non-polarizable $Ag^+/AgCl$ electrodes placed in contact with the post-ganglionic trunk and the ganglion body. The tissue was superfused at 1 ml/min with Krebs solution (containing hyoscine 2.6 μm) at 25°C and the potential difference across the electrodes monitored on a Servoscribe 1 s chart recorder. Addition of GABA or carbachol to the superfusate produced a dose dependent depolarization of the ganglion (Bowery & Brown, 1974). Concurrent application of PTBO derivatives antagonized the depolarizing action of GABA but not that of carbachol.

Spinal cords were dissected from decerebrated frogs and hemisected. Half-cords were transferred to a cooled perfusion apparatus (10°C) and dorsal roots mounted on $Ag^+/AgCl$ electrodes for DC recordings. The trans-synaptic actions of drugs were eliminated by the addition of procaine to the superfusing solutions as described by Evans & Watkins (1975) and Tris buffer was used to maintain pH neutrality. Application of GABA, glycine or glutamate (0.5 to 4 mM) produced dose-dependent depolarization of dorsal roots. Concurrent exposure to the PTBO compounds produced antagonism of the GABA-induced depolarization but did not reduce the glutamate or glycine responses.

In both ganglion and dorsal root the potency ranking of the compounds as GABA antagonists was IPTBO > EPTBO > PPTBO which is in the same order as the convulsant potency. The potency of IPTBO as a GABA antagonist was comparable with that of bicuculline methochloride and picrotoxin. It was, therefore, concluded that the PTBO compounds are effective and specific GABA antagonists when tested on either preparation. The potency ranking suggests that the convulsant properties of the PTBO series may be due to antagonism of the actions of synaptically-released GABA.

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Evidence for a specific somatosensory receptor in the cat skin that responds to irritant chemicals

R.W. FOSTER & A.G. RAMAGE

Department of Pharmacology, Materia Medica and Therapeutics, The University, Manchester M13 9PT.

The irritant chemical dibenzoxazepine (CR) produces a sensation of burning pain when applied to the human skin (Ballentyne, Beswick & Price-Thomas, 1973) and acts on somatosensory receptors in the cat related to unmyelinated nerve fibres (Foster & Ramage, 1975). Further investigations have sought to classify the type of sensory receptor acted upon by CR and by *w*-chloroacetophenone (CN), *o*-chlorobenzylidene malononitrile (CS), *n*-nonyl vanillylamide (VAN) and capsaicin (CAP).

Cats were anaesthetized with α-chloralose (70–90 mg/kg). Multifibre or single unit activity was recorded (Iggo, 1960) from the saphenous nerve.

Irritants (5×10^{-4} M in saline to 10^{-1} M in alcohol) were tested by topical application to the receptor area. Analysis of results employed a computer method (Foster & Ramage, 1976).

In 18 low threshold alpha mechanoreceptor units activity was only induced indirectly when local oedema was caused by the irritant.

Twenty moderate to high threshold alpha delta mechanoreceptor units which are believed to be responsible for a sensation of sharp pain (Landau & Bishop, 1958), were not activated by the irritants; nor were 10 low threshold C-mechanoreceptor units.

Very high threshold C-mechanoreceptor units, which adapt rapidly, and a cold thermoreceptor unit were not activated by the irritants. A warm thermoreceptor unit did show an increase in activity to CR 10^{-4} M (Foster & Ramage, 1975) but

this was an indirect effect associated with erythema.

Increase in activity was consistently induced by these irritants in 17 moderate–high threshold C-mechanoreceptor units (with conduction velocities 0.3–1.0 m/s). The order of relative potency of the irritants was VAN > CAP > CR > CN > CS. CN, CR and VAN generally induced rapid tachyphylaxis and cross tachyphylaxis. When a receptor had developed tachyphylaxis to VAN, exposure to CN and CR failed to elicit activity. However when a receptor had developed tachyphylaxis to CN and CR, exposure to VAN still elicited activity. CAP seemed in this respect to be similar to VAN.

The onset of response to CR, CN and CS (5×10^{-4} M) showed a delay of 5.0–8.1 min whereas VAN was immediately (< 1.4 min) effective. When CR was applied in an alcoholic solution of 10^{-1} M, or the skin over the receptor area was broken, onset of activity was immediate. This suggests that the delay was mainly due to the permeability barrier of the skin. The average duration of action of most of these irritants was 24.3 min, though the action of CAP was briefer (approx 10 min).

The observation that these irritants affect selectively high-moderate C-mechanoreceptor units is consistent with the concept that C-fibre stimulation is associated with a sensation of dull burning pain (Landau & Bishop, 1958). Thus these chemical irritants could represent a useful tool for identifying peripheral nociceptors.

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Profiles of different anti-allergy effects of a new histamine antagonist, BM 15,100

E.S.K. ASSEM & E.K.S. CHONG

Department of Pharmacology, University College, London.

Several anti-allergy compounds possess multiple actions on the anaphylactic mechanism, including inhibition by H_1 histamine-receptor blocking agents of antigen-induced histamine release. This effect, was shown by Lichtenstein & Gillespie, 1975, in the isolated, sensitized human leucocyte preparation, *in vitro*, by concentrations of the order of 10^{-4} M. The high concentrations required for inhibition lead these authors to doubt the practical significance of their finding. We investigated a new histamine antagonist, BM 15,100:3,4-dimethyl-7-[4-(*p*-chlorobenzyl)-piperazin-1-yl]-propoxycoumarin. dihydrochloride, (Boehringer Mannheim), assessing its antagonism to histamine and other agonists. Its ability to inhibit anaphylactic histamine release in the human leucocyte test model was also investigated. Histamine release was measured by a spectrofluorometric technique.

We found BM 15,100 to be a potent antagonist of histamine in guinea-pig ileum, with a pA_2 of 9.8, after 3 min pre-incubation with antagonist, and in guinea-pig spiral tracheal strips.

Concentrations exceeding 10^{-6} M lead to irreversible antagonism and lack of recovery, which could not be averted by increasing the agonist concentration. BM 15,100 also showed relatively weak antagonism of slow reacting substance of anaphylaxis, 5-hydroxytryptamine, prostaglandins E_1, E_2 and $F_{2\alpha}$, bradykinin, and angiotensin in isolated guinea-pig ileum, with pA_2 values ranging from 5.6 to 6.1 for all of these agonists. The compound also antagonized PGE(s), $PGF_{2\alpha}$, and angiotensin in rat uterus, with pA_2 values of similar order. This compound also inhibited antigen-induced histamine release from sensitized human leucocytes, but the dose-response curve exhibited a point of inflexion. Thus, small inhibition was seen with 10^{-7} M which increased to a maximum of 75 to 100% with concentrations ranging from 10^{-6} to 10^{-5} M, but further increase to 10^{-4} M