## Effects of prostacyclin ($PGI_2$), $PGI_1$ and 6-oxo-$PGF_{1\alpha}$ on the rat gastric mucosa

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Prostacyclin ($PGI_2$) is an unstable potent vasodilator, which can be formed by vascular tissue and the rat stomach (Gryglewski, Bunting, Moncada, Flower & Vane, 1976). We have now investigated the effects of $PGI_2$, its stable degradation product 6-oxo-$PGF_{1\alpha}$, and 6β-$PGI_1$, a 5,6-dihydro prostacyclin (Johnson, Lincoln, Thompson, Nidy, Mizsak & Axen, 1977) on the rat gastric mucosa.

The inhibition of pentagastrin (0.5 μg $kg^{-1}min^{-1}$)-induced gastric acid secretion and the change in mucosal blood flow (MBF) in the urethane-anaesthetised rat was determined as previously described (Main & Whittle, 1973). $PGI_2$ (0.25–5 μg $kg^{-1}min^{-1}$ i.v.) caused a dose-dependant fall in systemic arterial blood pressure and inhibition of acid output; the $ID_{50}$ (dose causing 50% inhibition) was 0.5 μg $kg^{-1}min^{-1}$ (infused i.v. for 30 min) compared with an $ID_{50}$ of 1 μg $kg^{-1}min^{-1}$ for $PGE_2$. Subcutaneous administration of $PGI_2$ (50–200 μg/kg) likewise inhibited acid output ($ID_{50}$, 100 μg/kg, s.c.). 6-oxo-$PGF_{1\alpha}$ had little effect on acid output in doses up to 50 $\mu g^{-1}kg^{-1}min$ i.v. for 30 minutes. However, the stable prostacyclin analogue, $PGI_1$ inhibited acid secretion ($ID_{50}$, 4 μg $kg^{-1}min^{-1}$ i.v.) and in these antisecretory doses, it was less active than $PGI_2$ as a vasodepressor.

During the inhibition of acid secretion by $PGI_2$, the ratio of MBF to acid output increased. Furthermore, $PGI_2$ (0.5 $\mu g^{-1}kg^{-1}min$, i.v.) increased resting MBF, indicating a direct vasodilator action on the mucosa.

In the isolated perfused whole rat-stomach preparation (Bunce & Parsons, 1976), $PGI_2$ added to the serosal solution (pH 7.6, 37°C) inhibited histamine ($5 \times 10^{-5}$ M)-induced acid output with an $ID_{50}$ of $6 \times 10^{-6}$M. Although $PGI_2$ appeared less active than $PGE_2$ ($ID_{50}$, $10^{-6}$ M) in this preparation, this may well result from the rapid breakdown of $PGI_2$ under these *in vitro* conditions; the stable analogue, $PGI_1$, showed marked antisecretory activity ($ID_{50}$, $1.0 \times 10^{-6}$ M).

The inhibition of gastric mucosal erosions was assessed 3 h after administration of indomethacin (20 mg/kg s.c.) as previously described (Whittle, 1976). Repeated subcutaneous administration of $PGI_2$, $PGI_1$ and 6-oxo-$PGF_{1\alpha}$ reduced the incidence and severity of the lesions, with an $ID_{50}$ of 35, 30 and 500 μg $kg^{-1}h^{-1}$ respectively. Likewise, a single subcutaneous injection of $PGI_2$ and $PGI_1$ immediately prior to indomethacin, inhibited the erosions, with an $ID_{50}$ of 350 and 200 μg/kg s.c. respectively compared to 450 μg/kg s.c. for $PGE_2$. 6-oxo-$PGF_{1\alpha}$ had little activity in single doses up to 500 μg/kg s.c.

The present findings indicate that prostacyclin exhibits many of the actions previously ascribed to $PGE_2$, being a potent mucosal vasodilator, an inhibitor of gastric acid secretion and an inhibitor of erosion formation in the rat. The interaction and relative roles of $PGI_2$ and $PGE_2$ in the gastric mucosa remains to be clarified.

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## The renal haemodynamic and excretory actions of prostacyclin ($PGI_2$) in anaesthetized dogs

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Prostacyclin ($PGI_2$) is a newly discovered arachidonic acid metabolite synthesized in vascular walls of different species including man. $PGI_2$ relaxes a variety of vascular muscle strips *in vitro* (Bunting, Gryglewski, Moncada & Vane, 1976) and is a strong hypotensive in rabbits and rats (Armstrong, Lattimer, Moncada & Vane, 1977).

As prostaglandins have profound stimulatory actions on renal haemodynamics and excretion in a variety of species (McGiff & Itskovitz, 1973) we have measured the renal actions of $PGI_2$ in anaesthetized dogs.