

of potency for the PG's studied on the isolated guinea-pig and rat uterus. This provides further evidence for the existence of different PG receptors mediating contractions of these two uterine smooth muscle preparations.

We thank Upjohn Co Ltd and ICI Ltd for the gift of prostaglandins. S.K.W. is a Glaxo-Allenbury's supported S.R.C. (CASE) Award student.

### **Dose-dependent nature of the interaction of fibrinogen-degradation products and 5-hydroxytryptamine on various vascular smooth muscle preparations**

C. FORSTER, J. MOHAN & E.T. WHALLEY

*Department of Neurosurgery, Manchester Royal Infirmary and Department of Pharmacology, Materia Medica and Therapeutics, University of Manchester, Manchester M13 9PT*

It has been shown that fibrin or fibrinogen degradation products (FDP's) can potentiate the effect of 5-hydroxytryptamine (5-HT) on various smooth muscle preparations (Buluk & Malofiejew, 1969). This study investigates further the interaction between FDP's and 5-HT on three vascular smooth muscle preparations: rabbit aortic strip (Rb.A); rat aortic strip (R.A.) and human basilar arterial strip (H.Ba). A crude preparation of FDP's was produced in the following way. Plasma from citrated blood of normal healthy human volunteers was thoroughly mixed with 2000 units of streptokinase and incubated for 90 min, after which time the reaction was stopped by the addition of 500 units/ml of aprotinin (Trasylol®). Aliquots of the incubate were then immediately deep frozen or kept cold until required.

A 90 min incubation period was chosen since we have recently shown that a standard 0.1 ml aliquot of incubate taken at this time produces a maximum potentiation of a response to a standard concentration of 5-HT on various vascular smooth muscles (Forster, Mohan & Whalley, 1979). R.A., Rb.A. and H.BA. strips were bathed in aerated Krebs-Henslett solution at 37°C and allowed to equilibrate for at least 2 hours. After full concentration effect curves to 5-HT were produced, the tissues were then challenged repeatedly with a threshold concentration of 5-HT, the contractions being recorded isometrically

### **References**

- BERGSTRÖM, S., CARLSON, L.A. & WEEKS, J.R. (1968). The prostaglandins: a family of biologically active lipids. *Pharmac. Rev.*, **20**, 1-48.
- DUKES, M., RUSSELL, W. & WALPOLE, A.L. (1974). Potent luteolytic agents related to prostaglandin F<sub>2t</sub>. *Nature. Lond.*, **250**, 330-331.

and displayed on a Grass Polygraph. When a constant threshold response was obtained, increasing volumes of the crude FDP sample were added to each bath, and left in contact for 1 min without washing out. The threshold concentration of 5-HT was then added. This procedure was repeated using an EC<sub>50</sub> of 5-HT.

Small volumes of the FDP incubate (<100 µl) exhibited no intrinsic activity on any of the tissues, however with larger volumes (100-800 µl) a dose-dependent slow-sustained contraction developed which was always preceded by a dose-dependent transient relaxation. Both the threshold concentration and EC<sub>50</sub> of 5-HT were potentiated in a dose-dependent fashion by increasing volumes of the FDP sample. Citrated plasma or streptokinase added alone possessed neither intrinsic activity nor the ability to potentiate the responses to 5-HT on any of the preparations.

Tovi, Nilsson & Thulin (1973) have demonstrated that there are increased levels of FDP's in the cerebrospinal fluid (CSF) following subarachnoid haemorrhage in humans. It is suggested that FDP's in CSF following rupture of an intracranial aneurysm may play some role in the intense cerebral vasospasm which can often be the cause of morbidity in this condition.

### **References**

- BULUK, K. & MALOFIEJEW, M. (1969). The pharmacological properties of fibrinogen degradation products. *Br. J. Pharmac.*, **35**, 79-89.
- FORSTER, C., MOHAN, J. & WHALLEY, E.T. (1979). Interaction of fibrin degradation products and 5-hydroxytryptamine on various vascular smooth muscle preparations: possible role in cerebral vasospasm. *Proceedings of 2nd Workshop Symposium on Cerebral Vasospasm* (In Press).
- TOVI, D., NILSSON, I.M. & THULIN, C.A. (1973). Fibrinolytic activity of the cerebrospinal fluid after subarachnoid haemorrhage. *Acta. Neurol. Scand.* **49**, 1-9.