and voltage-dependent depression of V_{max} was studied in guinea-pig ventricular muscle perfused with Tyrode solution by using conventional micro-electrode technique.

The resting block (time-independent block of V_{max}) of Quinidine (0.01mM) was facilitated in a concentration-dependent manner (0.03mM—1mM). Quinidine produced depression of V_{max} in a rate-dependent manner (RDB was seen under inter-stimulus interval 4800ms and was enhanced with the increase of inter-stimulus interval 4800ms to 250ms), and it was facilitated by sodium salicylate in a concentration-dependent manner. The rate of onset of quinidine plus sodium salicylate's RDB (2.42 ± 0.3 beats) became faster than before ($T_{on} = 3.30 \pm 0.6$ beats). Quinidine depressed V_{max} in more depolarized membrane and this was attributed to the negative shift of the curve relating V_{max} to the resting potential along the voltage axis, and the more negative shift was produced by sodium salicylate. It is suggested that the facilitatory effect of sodium salicylate on quinidine-induced fast Na^+ channel block was seen not only normal resting potential, but depolarized potential induced by a certain condition such as ischemic state of the heart.

-180- INHIBITORY EFFECTS OF MEXILETINE AND LIDOCAINE ON THE CALCIUM CURRENT OF SINGLE VENTRICULAR MYOCYTES

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We studied the effects of the Class I-b anti-arrhythmic agents, lidocaine (Lido) and mexiletine (Mex), on the calcium current of the guinea pig single ventricular myocytes using tight-seal whole-cell voltage and current clamp. Firstly the effects on action potential duration (APD) were examined. Mex (30 μ M) significantly shortened the APD by 38%; Lido also shortened the APD, but the shortening was not statistically significant. In voltage clamp experiment, Mex at the concentrations of 10, 30 and 100 μ M decreased I_{Ca} by 23.0, 29.0 and 55.4%, respectively, while Lido decreased it by only 8.9, 16.8 and 25.2%. Inward rectifier K current (I_{K1}) and voltage and time dependent K current (I_K) were not changed. At all concentrations tested, a potency of I_{Ca} inhibition by Mex was significantly greater than that of Lido ($p < 0.05$). The maximum inhibition (I_{max}) and apparent dissociation constant (K_d) were calculated from dose-response relationship. I_{max} and K_d were 70.0% and 34.4 μ M for Mex and 32% and 27.4 μ M for Lido. The findings suggest that Mex has a greater "efficacy" in blocking the Ca channels, albeit there's little difference in the "affinity" of the two drugs. The main anti-arrhythmic effect of these drugs would be a blockade of the sodium channel. However, the difference in the potency of Ca-antagonism is important to explain the alleged difference in the eligibility to suppress some clinical ventricular arrhythmias.

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BLOCKING EFFECTS OF CESIUM AND BARIUM ON THE INWARD-RECTIFIER K CHANNEL IN THE VENTRICULAR CELL MEMBRANE OF THE GUINEA-PIG

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It is known that both Cs and Ba block i_{K1} current and depolarize the resting membrane. With depolarization, Ba causes spontaneous automaticity, but Cs did not. To elucidate the differences in the effects of Cs and Ba on i_{K1} , effects of these two ions on the inward-rectifier K channel (I_{Krec}) were examined using "cell-attached" patch clamp technique. Enzymatically dispersed cells from the guinea-pig ventricle were used. In the single channel current, both Cs and Ba blocked I_{Krec} more strongly with higher concentrations of ions and with hyperpolarizing the membrane. The blocking kinetics of Cs were much faster than those of Ba. From the kinetic analyses, it was shown that Ba binds the site in the channel which senses 0.46 of the membrane potential. In the case of Cs, the value was 1.57, which suggests that Cs blocks the channel cooperatively with K. Furthermore, analyses of burst kinetics and ensemble averaged current disclosed that Cs blocks the channel only in its open state and that Ba blocks it independently from the control kinetics of the channel. Therefore, it was concluded that Cs and Ba block I_{Krec} by binding different sites of the channel with different kinetics.

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DUAL EFFECT OF METHYLXANTHINES ON THE TRANSIENT INWARD CURRENT OF SHEEP PURKINJE FIBERS

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The actions of different concentrations of caffeine, theophylline and aminophylline on the transient inward current (TI) were studied in sheep Purkinje fibers by means of a two microelectrode voltage clamp method.

The following results were obtained. At a low concentration (1 mM), caffeine: 1) induced a TI when this current was not already present; 2) increased the amplitude and decreased the time to peak of an already present TI; 3) shifted the depolarizing threshold for the appearance of TI to more negative and the repolarizing threshold to less negative values; 4) increased the effect of low concentration of strophanthidin on TI; 5) exaggerated the effects of high calcium solutions on TI; 6) enhanced the effects of trains of clamps and of longer clamp steps on TI. At a high concentration (8 mM), caffeine abolished TI. Intermediate concentration of caffeine had intermediate effect on TI. Theophylline and aminophylline had actions similar to those of caffeine.

It is concluded that methylxanthines suppress TI