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THE EFFECT OF UROGASTRONE ENCAPSULATED IN INTACT ERYTHROCYTES ON GASTRIC SECRETION IN THE RAT

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Urogastrone (Gray et al 1940) was discovered following observations that urine extracts from pregnant women had a beneficial effect on experimental ulcers in dogs (Gray et al 1939). This finding correlated with clinical observations of a low incidence of peptic ulceration during pregnancy. Urogastrone is a mixture of two peptides (52 and 53 amino acids) which strongly inhibit gastric secretion in laboratory animals. It has strong similarities with mouse epidermal growth factor. Since peptides are rapidly degraded in vivo we have attempted to prolong the anti-secretory activity of urogastrone by encapsulating urogastrone in erythrocytes and testing the preparation against the free hormone in the rat.

Urogastrone (Sigma Chemical Co Poole, Dorset) was iodinated with I^{125} using chloramine T (Hunter & Greenwood, 1962) and the radiolabelled compound was added to unlabelled hormone to act as a tracer. Urogastrone was encapsulated in rat erythrocytes by a modified preswell technique involving hypotonic swelling of cells (Pitt et al 1983). Optimum loading was found to be 1.06 mg/ml of packed cells (haematocrit value 76) representing a 17.6% encapsulation efficacy with 3% of the hormone attaching to the cell surface. When these cells (1 ml packed cells) were injected iv into rats (4 per group) the half life of the returned preparation was found to be 10 days. Erythrocytes returned to the circulation were labelled with fluorescein. The effect of this preparation was compared with that of the free hormone injected iv on carbachol induced gastric secretion in the anaesthesized rat. A calibrated pH meter connected to a recorder was used to monitor acid output in the perfusate. Basal acid output was recorded for 15 min before stimulation with carbachol. Cimetidine (40 mg/kg^{-1}) was used as a control. The perfusion technique employed was as described by Smith et al (1978). On a comparative basis free urogastrone inhibited acid secretion by 78 ± 9% (6) and encapsulated urogastrone inhibited acid secretion by 54 ± 8% (6) However encapsulated urogastrone was still inhibiting acid secretion at 2h when the experiment was terminated. The effect of free urogastrone lasted for 50 min. Cimetidine inhibited acid secretion by 87 ± 5% (4) and the effect lasted for 75 min. Results are mean ± sem (No of experiments). In in vitro dialysis experiments over 6h a steady state diffusion of drug from erythrocytes was observed with about 2% of the encapsulated drug leaving the cells per h.

The urogastrone obtainable was a relatively crude preparation but the encapsulation of peptide hormones represents an extension of the use of erythrocytes as a slow release drug delivery system.

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