previous studies canine myocardium has been shown to be as sensitive as human myocardium to the isomers of propranolol (Coltart & Meldrum, 1971).

The effect of varying concentrations of indoramin was studied on the action potential and contractile response of strips of canine ventricular muscle *in vitro*. Electrophysiological parameters were measured by conventional microelectrode techniques and contractile responses were assessed simultaneously by a strain gauge. At a concentration which occurs in human plasma after oral hypotensive doses of indoramin ($2{\cdot}6\times10^{-7}$ M), there was a statistically significant ($P=<0{\cdot}001$) decrease in V_{max} of depolarization, whereas resting potential, action potential amplitude, repolarization time and the contractile response were unchanged. Only with much higher concentrations of indoramin ($2{\cdot}6\times10^{-5}$ M–$4{\cdot}16\times10^{-4}$ M) was a reduction of contractile response demonstrated. In this respect, indoramin differed from (±)-propranolol which showed a clear dissociation between the concentration of the drug producing maximal β-blockade in man and that demonstrating a quinidine-like decrease of the V_{max} of depolarization on the human myocardial action potential (Coltart, 1971; Coltart & Meldrum, 1971).

Indoramin is of interest because it has a membrane stabilizing effect *in vitro* at a concentration which occurs in human plasma after administration of effective hypotensive doses of the drug, but the electrophysiological change is not accompanied by direct depression of the myocardial contractile response. Thus the alteration in myocardial contractility caused by indoramin would seem to be due to other properties, possibly including blockade of cardiac α-adrenoreceptors (Govier, 1968). Unlike propranolol, therapeutic concentrations of indoramin produce a decrease in the depolarization rate of the myocardium which may prove beneficial in the suppression of cardiac arrhythmias.

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Relative potency of intravenous prinodolol and propranolol in man

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Prinodolol (LB 46) a β-adrenoceptor blocking drug, is 4·6 times more potent than propranolol on isolated tissues (Saameli, 1967) and 20–40 times more potent than propranolol when administered orally to man (Hill & Turner, 1969).

This communication compares the effects of intravenous administration of prino-

dolol and propranolol. The plasma half life of prinodolol was found to be 3·34 h (S.D.±0·24). This compares with a value of 2·34 h (S.D.±0·22) for propranolol (Shand, Nuckolls & Oates, 1970).

Preliminary double blind studies in four volunteers showed that intravenous prinodolol (0·25 and 0·5 mg) produced a dose-response inhibition of tachycardia induced by isoprenaline aerosol and that the effect of propranolol (5 mg) was intermediate between the two doses of prinodolol.

In a double blind definitive study, prinodolol (0·1 and 0·5 mg) and propranolol (2 and 10 mg) were administered intravenously to four normal male subjects (20–40 years) and the inhibition of exercise tachycardia measured at 15, 60 and 240 min after injection, using a bicycle ergometer, and an electrocardiograph for recording heart rate. At rest the dose-response relationship for the two drugs was in opposite directions, propranolol producing a fall and prinodolol a rise in resting heart rate. Both drugs produced a significant dose-dependent inhibition of exercise tachycardia throughout the experimental period. The potency ratio of prinodolol to propranolol was between 5 and 10 to 1.

Measurement of plasma concentrations of both drugs (propranolol by the method of Shand, Nuckolls & Oates (1970) and prinodolol by a slight modification of that used by Pacha (1969)) showed that the mean concentration of prinodolol 15 min after the administration of 0·5 mg was 6·2 ng/ml (S.D.±1·6) and that of propranolol 15 min after administration of 10 mg was 88·5 ng/ml (S.D.±15·6). There was a linear fall in heart rate with increasing log plasma drug concentration and this was similar for both compounds in all subjects. The common slope was b=−12·6, indicating that a 10-fold increase in plasma concentration of either drug would produce a mean decrease in heart rate of 12·6 beats/minute.

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Interaction between phosphodiesterase inhibitors and catecholamines on contractions of the cat soleus muscle

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β-Adrenoceptor agonists produce a decrease in peak tension and an increase in the rate of relaxation of the maximal twitch of the slow-contracting cat soleus muscle (Bowman & Zaimis, 1958). The effect is consistent with an enhanced rate of decline of the active state of the stimulated muscle. The changes produced in the unit of contraction result in a marked decrease in fusion and in tension when subtetanic contractions are elicited by frequencies of stimulation that include the physiological range (5–15 Hz). This effect of β-adrenoceptor agonists also occurs in slow-contracting