# Effect of Picotamide on Prostacyclin Production by Human Endothelial Cells

Dear Sir,

Picotamide, a derivative of 4-methoxy-isophtalic acid, has been recently shown to inhibit thromboxane synthetase as well as thromboxane receptors in vitro and in vivo (1). Due to these effects the compound has a potential usefulness as antithrombotic agent (2). In order to further elucidate the pharmacological properties of picotamide we investigated the effect of this compound on $PGI_2$ production by cultured endothelial cells. Human endothelial cells, obtained from umbilical cords as described by Jaffe et al. (3), were grown in vitro and subcultured in 24-well cluster plates as previously described (4). To measure the effect of picotamide on $PGI_2$ production, endothelial cell monolayers were washed twice with Dulbecco buffered saline (DBS) and then incubated for 30 min at 37° C with 0.5 ml of DBS containing picotamide at final concentrations ranging between 1.5 and 390 μg/ml. This compound was added to DBS as ethanolic solution. Final ethanol concentration was 0.04% (w/v). At this concentration, and in a similar experimental set up, ethanol had been demonstrated to have a moderate stimulatory effect on $PGI_2$ production (4). In control experiments the same ethanol dose was thus used. At the end of incubation the supernatants were frozen and kept at −70° C until the assay could be performed. Concentrations of 6-keto-$PGF_{1\alpha}$ in the supernatants were assayed by radioimmunoassay. The effect of the various doses of picotamide on endothelial $PGI_2$ is reported in Table 1. No significant reduction of $PGI_2$ production was observed for picotamide concentrations up to 6 μg/ml. At higher picotamide concentrations the inhibition was dose-dependent up to 24 μg/ml where a 50% inhibition was achieved; higher picotamide concentrations caused a substantially similar $PGI_2$ decrease thus suggesting some enzymatic non-competitive type inhibition. The degree of $PGI_2$ inhibition was not raised when the time of exposure of endothelial cells to the drug was increased. The effect of picotamide on $PGI_2$, although moderate, shows that the pharmacological properties of this compound are more complex than earlier recognized. It can be suggested that the inhibition of thromboxane synthesis, thromboxane receptors and $PGI_2$ synthesis might all derive from a more general effect of this molecule which requires further studies in order to be elucidated. In considering picotamide as potential antithrombotic agent, it has to be remarked that the inhibition of $PGI_2$ observed in vitro is moderate and requires picotamide levels much higher than those achieved in vivo following oral administration. On this basis it is possible that the use of appropriate doses of picotamide in vivo could allow to block thromboxane synthesis and thromboxane effect without affecting $PGI_2$.

*Table 1* Effect of picotamide on endothelial $PGI_2$

| Picotamide dose (μg/ml) | 6-keto-$PGF_{1\alpha}$ (% of control)* |
|---|---|
| 1.5 | 103 |
| 3 | 105 |
| 6 | 95 |
| 12 | 75 |
| 24 | 52 |
| 48 | 47 |
| 192 | 48 |
| 384 | 44 |

* Results of three individual experiments are listed.

Yours sincerely
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## References

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