

## Inhibitory effect of L-ascorbic acid on the yield of prostaglandin F from the guinea-pig uterine homogenates

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Poyser (1972) demonstrated that homogenized guinea-pig uterus has the ability to biosynthesize prostaglandins from endogenous precursors and that this process can be inhibited by indomethacin. Earlier studies (van Dorp, 1971) have shown that certain antioxidants, such as  $\alpha$ -tocopherol and propylgallate, have inhibitory effects on the biosynthesis of prostaglandins. The experiments here reported were carried out to determine whether L-ascorbic acid (L-AA), which forms an oxidation-reduction system in the body, would have an effect on the *in vitro* yield of prostaglandin F from guinea-pig uterine homogenate.

Guinea-pigs fed on the normal diet were killed on day 14 of the oestrous cycle and the uteri were removed. Each uterus was freed of fat and blood and homogenized mechanically in ice-cold Krebs solution for 10 minutes. More Krebs solution was added to give a final tissue concentration of 100 mg/ml. In each experiment, tissue from one animal was incubated with a range of L-AA concentrations. Four tubes were set up for each concentration of L-AA and for tissue samples to which no L-AA was added. All replicates contained 200  $\mu$ l of homogenate to which 25  $\mu$ l volumes of either Krebs solution or L-AA in Krebs solution were added. In the latter case, the concentration of L-AA was designed to yield the final concentration of ascorbic acid shown in the table. All the tubes were incubated for one hour at

37°C. To the tubes in Group A, nine volumes of 96% ethanol were added prior to incubation while to all other tubes ethanol was added at the end of incubation so as to terminate prostaglandin synthesis (Ånggård & Samuelsson, 1965). From all incubated tubes PGF was extracted and assayed as described earlier (Sharma, Hibbard, Hamlett & Fitzpatrick, 1973). The effect of L-AA additions on pH was determined before but not after incubation.

The results shown in the table indicate that additions of varying concentrations of L-AA have an inhibitory effect on the yield of PGF from the uterine tissue homogenates. Although an ascorbic acid-dependent effect seems to be lacking at higher concentrations, there is a possibility that such relationship does exist at lower concentrations. However, since in other tissues prostaglandin inhibition appears to be pH-dependent (Rose & Collins, 1974) and since the number of observations for the lower concentrations of ascorbic acid in the present investigation is limited, further work would be required to clarify this point.

### References

- ÅNGGÅRD, E. & SAMUELSSON, B. (1965). Biosynthesis of prostaglandins from arachidonic acid in guinea-pig lung. *J. Biol. Chem.*, **210**, (9), 3518-3521.
- POYSER, N.L. (1972). Production of prostaglandins by the guinea-pig uterus. *J. Endocrin.*, **54**, 147-159.
- ROSE, A.J. & COLLINS, A.J. (1974). The effect of pH on the production of prostaglandins  $E_2$  and  $F_{2\alpha}$  and a possible pH-dependent inhibitor. *Prostaglandins*, **8**, (4), 271-283.
- SHARMA, S.C., HIBBARD, B.M., HAMLETT, J.D. & FITZPATRICK, R.J. (1973). Prostaglandin  $F_{2\alpha}$  concentrations in peripheral blood during the first stage of normal labour. *Br. med. J.*, **1**, 709-711.
- VAN DORP, D.A. (1971). Recent developments in the biosynthesis and the analysis of prostaglandins. *Ann. N.Y. Acad. Sci.*, **180**, 181-199.

**Table 1** Prostaglandin F content of guinea-pig uterine homogenate ng/100 mg tissue

Groups	A	B	C	D	E	F	G	H	I
L-ascorbic acid ( $\mu$ g/ml homogenate)	—	—	6.25	12.5	25	50	125	625	1250
pH before incubation	7.42	7.42	7.41	7.40	7.37	7.32	7.17	5.93	4.51
PGF content (mean $\pm$ s.e.)	31.6 $\pm$ 4.3 (n = 8)	119.5 $\pm$ 10.5 (n = 8)	97.6 $\pm$ 9.4 (n = 3)	84.1 $\pm$ 7.9 (n = 3)	70.3 $\pm$ 8.7 (n = 8)	63.6 $\pm$ 10.2 (n = 3)	67.3 $\pm$ 3.9 (n = 8)	91.8 $\pm$ 2.8 (n = 5)	67.9 $\pm$ 1.5 (n = 5)
Level of significance from Group B	<0.01	—	>0.05	<0.05	<0.01	<0.01	<0.01	<0.05	<0.01