

Further studies on the depressant action of tetracyclines plus ascorbic acid on the rabbit ear artery

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We have described previously (McCullough & Wallace, 1975) a depressant action on constrictor responses to noradrenaline and histamine of a mixture of oxytetracycline (10^{-4} mol/l) and ascorbic acid (1.1×10^{-3} mol/l) added to the perfusate of the isolated rabbit ear artery. In the present study this effect is examined in greater detail.

The depressant effect of the mixture was greater after 90 min prior incubation of the perfusate at 37°C than when the mixture had been made up immediately before perfusion began—61% reduction ($P < 0.01$) as compared with 24% reduction ($P < 0.05$) in responses to 10 ng noradrenaline.

Varying the concentration of oxytetracycline from 5×10^{-5} mol/l to 2×10^{-4} mol/l while holding the concentration of ascorbic acid constant at 1.1×10^{-3} mol/l had no appreciable effect on the depressant action of the mixture. However, when the oxytetracycline concentration was held constant at 10^{-4} mol/l the concentration of ascorbic acid was critical. At a concentration of 0.55×10^{-3} mol/l ascorbic acid the response to 10 ng noradrenaline was depressed by 46%, at 1.1×10^{-3} mol/l it was depressed by 61% and at 2.2×10^{-3} mol/l it was depressed by 90% ($P < 0.01$ in all cases).

When the oxytetracycline in the mixture was replaced by tetracycline, demethylchlortetracycline or minocycline (all 10^{-4} mol/l) the constrictor responses were significantly ($P < 0.02$) depressed in all cases; the extent of the depression was similar (60–80%) to that produced by oxytetracycline.

When the oxytetracycline was replaced by chloramphenicol or cloxacillin (10^{-4} mol/l) there was a significant ($P < 0.05$) inhibition of the constrictor responses but this inhibition was much less than that obtained with oxytetracycline (Figure 1) and similar to

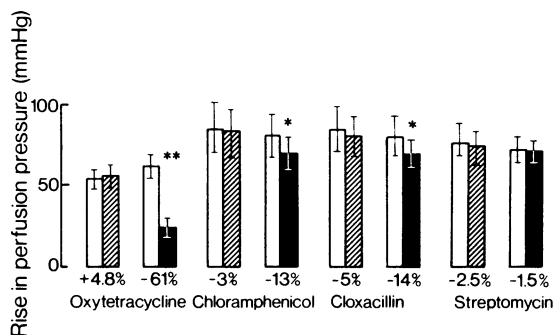


Figure 1 Effect of oxytetracycline, chloramphenicol, cloxacillin and streptomycin (all 10^{-4} mol/l) alone (hatched rectangles) and when mixed with ascorbic acid (1.1×10^{-3} mol/l) (black rectangles). (Open rectangles), control responses to noradrenaline 10 ng.

The results are means with standard errors from six experiments. ** $P < 0.01$; * $P < 0.05$; Paired *t* test; no other differences significant.

that produced by ascorbic acid alone (McCullough & Wallace, 1975). With streptomycin (10^{-4} mol/l) there was no significant effect on constrictor responses.

The results are consistent with the hypothesis that the depressant effect of the mixture is related to an interaction between the tetracycline and ascorbic acid in which the concentration of the ascorbic acid is the more critical, the tetracycline possibly playing a catalytic role.

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Reference

- McCULLOUGH, D.A. & WALLACE, W.F.M. (1975). Inhibition of constrictor responses of the rabbit ear artery by a mixture of oxytetracycline and ascorbic acid. *Br. J. Pharmac.*, **54**, 261–262P.