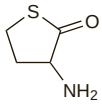
Homocysteine Thiolactone Hydrochloride

3-Aminodihydro-2(3*H*)-thiophenone hydrochloride.

C_4H_8ClNOS = 153.6.

CAS — 10593-85-8 (homocysteine thiolactone); 3622-59-1 (homocysteine thiolactone hydrochloride).



(homocysteine thiolactone)

Profile

Homocysteine thiolactone has been used in preparations for the treatment of liver disorders. Its hydrochloride salt has been used as a mucolytic. Homocysteine thiolactone is a metabolite of homocysteine and has been implicated in the pathogenesis of some cardiovascular diseases (see p.1941).

◊ References.

1. Chwatko G, Jakubowski H. Urinary excretion of homocysteine-thiolactone in humans. *Clin Chem* 2005; **51:** 408–15.
2. Jakubowski H. The molecular basis of homocysteine thiolactone-mediated vascular disease. *Clin Chem Lab Med* 2007; **45:** 1704–16.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Filogaster†.

Horseradish

Armoracia; Meerrettich; Rábano rusticano; Raifort.

Profile

Horseradish, the root of *Cochlearia armoracia* (*Armoracia rusticana*; *Nasturtium armoracia*; *Radicula armoracia*) (Cruciferae), has diuretic and antiseptic properties and stimulates the digestion. It is used in gastrointestinal, respiratory-tract, and urinary-tract disorders, and has also been used externally.

Horseradish is widely used as a food flavouring and condiment.

Homoeopathy. Horseradish has been used in homoeopathic medicines under the following names: Cochlearia armoracia; Coch. ar.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Garlic and Horseradish + C Complex; Garlic, Horseradish, A & C Capsules†; Procold†; ***Braz.:*** Infantoss†; ***Ger.:*** Angocin Anti-Infekt N; ***Malaysia:*** Horseradish Plus†; ***Switz.:*** Kernosan Elixir; Pectosan N†; Sanogencive; ***UK:*** Mixed Vegetable Tablets.

Hyaluronic Acid *(BAN)*

Hialurónico, ácido. (1→3)-*O*-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)-(1→4)-*O*-β-D-glucopyranosiduronan.

CAS — 9004-61-9.

ATC — D03AX05; M09AX01; S01KA01.

ATC Vet — QD03AX05; QM09AX01; QS01KA01.

NOTE. The term Hyaluronan is used to cover both hyaluronic acid and sodium hyaluronate.

Sodium Hyaluronate *(BANM)*

Hialuronato sódico; Hyaluronate Sodium *(USAN)*; Natrii hyaluronas; Natrio hialuronatas; Nátrium-hialuronát; Natriumhyaluronaatti; Natriumhyaluronat; Natrium-hyaluronát; Sodium, hyaluronate de; Sodyum Hiyalüronat.

CAS — 9067-32-7.

ATC — D03AX05; M09AX01; S01KA01.

ATC Vet — QD03AX05; QM09AX01; QS01KA01.

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

Ph. Eur. 6.2 (Sodium Hyaluronate). The sodium salt of hyaluronic acid, a glycosaminoglycan consisting of D-glucuronic acid and *N*-acetyl-D-glucosamine disaccharide units. It is extracted from cocks' combs or obtained by fermentation from streptococci (Lancefield Groups A and C). A white or almost white, very hygroscopic powder or a fibrous aggregate. Sparingly soluble to soluble in water; practically insoluble in dehydrated alcohol and in acetone. A 0.5% solution in water has a pH of 5.0 to 8.5. Store in airtight containers. Protect from light and humidity.

Adverse Effects

There have been reports of a transient rise in intra-ocular pressure when sodium hyaluronate was given into the eye. When injected into the knee, pain and inflammation may occur at the injection site. There have also been occasional reports of hypersensitivity, including, rarely, anaphylaxis.

Effects on the eyes. Crystalline deposits on intra-ocular lenses have been reported in patients after use of a high viscosity sodium hyaluronate preparation during cataract surgery.[1]

1. Jensen MK, *et al.* Crystallization on intraocular lens surfaces associated with the use of Healon GV. *Arch Ophthalmol* 1994; **112:** 1037–42.

Effects on the skin. A cutaneous granulomatous reaction has been reported in a woman 5 weeks after treatment with synthetic hyaluronic acid for cosmetic use as a dermal filler.[1] All cutaneous lesions resolved spontaneously within 3 months without scarring.

1. Ghislanzoni M, *et al.* Cutaneous granulomatous reaction to injectable hyaluronic acid gel. *Br J Dermatol* 2006; **154:** 755–8.

Inflammatory reaction. Severe peritoneal inflammation has been reported[1] after use of a sodium hyaluronate-based bioresorbable membrane to prevent postoperative adhesion formation.

1. Klingler PJ, *et al.*. Seprafilm -induced peritoneal inflammation: a previously unknown complication: report of a case. *Dis Colon Rectum* 1999; **42:** 1639–43.

Uses and Administration

Hyaluronic acid is widely distributed in body tissues and intracellular fluids, including the aqueous and vitreous humour, and synovial fluid; it is a component of the ground substance or tissue cement surrounding cells.

A viscous solution of sodium hyaluronate is used during surgical procedures on the eye, for example for cataract extraction. Introduction of the solution into the anterior or posterior chamber via a fine cannula or needle allows tissues to be separated during surgery and protects them from trauma. Sodium hyaluronate eye drops 0.1% are also used for the relief of dry eye and as a contact lens lubricant.

Sodium hyaluronate is given by intra-articular injection in the treatment of osteoarthritis of the knee. Doses vary according to the preparation used, but are of the order of 20 to 25 mg once weekly for 5 weeks or up to 30 mg once weekly for 3 or 4 weeks; it is generally recommended that the treatment course for any individual joint should not be repeated within 6 months. Sodium hyaluronate is also used during arthroscopic procedures to flush out irrigating solutions and act as a temporary substitute for synovial fluid.

Hyaluronic acid is applied topically to promote wound healing. Zinc hyaluronate has also been used. A film containing sodium hyaluronate and carmellose is used to prevent surgical adhesion. Sodium hyaluronate has also been used in the management of lesions of the oral mucosa.

Hylans, which are polymers derived from hyaluronic acid, are used similarly for osteoarthritis and wound care.

Sodium hyaluronate instilled intravesically has been used as a temporary replacement of the glycosaminoglycan layer in the bladder for the symptomatic treatment of interstitial cystitis.

Topical formulations of diclofenac in hyaluronic acid (CT-1101, AT-2101) are used in the treatment of actinic keratoses (but distinguish from an oral formulation of isofagomine tartrate (p.2327) under investigation for use in Gaucher disease that also carries the code AT-2101).

Hyaluronic acid has been used as a dermal filler for the correction of moderate to severe facial wrinkles and folds (see Photoageing, p.1581).

◊ Reviews.

1. Goa KL, Benfield P. Hyaluronic acid: a review of its pharmacology and use as a surgical aid in ophthalmology, and its therapeutic potential in joint disease and wound healing. *Drugs* 1994; **47:** 536–66.
2. Adams ME, *et al.* A risk-benefit assessment of injections of hyaluronan and its derivatives in the treatment of osteoarthritis of the knee. *Drug Safety* 2000; **23:** 115–30.

Actinic keratoses. For references to the use of diclofenac in a hyaluronic acid gel in the treatment of actinic keratoses, see p.46.

Dry eye. The usual management of dry eye (p.2140) is with artificial tears. Sodium hyaluronate has also been reported to be of some benefit. Alleviation of symptoms[1-3] and an increase in tear film stability[1,2] has been shown after topical application of sodium hyaluronate solution (0.1 or 0.2%) compared with saline-based placebo solutions. However, another study[4] failed to show any advantage over placebo, although it has been suggested[4,5] that sodium hyaluronate might play a role in maintaining a healthy corneal epithelium.

1. Mengher LS, *et al.* Effect of sodium hyaluronate (0.1%) on break-up time (NIBUT) in patients with dry eyes. *Br J Ophthalmol* 1986; **70:** 442–7.
2. Sand BB, *et al.* Sodium hyaluronate in the treatment of keratoconjunctivitis sicca: a double masked clinical trial. *Acta Ophthalmol (Copenh)* 1989; **67:** 181–3.
3. Condon PI, *et al.* Double blind, randomised, placebo controlled, crossover, multicentre study to determine the efficacy of a 0.1% (w/v) sodium hyaluronate solution (Fermavisc) in the treatment of dry eye syndrome. *Br J Ophthalmol* 1999; **83:** 1121–4.
4. Shimmura S, *et al.* Sodium hyaluronate eyedrops in the treatment of dry eyes. *Br J Ophthalmol* 1995; **79:** 1007–11.
5. Aragona P, *et al.* Long term treatment with sodium hyaluronate-containing artificial tears reduces ocular surface damage in patients with dry eye. *Br J Ophthalmol* 2002; **86:** 181–4.

Osteoarthritis. In osteoarthritis, the size and concentration of hyaluronic acid molecules naturally present in synovial fluid is reduced. Thus, one approach in the management of osteoarthritis (p.11) of the knee is viscosupplementation of the synovial fluid by the intra-articular injection of hyaluronic acid or its derivatives. Such injections may reduce pain over 1 to 6 months but may be associated with a short-term increase in knee inflammation; there is some suggestion that any benefit is longer lasting than with intra-articular corticosteroids. Some studies suggest that viscosupplementation may be an effective option for patients who are unable to take oral NSAIDs or have regular intra-articular corticosteroids, and who are unsuitable candidates for joint replacement surgery, although there appears to be considerable variability in clinical response between products, as well as in the variables being assessed and length of treatment.

References.

1. Altman RD, Moskowitz R. Intraarticular sodium hyaluronate (Hyalgan) in the treatment of patients with osteoarthritis of the knee: a randomized clinical trial. *J Rheumatol* 1998; **25:** 2203–12. Correction. *ibid.* 1999; **26:** 1216.
2. Anonymous. Hyaluronan or hylans for knee osteoarthritis? *Drug Ther Bull* 1999; **37:** 71–2.
3. Huskisson EC, Donnelly S. Hyaluronic acid in the treatment of osteoarthritis of the knee. *Rheumatology (Oxford)* 1999; **38:** 602–7.
4. Wobig M, *et al.* The role of elastoviscosity in the efficacy of viscosupplementation for osteoarthritis of the knee: a comparison of hylan G-F 20 and a lower-molecular-weight hyaluronan. *Clin Ther* 1999; **21:** 1549–62.
5. Felson DT, Anderson JJ. Hyaluronate sodium injections for osteoarthritis: hope, hype, and hard truths. *Arch Intern Med* 2002; **162:** 245–7.
6. Lo GH, *et al.* Intra-articular hyaluronic acid in treatment of knee osteoarthritis: a meta-analysis. *JAMA* 2003; **290:** 3115–21.
7. Bellamy N, *et al.* Viscosupplementation for the treatment of osteoarthritis of the knee. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 09/05/06).

Wound healing. Hyaluronic acid has been used to aid wound healing,[1,2] the overall management of which is discussed on p.1585.

1. Soldati D, *et al.* Mucosal wound healing after nasal surgery: a controlled clinical trial on the efficacy of hyaluronic acid containing cream. *Drugs Exp Clin Res* 1999; **25:** 253–61.
2. Harris PA, *et al.* Use of hyaluronic acid and cultured autologous keratinocytes and fibroblasts in extensive burns. *Lancet* 1999; **353:** 35–6.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Aquify; Artflex; Dropstar; Gengigel; Hialudorf; Hyalart†; Hyasol; Iuronicoderm; Lacripharma†; Maxiostenil; Miniostenil; Provisc; Synvisc; ***Austral.:*** AMO Vitrax; Fermathron†; Healon; Ophthalin; Provisc; Synvisc; Vismed†; ***Austria:*** Artzal; Connettivina; Etamucin; Hyalgan; ***Belg.:*** Gengigel; Healon†; Hyalgan; ***Braz.:*** Healon; Hyaludermin; Polireumin; Suprahyal; Synvisc; ***Canad.:*** Biolon†; Cystistat; Eyestil†; Healon†; Hyalgan; Hyalofill†; NeoVisc; Orthovisc; Suplasyn; Synvisc; ***Chile:*** Biolon; Eucerin Emulsion; Healon; Hyalgan; Lagricel Ofteno; Suprahyal; Synvisc; Toptear; ***Cz.:*** Curasan†; Healon†; Hyalgan; ***Denm.:*** Artz; Hyalgan; ***Fin.:*** Artzal; Healon†; Hyalgan; ***Fr.:*** Adant; Arthrum H; Effidia; Hyabak; Hyal-Drop; Hyalgan; Hyalofemme; Hyalofill; Hyalugel; Hylo-COMOD; Hyluprotect; Ialuset; Osteni; Provisc; Sinovial; Suplasyn; Synvisc; Vismed†; ***Ger.:*** Arthrease†; Biolan; Biolon; Dispasan; Endogel; Fermathron; Gelbag; Go-On; Healon†; Hy-GAG; Hya-ject; Hya-Ophtal†; Hyal-System†; Hyalart; Hyalubrix; Hylaform†; Hylan; Hylo-COMOD; Hylo-Vision; Hysan; Laservis; Orthovisc; Ostenil; Oxyal; Provisc; Suplasyn; Synvisc; TwinVisc; Viscoseal; Visiol; Vislube; Vismed; VisThesia; Xidan EDO; ***Gr.:*** Hyalart; ***Hong Kong:*** Connettivina; Go-On; Healon; Hialid; Hyalgan; Hyruan; Provisc†; Vismed; ***Hung.:*** Curiosin; Healon†; Hyalgan; Ial†; Ophthalin†; Provisc†; ***India:*** Halonix; Lghyal; Synvisc; Visial; ***Indon.:*** Adant; Durolane; Hialid; Hyalgan; Osflex; Suplasyn; ***Irl.:*** Hyalgan; Ophthalin†; Provisc†; Suplasyn; ***Israel:*** Adant; Arthrease; Biolon; Curavisc; Eyecon; Healon; Hylo-COMOD; Hysan; Ophthalin; Orthovisc; Suplasyn; Synvisc†; ***Ital.:*** Artz; Connettivina; Dropstar; Durolane; Go-On; Hy-Drop; Hyabak; Hyalart; Hyalgan; Hyalistil; Hylo-COMOD; Hyluprotect; Ial; Ialect†; Ialum; Ialurex; Inilens; Ocustil†; Ophtalin; Oxyal; Provisc; Synocrom; Synvisc; Vismed; ***Jpn:*** Hyalein; Suvenyl; ***Malaysia:*** Curiosin; Gengigel; Go-On; Healon†; Hyal; Hyalgan; Hyruan; Laservis†; Provisc; Sinovial; Synvisc; Viscoseal; Visiol; Vislube; Vismed; ***Mex.:*** Biolon; Hyasol; Lagricel; Suprahyal; Synvisc; Zonaker; ***Mon.:*** Oxyal; ***NZ:*** AMO Vitrax†; Healon; Hylaform; Ophthalin; Provisc; Synvisc; ***Philipp.:*** Hialid; Provisc; ***Pol.:*** Hyalgan; Synvisc; ***Port.:*** Artz; Gengigel†; Hyalart; Hyalofill†; Hylo-COMOD†; ***Rus.:*** Curiosin (Куриозин); Healon (Хеалон)†; Hylo-COMOD (Хило-КОМОД); ***S.Afr.:*** AMO Vitrax; Biolon; Biolone; Healon; Provisc; ***Singapore:*** AMO Vitrax†; Healon†; Hialid; Hyalgan; Hylaform; Provisc; Restylane†; Suplasyn; Synvisc; ***Spain:*** Hyalart; Hyalgan; ***Swed.:*** Artzal; Hyalgan; Synvisc; ***Switz.:*** Fermavisc; Healon†; Hyal-Drop; HycoSan5; Hylo-COMOD; Hysan; Ial; Ialugen; Laservis; Ostenil; Rhinogen; Sinovial; Suplasyn; Synvisc; Viscoseal; Visiol; Vislube; Vismed; ***Thai.:*** Adant; Connettivina†; Healon†; Hialid; Hyalgan; Hyruan; Ial; Ophthalin; Provisc; Synvisc; ***Turk.:*** Adant; Amvisc; Biolon; Healon; Hyalgan; Ial; Ophtalin Plus; Ostenil; Provisc; Synvisc; ***UK:*** Arthrease; Cystistat; Euflexxa; Fermathron; Gengigel; Healonid†; Hyabak; Hyalgan; Hyalofill; Hycosan; Ophthalin; Optrex Contact Lens Friendly Eye Drops; Orthovisc; Ostenil; Supartz†; Suplasyn; Synocrom; Synvisc; Viscoseal; ***USA:*** AMO Vitrax; Amvisc; Bionect; Coease; Euflexxa; Healon; Hyalgan; Hylaform; Hylira; Juvederm; Orthovisc; Perlane; Restylane; Shellgel; Supartz; Synvisc; ***Venez.:*** Healon†; Hyalgan; Lagricel Ofteno; Provisc†; Suprahyal; Synvisc; Toptear.

Multi-ingredient: ***Arg.:*** Blink Contacts; Cellskinlab Hydragel B5; Cremisona†; Culuflex H; Epitheliale AH; Estri-Atlas; Hyalcrom; Hyalcrom NF; Hyanac†; Hydratone†; Ingebrax; Iuronico Biotic; Lacrimax; Maxilac; Maxus; Muvar; Panoxi; Timed 0.5; Viscoat; Vita-C Derms's; Yusin Tears II; ***Austral.:*** Blink Contacts; Duovisc; Viscoat; ***Belg.:*** Physiologica; ***Chile:*** Hydrating B5 Gel; Ureadin Rx RD; ***Cz.:*** Curiosin†; Ialugen Plus; ***Fr.:*** Cicaplast; Cicatridine; Hyalogran; Hyarhinol; Ialuset Plus; Mucogyne; Saugella; Tonimer; Viscoat; ***Ger.:*** Duovisc; Hylo-Care; Viscoat; ***Hong Kong:*** Duovisc†; Viscoat†; ***Hung.:*** Ialugen Plus; Viscoat†; ***Israel:*** Aphtagone; Aptha-X; Gelclair†; ***Ital.:*** Altergen; Connettivina Plus; Dropyal; Idroskin C; Migel; Osmogel; Sirmiogel†; Trofo 5; Viscoat; ***Malaysia:*** Duovisc; Viscoat; ***Mex.:*** Cetopic; Emolin Neo; Grimal; Hyalcrom NF; Hyalox; ***Mon.:*** Monasens; ***NZ:*** Viscoat; ***Philipp.:*** Viscoat; ***Port.:*** Synchrorose; Synchrovit; ***Rus.:*** Hylozar-COMOD