Troxipide *(rINN)*

Troxipida; Troxipidum. (±)-3,4,5-Trimethoxy-*N*-3-piperidylbenzamide.

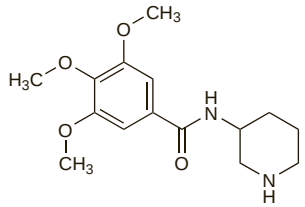
Троксипид

$C_{15}H_{22}N_2O_4$ = 294.3.

CAS — 30751-05-4.

ATC — A02BX11.

ATC Vet — QA02BX11.



Profile

Troxipide is used for its cytoprotective properties in the treatment of gastritis and peptic ulcer disease (p.1702) in a usual oral dose of 100 mg three times daily, after food.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Aplace.

Urogastrone

Anthelone; EGF-URO; Epidermal Growth Factor; Murodermina; Uroanthelone; Uroenterone; Urogastrona.

Урогастрон

CAS — 9010-53-1.

Pharmacopoeias. *Chin.* includes monographs for recombinant human epidermal growth factor suitable for external use.

Uses

Urogastrone is a polypeptide first isolated from human urine. Two forms have been identified, β and γ urogastrone. The β form consists of 53 amino acids and is distinguishable from the γ form by an additional terminal arginine residue. The β form is reported to be identical to human epidermal growth factor and this term is widely used in the literature.

Urogastrone inhibits gastric acid secretion and has been tried in the treatment of peptic ulcer disease and other gastrointestinal disorders but its rapid destruction in the stomach has limited its clinical use.

It is a potent stimulator of cellular proliferation and has also been used as an aid to wound healing.

◊ Reviews.

1. Burgess AW. Epidermal growth factor and transforming growth factor α. *Br Med Bull* 1989; **45:** 401–24.
2. Miyazawa K. Role of epidermal growth factor in obstetrics and gynecology. *Obstet Gynecol* 1992; **79:** 1032–40.
3. Grazul-Bilska AT, *et al.* Wound healing: the role of growth factors. *Drugs Today* 2003; **39:** 787–800.
4. Klenkler B, Sheardown H. Growth factors in the anterior segment: role in tissue maintenance, wound healing and ocular pathology. *Exp Eye Res* 2004; **79:** 677–88.

Gastrointestinal disorders. Intravenous infusion of urogastrone 250 nanograms/kg over 1 hour has been reported[1,2] to reduce the secretion of gastric acid in patients with duodenal ulcer (p.1702) or the Zollinger-Ellison syndrome (p.1704). Ulcer pain was relieved 30 to 60 minutes after the start of the infusion.[2] A dose of 100 nanograms/kg per hour by intravenous infusion has been used with partial success in an infant with microvillous atrophy[3] and was apparently beneficial in an infant with necrotising enteritis.[4]

Human epidermal growth factor has also shown some promise in the treatment of active ulcerative colitis. In a small study,[5] patients received daily enemas containing either recombinant human epidermal growth factor (5 micrograms in 100 mL) or placebo; all patients also received oral mesalazine. Ten of the 12 patients in the urogastrone group were in remission after 2 weeks treatment compared with 1 of the 12 patients in the placebo group, and this benefit was maintained for up to 12 weeks.

1. Koffman CG, *et al.* Effect of urogastrone on gastric secretion and serum gastrin concentration in patients with duodenal ulceration. *Gut* 1982; **23:** 951–6.
2. Elder JB, *et al.* Effect of urogastrone in the Zollinger-Ellison syndrome. *Lancet* 1975; **ii:** 424–7.
3. Walker-Smith JA, *et al.* Intravenous epidermal growth factor/urogastrone increases small-intestinal cell proliferation in congenital microvillous atrophy. *Lancet* 1985; **ii:** 1239–40.
4. Sullivan PB, *et al.* Epidermal growth factor in necrotising enteritis. *Lancet* 1991; **338:** 53–4.
5. Sinha A, *et al.* Epidermal growth factor enemas with oral mesalamine for mild-to-moderate left-sided ulcerative colitis or proctitis. *N Engl J Med* 2003; **349:** 350–7.

Wound healing. For a general discussion of the management of wounds and ulcers, see p.1585.

In a randomised double-blind study in 61 patients with diabetic foot ulcers, adding human epidermal growth factor 0.04% to an ulcer cream containing protein-free bovine blood extract was shown to significantly enhance wound healing and reduce healing time compared with either the cream alone or the cream plus human epidermal growth factor 0.02%.[1] Topical application of recombinant human epidermal growth factor 0.02% has also been reported to reduce pain and promote healing of exfoliated skin lesions in a patient with drug-induced Stevens-Johnson syndrome.[2]

The effect on the rate of wound healing of a cream containing sulfadiazine silver plus recombinant human epidermal growth factor (10 micrograms/mL) was compared with sulfadiazine silver alone in 12 patients each requiring skin grafts at 2 donor sites.[3] The cream containing epidermal growth factor accelerated the rate of epidermal regeneration in all patients and reduced the average time to 100% healing by about 1.5 days. Patients were followed up for a maximum of 1 year after cessation of therapy and no complications or clinical evidence of neoplasia at the healed donor sites occurred.

In contrast, recombinant human epidermal growth factor as an ophthalmic solution containing 30 or 100 micrograms/mL was investigated in patients who had undergone keratoplasty, but the weaker solution had no effect on the rate of re-epithelialisation, and the more concentrated one was actually associated with slower healing.[4]

1. Tsang MW, *et al.* Human epidermal growth factor enhances healing of diabetic foot ulcers. *Diabetes Care* 2003; **26:** 1856–61.
2. Tsang MW, *et al.* The use of recombinant human epidermal growth factor (rhEGF) in a gentleman with drug-induced Steven Johnson syndrome. *Dermatol Online J* 2004; **10:** 25.
3. Brown GL, *et al.* Enhancement of wound healing by topical treatment with epidermal growth factor. *N Engl J Med* 1989; **321:** 76–9.
4. Dellaert MMMJ, *et al.* Influence of topical human epidermal growth factor on postkeratoplasty re-epithelialisation. *Br J Ophthalmol* 1997; **81:** 391–5.

Preparations

Proprietary Preparations (details are given in Part 3)

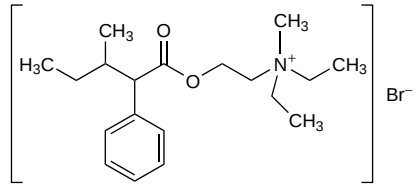
Multi-ingredient: ***Chile:*** FCE; Hebermin†.

Valethamate Bromide

Valetamat Bromür; Valetamato, bromuro de. Diethylmethyl[2-(3-methyl-2-phenylvaleryloxy)ethyl]ammonium bromide.

$C_{19}H_{32}BrNO_2$ = 386.4.

CAS — 16376-74-2 (valethamate); 90-22-2 (valethamate bromide).



Profile

Valethamate bromide is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1219). It has been given orally, by injection or rectally in the symptomatic treatment of visceral spasms.

Preparations

Proprietary Preparations (details are given in Part 3)
India: Epidosin; Valosin; ***Indon.:*** Epidosin; ***Turk.:*** Epidosin.

Multi-ingredient: ***Turk.:*** Epidosin Compozitum.

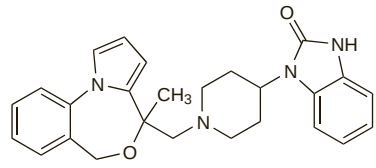
Zaldaride *(rINN)*

CGS-9343B (zaldaride maleate); Zaldarida; Zaldaridum. (±)-1-{1-[(4-Methyl-4*H*,6*H*-pyrrolo[1,2-*a*][4,1]benzoxazepin-4-yl)methyl]-4-piperidyl}-2-benzimidazolinone.

Зальдарид

$C_{26}H_{28}N_4O_2$ = 428.5.

CAS — 109826-26-8 (zaldaride); 109826-27-9 (zaldaride maleate).



Profile

Zaldaride is a calmodulin antagonist that has been investigated as the maleate for the treatment of diarrhoea.

Diarrhoea. Studies in patients with travellers' diarrhoea (p.1694) have indicated that zaldaride in oral doses of 20 mg as the maleate four times daily is an effective antidiarrhoeal.[1,2] It was somewhat less effective than loperamide when given without a loading dose,[2] but a regimen of 40 mg initially, followed by 20 mg, about every 6 hours was as effective as loperamide 4 mg initially followed by 2 mg after each unformed stool.[3]

1. DuPont HL, *et al.* Zaldaride maleate, an intestinal calmodulin inhibitor, in the therapy of travelers' diarrhea. *Gastroenterology* 1993; **104:** 709–15.
2. Okhuysen PC, *et al.* Zaldaride maleate (a new calmodulin antagonist) versus loperamide in the treatment of traveler's diarrhea: randomized, placebo-controlled trial. *Clin Infect Dis* 1995; **21:** 341–4.
3. Silberschmidt G, *et al.* Treatment of travellers' diarrhoea: zaldaride compared with loperamide and placebo. *Eur J Gastroenterol Hepatol* 1995; **7:** 871–5.