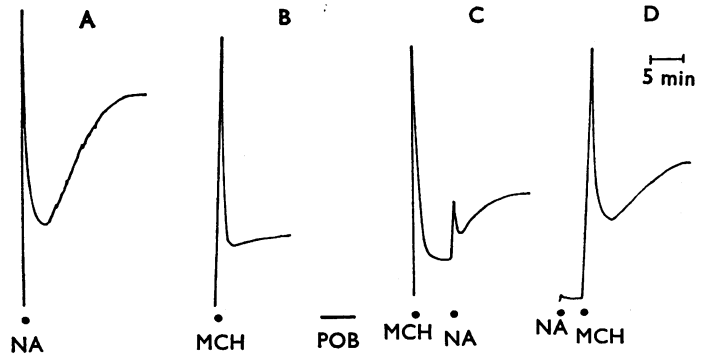

FIG. 1. Reversal of α-adrenoceptor blockade by methacholine (MCh). Doses of agonists are added at the dots. Between B and C the tissue was exposed to sufficient phenoxybenzanine (POB) to block noradrenaline (NA) (compare A and D). In C and D the agonists are added cumulatively.

adrenaline could be reversed by the addition of atropine, phentolamine or tolazoline during the response. Further treatment with POB only reduced the response to noradrenaline in proportion to the reduction in response to methacholine. We suggest that activation of muscarinic receptors uncovers new α-adrenoceptors (not susceptible to phenoxybenzamine) or reverses the effect of phenoxybenzamine temporarily without causing dissociation of phenoxybenzamine. The latter hypothesis would explain previous studies of the ability of cocaine to potentiate effects of maximal doses of noradrenaline in phenoxybenzamine-treated tissues (Nakatsu & Reiffenstein, 1968). However, the vas deferens does not normally respond to 5-hydroxytryptamine ($1–2 \times 10^{-4}$ M) but does so in the presence of methacholine, suggesting new 5-hydroxytryptamine sensitive receptors have been uncovered, or activated.

REFERENCE

NAKATSU, K. & REIFFENSTEIN, R. J. (1968). Increased receptor utilization: mechanism of cocaine potentiation. *Nature, Lond.*, **217**, 1276–1277.

Active factors in the venom duct of *Conus californicus*

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Marine snails of the genus *Conus* have an elaborate venom apparatus (Halstead, 1965) and produce a potent venom which can be lethal to humans. *C. californicus* feeds on other molluscs and worms (Saunders & Wolfson, 1961) but the venom from the species is also lethal to mice and rabbits. The toxic components of the venom are produced in a convoluted venom duct (Whysner & Saunders, 1963).

Because certain molluscs are the natural prey of *C. californicus* we decided to test the activity of venom duct extracts on some molluscan preparations in an initial attempt to determine the natural mechanism of action of the components of the venom.

Extracts prepared in artificial sea water produced an initial relaxation of the *Mytilus* anterior byssus retractor muscle similar to that caused by high concentrations of 5-hydroxytryptamine, and then a blockade of neurally induced contractions.

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The same extracts produced marked 5-hydroxytryptamine-like inotropic and chronotropic effects on the isolated *Mercenaria* heart. Paper chromatography in two solvent systems confirmed the presence of 5-hydroxytryptamine in the extracts. Quantitative estimates based on bioassay and chromatography showed that the concentration of 5-hydroxytryptamine in the extracts was very high, representing 1–2 mg of base/g wet weight of venom duct. No 5-hydroxytryptamine was detected in the venom bulb.

Extracts of venom duct prepared in snail saline had complex effects on the electrical activity of the three giant neurones located in each buccal ganglion of *Helix aspersa* (Cottrell, 1971). Extracts caused both depolarization and spike firing, and blockade of the synaptic inputs from the cerebro-buccal connectives.

Crude extracts were fractionated on a 21×1 cm column of Bio-Gel P2 (50–100 mesh) into a low MW fraction, a fraction containing substances with a MW of about 1,000, and a high MW fraction. Factors in the high MW fraction, but in neither of the other fractions, had pronounced effects on the responses of the individual neurones during stimulation of the cerebro-buccal connectives. The experimental results showed that there was a factor which blocked synaptic transmission and a factor which could block axonal conduction.

The data therefore suggest that there are at least three different active factors in the venom duct of *C. californicus*. The very high concentration of 5-hydroxytryptamine is another example of the abundance of this amine in the venom apparatus of invertebrate species of different phyla (Welsh, 1964).

REFERENCES

COTTRELL, G. A. (1971). Synaptic connections made by two serotonin-containing neurones in the snail (*Helix pomatia*). *Experientia*, **27**, 813.

HALSTEAD, B. W. (1965). *Poisonous and Venomous Marine Animals of the World*, Vol. **1**, 1–994 pp. Washington, D.C.: U.S. Government Printing Office.

SAUNDERS, P. R. & WOLFSON, F. (1961). Food and feeding behaviour in *Conus californicus*. *The Veliger*, **3**, 73–76.

WELSH, J. H. (1964). Composition and mode of action of some invertebrate venoms. *Ann. Rev. Pharmac.*, **4**, 293–304.

WHYSNER, J. A. & SAUNDERS, P. R. (1963). Studies on the venom of the marine snail *Conus californicus*. *Toxicon*, **1**, 113–122.

Effect of vasopressin and of adenosine triphosphate on the flat preparation of rabbit rectum

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Woo & Somlyo (1967) describe a predominantly excitatory response to vasopressin (10 mU/ml) of the longitudinal muscle strip from the rabbit distal colon. Gilmore & Vane (1970), on the other hand, report that vasopressin (4–14 μU/ml) has an inhibitory effect on the longitudinal muscle of the rabbit rectum, with an after-contraction at higher concentrations (33–133 μU/ml). We have now used the flat preparation of rabbit rectum (Mackenna & McKirdy, 1970) to examine the effect of vasopressin (Pitressin; Parke-Davis) on the longitudinal and circular layers of the muscularis externa. In a study of inhibitory agents, we have also examined the effect of adenosine triphosphate which Burnstock, Campbell, Satchell & Smythe (1970) have suggested to be the transmitter substance released by non-adrenergic inhibitory neurones in the gut.