

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  $\mu$ U/ml) has an inhibitory effect on the longitudinal muscle of the rabbit rectum, with an after-contraction at higher concentrations (33–133  $\mu$ U/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.

The response to vasopressin (1-100  $\mu\text{U/ml}$ ) was rather variable in character but a general pattern was discernible. Both layers of the muscularis externa typically showed a biphasic response to vasopressin composed of inhibition (fall in tension) followed by excitation (rise in tension above baseline level). Inhibition of both layers became apparent at about the same time, but the longitudinal layer usually led the circular in the subsequent excitation.

The response of the flat preparation to adenosine triphosphate (B.D.H.) was even more variable than that to vasopressin. In concentrations of  $10^{-4}$ - $3 \times 10^{-4}$  g/ml, adenosine triphosphate usually produced prolonged inhibition selectively of the circular layer, frequently accompanied by excitation of the longitudinal layer. On repeated exposure, the flat preparation showed tachyphylaxis to both adenosine triphosphate ( $10^{-4}$ - $3 \times 10^{-4}$  g/ml) and vasopressin (1-100  $\mu\text{U/ml}$ ). The responses to both vasopressin and adenosine triphosphate were qualitatively unaltered in the presence of tetrodotoxin ( $10^{-7}$  g/ml).

The biphasic response to vasopressin (1-100  $\mu\text{U/ml}$ ) recordable from the longitudinal muscle is probably comparable with the inhibition and after-contraction found by Gilmore & Vane (1970) in response to high concentrations of vasopressin. With regard to the suggestion that adenosine triphosphate is the non-adrenergic inhibitory transmitter, it seems surprising that adenosine triphosphate ( $10^{-4}$ - $3 \times 10^{-4}$  g/ml) should produce its inhibitory effect predominantly on circular muscle, since Furness (1969) has shown that non-adrenergic inhibitory nerves supply the longitudinal as well as the circular layer of the muscularis externa of the rabbit distal colon.

#### REFERENCES

- BURNSTOCK, G., CAMPBELL, G., SATCHELL, D. & SMYTHE, A. (1970). Evidence that adenosine triphosphate or a related nucleotide is the transmitter substance released by non-adrenergic inhibitory nerves in the gut. *Br. J. Pharmac.*, **40**, 668-688.
- FURNESS, J. B. (1969). An electrophysiological study of the innervation of the smooth muscle of the colon. *J. Physiol., Lond.*, **205**, 549-562.
- GILMORE, N. J. & VANE, J. R. (1970). A sensitive and specific assay for vasopressin in the circulating blood. *Br. J. Pharmac.*, **38**, 633-652.
- MACKENNA, B. R. & MCKIRDY, H. C. (1970). A simple method for investigating the functional relationship of the longitudinal and circular layers of the muscularis externa of the rabbit bowel, using a "flat" preparation. *J. Physiol., Lond.*, **211**, 18P.
- WOO, C.-Y. & SOMLYO, A. P. (1967). Interaction of magnesium with vasopressin in intestinal smooth muscle. *J. Pharmac. exp. Ther.*, **155**, 357-366.

#### Relationships between stereospecificity and chemical structure (T)

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#### Mechanism of the facilitatory action of edrophonium in cat skeletal muscle (T)

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