Production of prostaglandin-like materials by rat tail skin in response to injury

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Wounding of the skin is followed by the development of an acute inflammatory reaction in which prostaglandin-like substances (PGLA) might also be produced. The production of PGLA from an isolated rat tail preparation, in response to wounding was investigated using a cascade superfusion technique (Henman, Naylor & Leach, 1978).

Skin of male rats (CFE strain 200–300 g) was removed from the tail and after discarding the tip area, an 8–10 cm strip was prepared. The strip was superfused on its dermal surface with Krebs-Henseleit solution (3 ml/min) at 37°C and the superfusate was then combined with additional Krebs-Henseleit solution (1 ml/min) containing a mixture of antagonists and indomethacin (2.8 μM) to render the assay tissues more sensitive and selective for prostaglandin assay (Gilmore, Vane & Wyllie, 1968; Ellis, Oelz, Roberts, Payne, Sweatman, Nies & Oates, 1976). Transverse full thickness skin wounds were made with surgical scissors to the superfused preparation *in situ*.

Application of full thickness wounds to the rat tail skin always produced a series of characteristic responses in the assay tissues. Rat fundic strip (RFS), rat colon (RC) and chick rectum (CR) preparations contracted whilst spirally cut rabbit mesenteric artery (RbMA) and transverse stomach strip (RbSS) relaxed. The wound responses could be mimicked by addition of prostaglandin E_2 (PGE_2) which suggested the production of a prostaglandin E_2-like (PGE_2-like) material in the superfusate as a result of wounding. Further experiments using spirally cut bovine coronary artery strip indicated the presence of a small amount of prostacyclin-like (PGI_2-like) material in the superfusate.

Using RFS as the assay tissue and measuring the area of each response with an electronic integrator, PGLA could be estimated in terms of ng. PGE_2 equivalents. The extent of the wound response was found to be proportional to the number of wounds inflicted. Using a standard wound stimulus of 8 full thickness cuts no significant difference in the output of PGLA could be detected when the wounds were applied to 4 separate regions of the tail strip.

Either of the cyclo-oxygenase inhibitors indomethacin (IM), (0.7 μM, 1.4 μM and 2.8 μM) or AH7170 (2-m(p-chloro-benzoyl) phenylpropionic acid) (3.4 μM and 17.3 μM) administered as infusions 1 min before and for 2 min during wounding decreased the output of PGLA expressed as a percentage inhibition of the control: (IM); 49.2, 69.5 and 83.0% and (AH7170); 70.6 and 95.2% respectively. Likewise, addition of arachidonic acid (AA), (1.6 μM, 3.3 μM, 6.6 μM) potentiated the PGLA output 28.0, 50.4 and 77.9%. Tail skins removed from rats pretreated with AH7170 (5 and 10 mg/kg, i.p.), 3 h previously also produced less PGLA than rats treated with vehicle alone 5 mg/kg giving 28.7% and 10 mg/kg, 50.5%.

On the basis of this evidence the isolated rat tail skin strip produces PGLA in response to a simple wounding procedure. Both PGE_2-like and PGI_2-like components have been shown to be present in the superfusate obtained after wounding. The amount of PGLA produced is proportional to the severity of the injury.

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References

ELLIS, E.C., OELZ, O., ROBERTS, L.J., PAYNE, N.A., SWEATMAN, B.J., NIES, A.S. & OATES, J.A. (1976). Coronary arterial smooth muscle contraction by a substance released from platelets: evidence that it is thromboxane A_2. *Science*, **193**, 1135–1137.

GILMORE, N., VANE, J.R. & WYLLIE, H. (1968). Prostaglandins released by the spleen. *Nature (Lond.)*, **218**, 1135–1140.

HENMAN, M.C., NAYLOR, I.L. & LEACH, G.D.H. (1978). A critical evaluation of the use of a cascade superfusion technique for the detection and estimation of biological activity. *J. Pharm. Meth.*, **1**, 13–26.