Reduction of prostaglandin E_2 to prostaglandin $F_{2\alpha}$ by an enzyme in sheep blood

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When prostaglandin E_2 (PGE_2) is incubated with sheep whole blood, it is converted to a more polar compound with chromatographic behaviour corresponding to prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$). Incubation of PGE_2 with the cellular fraction of blood caused similar conversion whereas incubation with cell-free plasma (prepared by centrifugation at 1875 *g* for 20 min) did not. When the cells were treated with 0.1 M phosphate buffer, causing red cell haemolysis, and the cellular debris separated by centrifugation and re-suspended in fresh 0.1 M phosphate buffer, a preparation was obtained which converted PGE_2 to $PGF_{2\alpha}$ and which could be used for further study of the factors responsible for the conversion. Duration of incubation was 75 min and substrate concentration was 1 μg/ml.

The product of the reaction was quantitatively assayed by liquid scintillation counting of an aliquot of the material following extraction and thin layer chromatography. The end-product in two thin layer chromatography systems behaved like $PGF_{2\alpha}$ and on radio gas chromatography the trimethylsilyl ether methyl ester derivative had a retention time corresponding to authentic [^{3}H]-$PGF_{2\alpha}$. Conclusive evidence of identification was obtained by combined gas liquid chromatography and mass spectrometry. There was no evidence that any $PGF_{2\beta}$ was formed. Prolonged incubation of the system at 50°C or a short incubation at 55°C and above destroyed the ability of the system to reduce PGE_2 to $PGF_{2\alpha}$. The reaction occurred over a narrow pH range with the optimum conversion at 37°C occurring at approximately pH 7. The heat lability and the pH dependence of the system would suggest that it is enzymatic in nature.

Substrate specificity studies have been performed on the enzyme system with prostaglandin E_1; 8-iso-prostaglandin E_1 and PGE_2. Prostaglandins E_1 and E_2 were equally good substrates, whereas 8-iso-prostaglandin E_1 was a poor substrate.

The evidence to date suggests that sheep blood cells contain an enzyme that is capable of reducing the 9-oxo group of the E series prostaglandins into the corresponding F_α prostaglandin. It is not yet possible to state that this enzyme is specific for prostaglandins.

There have been several reports of enzymes that are capable of reducing the 9-oxo group of the E series prostaglandins into one or both of the corresponding 9-hydroxy configurations (Schneider & Murray, 1973; Leslie & Levine, 1973; Hamberg & Samuelsson, 1969). The work presented here provides evidence for the presence in sheep whole blood of a similar enzyme. The biological significance of this conversion of PGE_2 to $PGF_{2\alpha}$ remains to be elucidated.

The work provides evidence for a similar enzyme in sheep whole blood; however, under identical conditions, blood from man, guinea-pig, horse, cat, cow, rat and pig were found incapable of metabolizing PGE_2. The biological significance of this conversion of PGE_2 to $PGF_{2\alpha}$ remains to be elucidated.

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