Effect of *p*-bromophenacyl bromide, an inhibitor of phospholipase A_2, on prostaglandin production by the guinea-pig uterus

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Membrane phospholipids are a probable source of arachidonic acid for prostaglandin synthesis, though this has still to be proven. Phospholipase A_2 (PLA_2) cleaves unsaturated fatty acids from phospholipids, so its inhibition should prevent prostaglandin production by tissues if phospholipids are involved. Para-bromophenacyl bromide (*p*-BPAB), an inhibitor of porcine pancreatic PLA_2 (Volwerk, Pieterson & de Haas, 1974) may be useful in studying arachidonic acid release from and prostaglandin synthesis by tissues. Its effect of these parameters has been examined *in vitro* on the guinea-pig uterus, a tissue which synthesizes predominantly prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) from endogenous precursors when homogenized and incubated *in vitro* (Poyser, 1972).

Uteri from guinea-pigs in dioestrus were homogenized in 15 ml Krebs solution and incubated for 90 min in the absence or presence of a known concentration of *p*-BPAB. Each uterus was so divided so as to act as its own control. $PGF_{2\alpha}$ synthesis was inhibited, but not completely, by *p*-BPAB (Table 1). A re-direction of synthesis towards PGE_2 did not occur as its synthesis was also inhibited ($63.0 \pm 4.3\%$; $n=5$) by *p*-BPAB (100 μg/ml). Metabolism of 9-[^{3}H]-$PGF_{2\alpha}$ (0.4 μCi) by the uterus was unaffected by *p*-BPAB (100 μg/ml) and remained undetectable ($n=2$).

The release of free arachidonic acid during incubation of the guinea-pig uterus was also measured in the absence or presence of *p*-BPAB (100 μg/ml). Indomethacin (50 μg/ml) was present in the Krebs solution during this study. The post-homogenization, pre-incubation level (μg/100 mg tissue) of free arachidonic acid in the uterus was 1.6 ± 0.4 ($n=5$), which rose to 4.5 ± 0.4 following incubation. This increase was inhibited by 75.9% with *p*-BPAB (the level of arachidonic acid being 2.3 ± 0.4) achieved possibly by inhibiting PLA_2. The amount of arachidonic acid available is, however, still far in excess of the amounts of prostaglandins normally synthesized by the uterus. It would appear that inhibition of arachidonic acid release does not account for the reduction in prostaglandin synthesis. Furthermore, the addition of exogenous arachidonic acid (10 μg/ml) to uterine incubates ($n=5$) did not overcome the inhibition of prostaglandin synthesis produced by *p*-BPAB. Apparently this compound also prevents the conversion of arachidonic acid into prostaglandins.

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References

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Table 1 Effect of *p*-bromophenacyl bromide (*p*-BPAB) on prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) synthesis by guinea-pig uterus homogenates *in vitro*.

Concentration of p-BPAB (μg/ml)	*% Inhibition of $PGF_{2\alpha}$ synthesis (mean ± s.e.)*	*No. of repetitions (n)*
1	6.6 ± 1.4	4
2	25.2 ± 7.3	4
5	38.4 ± 6.7	4
10	51.1 ± 7.0	3
25	53.0 ± 10.3	4
50	52.8 ± 5.2	4
100	68.0 ± 6.0	7
200	68.7 ± 6.0	5
400	77.0 ± 6.3	4