

P010 Inotropic effect of the diazepam-dopamine combination in rat heart: Role of cAMP

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Diazepam inhibits phosphodiesterase (PDE) type 4 and potentiates the effect of some 3',5'-cyclic adenosine monophosphate (cAMP)-dependent positive inotropic agents. The present study was undertaken to determine whether diazepam enhances the contractile response and cAMP levels induced by dopamine in electrically driven right ventricular strips of the rat heart, and the effects are compared with those of the typical PDE4 inhibitor rolipram. Dopamine (3-100 μ M) produced concentration-dependent positive inotropic effects which were augmented in the presence of 10 μ M diazepam, or 1 μ M rolipram. The diazepam induced enhancement of the positive inotropic effect of dopamine was not mimicked by 100 μ M γ -aminobutyric acid (GABA) nor it was antagonized by a 5 μ M concentration of the blockers of central and peripheral type benzodiazepine receptors, flumazenil and PK 11195. Diazepam and rolipram also potentiated the increase in cAMP levels produced by dopamine in this tissue. The results demonstrate that diazepam, like rolipram, augments the inotropic and biochemical effects of dopamine in rat myocardium. This effect is not mediated by benzodiazepine receptors but is probably the consequence of the PDE4 inhibitory activity of diazepam