Prostacyclin is produced in whole blood

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Prostacyclin (PGI_2) is the major product, via cyclo-oxygenase, of arachidonic acid metabolism in vascular tissue *in vitro* (Moncada, Gryglewski, Bunting & Vane, 1976) whereas in blood the major product is the labile platelet aggregating agent, thromboxane A_2 (TXA_2: Hamberg, Svensson & Samuelsson, 1975). PGI_2 is a potent inhibitor of platelet aggregation induced by several agents (arachidonic acid, prostaglandin endoperoxides, collagen, thrombin, ADP and adrenaline) (Moncada *et al.*, 1976) and causes vasodilatation (Armstrong, Lattimer, Moncada & Vane, 1978). It has been hypothesized that PGI_2 plays an important physiological role in preventing platelets clumping on blood vessel walls.

In thrombo-embolic disorders it would be an advantage to redirect prostaglandin endoperoxide (PGG_2, PGH_2) metabolism towards synthesis of prostacyclin. We have established that certain derivatives of imidazole are potent and specific inhibitors of thromboxane synthesis. We now report that these inhibitors can 'unmask' the prostacyclin pathway of PG endoperoxide metabolism in whole rabbit blood.

Thromboxane B_2 (the stable degradation product of TXA_2) and 6-oxo-$PGF_{1\alpha}$ (the stable degradation product of PGI_2) were each measured in blood by sensitive and specific radioimmunoassays after extraction and thin layer chromatographic separation (Salmon, 1978). Only low concentrations of TXB_2 and 6-oxo-$PGF_{1\alpha}$ were detected in stirred whole blood—1.89 ± 0.29 and 0.32 ± 0.06 ng/ml (mean ± s.e. mean) respectively. The addition of either arachidonic acid (50 μg) or collagen (10 μg) caused platelet aggregation and the amount of TXB_2 increased dramatically: in the case of collagen, to 21.56 ± 3.01 ng/ml; there was a small concurrent increase in the concentration of 6-oxo-$PGF_{1\alpha}$. Thrombin also caused an elevation of TXB_2 (8 ng/ml: 2 experiments) but this was less than with other aggregating agents. Low concentration of 1-*n*-butylimidazole (8 μM) prevented platelet aggegation induced by arachidonic acid and collagen and this was associated with decreased synthesis of TXB_2 which fell to 1.5 ± 0.24 ng/ml. However, the addition of the thromboxane synthetase inhibitor and the aggregating agent increased the concentration of 6-oxo-$PGF_{1\alpha}$; for example, the concentration of 6-oxo-$PGF_{1\alpha}$ after treating blood with collagen and 1-*n*-butylimidazole was 11.6 ± 1.26 ng/ml.

Which cell type is responsible for the production of 6-oxo-$PGF_{1\alpha}$? Our experiments have ruled out the possibility that platelets themselves or red blood cells can generate prostacyclin. The 'buffy coat' cells however, are a rich source of the prostacyclin synthesising enzymes.

These data indicate that when the conversion of PG endoperoxides to TXA_2 in blood is blocked, PGI_2 can be synthesised by components in the blood from the surplus endoperoxides, and strongly suggests a role for leucocytes in the control of platelet aggregability.

References

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