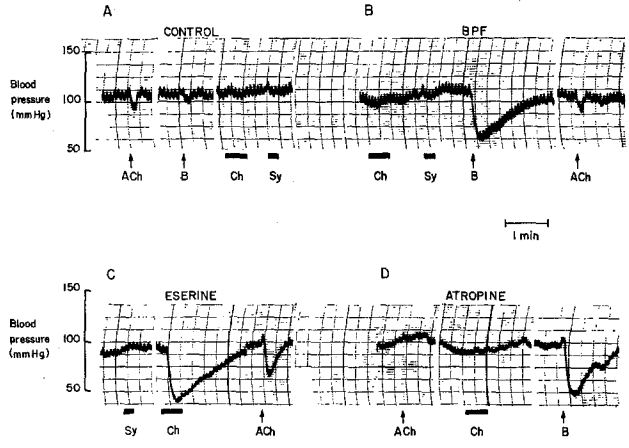
(Nutritional Biochemicals Corporation). Bradykinin, (Schwarz Bioresearch Inc).

Results. Effect of chorda lingual nerve stimulation on systemic blood pressure before and after eserine and BPF. 2 experiments were carried out with the objective of stabilizing either acetylcholine or kinin released locally in the submaxillary gland so that the systemic affects of a released transmitter or mediator could be detected. In one experiment, eserine was given in a cumulative dose of 400 $\mu g/kg^{-1}$ i.v. over a 5-min period; in the other experiment, the dose was s single one of 100 $\mu g/kg^{-1}$ i.v. Large doses of eserine may cause convulsions some time after administration. These may be reduced or eliminated by increasing the depth of anaesthesia. The more potent nonapeptide kinin potentiator was used in both experiments in a dose of 2 mg/kg^{-1} i.v. Whereas prior administration of eserine readily demonstrated the systemic 'spill-over' of acetylcholine following stimulation of the chorda lingual nerve, the nonapeptide failed to reveal any overflow of bradykinin despite the fact that it potentiated the hypotensive effect of bradykinin injected i.v. to a greater degree than eserine enhanced the effect of injected acetylcholine. Detailed results of one of these experiments are shown in the Figure.



Blood pressure of cat (2.7 kg) under chloralose anaesthesia. ACh, 0.01 μg acetylcholine. B, 1.0 μg bradykinin. Ch, stimulation of chorda lingual nerve. Sy, stimulation of cervical sympathetic nerve. Trace A: Control, showing effects of i.v. injection of acetylcholine, bradykinin and of chorda lingual and sympathetic nerve stimulation. Trace B: After injection of bradykinin potentiating factor (BPF), synethetic nonapeptide, 2 mg/kg^{-1} i.v. Marked potentiation of effect of injected bradykinin but there are again no systemic effects following stimulation of the chorda lingual or sympathetic nerves. Trace C: After injection of eserine, 400 $\mu g/kg^{-1}$ i.v. Chorda lingual nerve stimulation now results in a marked fall of the arterial blood pressure after a latency of approximately 10 sec. The effect of injected acetylcholine is also greater than in the control panel. Sympathetic nerve stimulation produces no systemic effects. Trace D: After injection of atropine, 250 $\mu g/kg^{-1}$ i.v. The effects of injected acetylcholine and of chorda lingual nerve stimulation are now completely blocked. Injected bradykinin is still potentiated.

In a second experiment, eserine (100 $\mu g/kg^{-1}$) was injected before the kinin potentiators. In this experiment, both the pentapeptide and the nonapeptide were injected (total dose, 4 mg/kg^{-1}) and the systemic effects of bradykinin were enhanced to an even greater degree than in the first experiment. Nonetheless, the systemic blood pressure revealed no trace of systemic overflow of kinin; again, however, overflow of acetylcholine on nerve stimulation was readily demonstrated after injection of eserine.

Effect of chorda lingual nerve stimulation on vasodilatation before and after BPF. In 2 other experiments, an attempt was made to potentiate vasodilatation in the submaxillary gland resulting from chorda lingual nerve stimulation by prior administration of a kinin potentiator. In one experiment, the nonapeptide was infused close arterially via the lingual artery (1 mg/kg^{-1}) and in the other the pentapeptide was injected i.v. (1 mg/kg^{-1}). Although the systemic hypotension to the intravenous injection of bradykinin was increased in both experiments by the potentiator, vasodilatation in the gland resulting from nerve stimulation was unaffected.

Discussion. Our results show that under equivalent conditions of potentiation of acetylcholine and kinin, although the release of acetylcholine following stimulation of the chorda lingual nerve can readily be demonstrated, there is no evidence of kinin release. We conclude, therefore, that kallikrein has no involvement in the mediation of the vasodilatation which occurs in the submaxillary gland during stimulation of the chorda lingual nerve. The physiological significance of salivary kallikrein remains obscure. The problem of the marked difference in sensitivity to atropine of the secretory and vasodilator effects of chorda lingual nerve stimulation has still not been resolved and also requires further study. It has been suggested, however, that the secretory and vascular smooth muscle cells both possess different cholinergic receptors but with markedly different sensitivities to atropine[4].

Zusammenfassung. Nachweis, dass bei Reizung des N. chorda lingualis der Katze ein Blutdruckeffekt ausbleibt, wenn ein Bradykinin potenzierender Faktor (Präparat BPF) zuvor gegeben wurde.

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The Effects of Cholinergic Drugs on the Motility of the Alimentary Canal of *Blennius pholis* L.

In view of the complex and unresolved problems which remain in understanding the control of gastrointestinal motility in teleosts[1,2] a study was undertaken in intact fish to explore the effects of drugs likely to influence motor activity of the alimentary tract. A locally available fish, *Blennius pholis* L., was selected principally because it is an example of a fish with no histologically defined stomach[3] and the results can be compared with in vivo studies on other fish, possessing stomachs, which have been reported from this laboratory[4].

Materials and methods. Mature specimens of *Blennius pholis* L., length 12.2–14.6 cm and weight 25–35 g, were collected from the rocky shores around Anglesey, tagged, and kept in the laboratory aquarium in tanks with circulating sea-water. Water temperature was continuously recorded and remained throughout the experiments, conducted June-August, within the range 15–17 °C. The fish were introduced to a diet of lug-worm, *Arenicola marina*, which after several days capture they accepted readily from the surface of the water immediately it was introduced. Social facilitation[5] appeared to play an important role in the early stages of artificial feeding. The fish were fed to excess on alternate days.

During experimental trials an 'Araldite' pellet, 2–3 mm diameter, was fed to each fish individually inside a piece of lug-worm. The time from feeding to appearance of the pellet in the faeces was recorded from each fish and used as a measure of the mechanical activity of the alimentary tract. Barium sulphate was mixed with the resin of the pellet to allow its progress to be monitored by X-ray screening. This enabled investigation of any differential effects of the drugs on the motility of arbitrarily defined fore-gut and hind-gut regions. This report however deals only with total clearance times i.e. the time elapsed between feeding and defaecation of the pellet.

Drugs were made up in teleost Ringer[6] and injected in 0.1 ml volumes into the coelomic cavity. 2 injections were administered during each experiment, approximately 1 h and 9 h after feeding. The following drugs were used: – acetylcholine chloride, acetyl-b-methylcholine chloride (methacholine), eserine sulphate, (Sigma), carbamylcholine chloride (carbachol), atropine sulphate, (B.D.H.).

Results and discussion. Of the 3 cholinesters tested only carbachol (0.05 mg/kg) stimulated motor activity of the alimentary tract. The mean clearance time, 17.7 h $\pm$ 0.99 ($\pm$ standard error), determined from 10 carbachol treated fish was significantly less ($P < 0.05$) than the mean clearance time, 20.1 h $\pm$ 0.61, determined from a group; of 35 untreated controls. Mean clearance times from fish treated with acetylcholine/eserine (1, 3 and 5 mg/kg) and methacholine (5 mg/kg) were not significantly different from those of their controls. These results may reflect the relative instability of acetylcholine or methacholine when released into the body fluids[7]. Both these compounds are more susceptible to cholinesterase activity than carbachol. Injection of an equimolecular concentration of the anticholinesterase, eserine, failed however to reveal any in vivo activity of acetylcholine which has been shown to contract isolated smooth muscle preparations of teleost gut [8–11], including preparations from *Blennius* (personal observation).

The action of carbachol in stimulating gut motilty may be via nicotinic or muscarinic receptors, or both, as this compound has been shown in mammals to be equally active at both sites[7]. Whilst it has been proposed that nicotinic receptors are the principal sites of cholinergic transmission in the teleost stomach[9] more recent evidence[4, 10, 11] has indicated that cholinergic transmission is predominantly muscarinic. Further evidence of a muscarinic site in *Blennius* is afforded by the observation that atropine, in otherwise untreated fish, decreased the rate of movement of food through the gut. The increase in clearance times was significant in 2 groups each of 10 fish treated with 3 mg/kg ($P < 0.05$) and 5 mg/kg ($P < 0.001$) atropine. Mean clearance times were respectively 21.3 h $\pm$ 0.27 and 22.7 h $\pm$ 0.47 compared with a mean control time of 19.9 h $\pm$ 0.44 determined from 36 untreated fish. If atropine acts as a selective muscarinic blocking agent, in the doses employed here, this would indicate the presence of cholinergic receptors on the smooth muscle cells. These results are consistent with other in vitro[11] and in vivo[4] studies reported from this laboratory[12].

Résumé. Les effets des cholinesters sur les mouvements spontanés du tractus alimentaire sont étudiés sur des poissons intacts. L'acétylcholine et la métacholine sont sans effets. Par ailleurs, une concentration de 0,05 mg/kg de carbachol produit un accroissement du mouvement spontané. Des concentrations de 3 et 5 mg/kg d'atropine inhibe le mouvement.

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The Effects of the 'Calcium-Antagonist', Prenylamine, on the Action Potential of Crayfish Muscle (*Oronectes virilis*)

Certain drugs that have been identified as 'Ca^{++}-antagonists' block excitation-contraction coupling in smooth muscle[1] and eliminate the inward flux of Ca^{++} during the action potential in the frog myocardium[2, 3]. The same drugs block the second, longer-lasting, delayed phase of Ca^{++} entry in the squid axon[4]. The present experiments were designed to test the effects of a Ca^{++}-antagonist on the action potential of crustacean muscle, which was the first experimental system in which Ca^{++} inflow was implicated in the genesis of spikes[5, 6].

Method. The observations were made on the contractor epimeralis and the superior extensor abdominalis medialis muscles of the crayfish, *Orconectes virilis*. The muscles were dissected in a van Harreveld's solution (v/H) containing 210.0 m*M* NaCl, 14.0 m*M* $CaCl_2$, 2.8 m*M* $MgCl_2$, 5.25 m*M* KCl, and 8.0 m*M* N-*Tris* (hydroxylmethyl) methyl-2-aminoethane sulfonic acid (TES) buffer pH 7.4. The Ca^{++}-antagonist tested was prenylamine lactate (N-(3,3-Diphenylpropyl)-α-methyl phenethylamine lactate; Segontin ®), which a was gift from the Hoechst Phar-