P28 INFLUENCE OF PINACIDIL ON CATECHOLAMINE SECRETION EVOKED BY CHOLINERGIC STIMUALTION AND MEMBRANE DEPOLARIZATION FROM THE RAT ADRENAL GLAND

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It has been known that potassium channel openers are a new class of molecules that have attracted general interest because of their potent antihypertensive activity in vivo and vasorelaxant activity in vitro (Hamilton and Weston, 1989). In the present study, it was attempted to examine the effect of the potassium channel opener on catecholamine (CA) secretion evoked by cholinergic stimulation, membrane depolarization and calcium mobilization from the isolated perfused rat adrenal gland. The perfusion of pinacidil (30-300 uM) into an adrenal vein for 20 min produced relatively dose-dependent inhibition in CA secretion evoked by ACh (5.32 mM), high K^+ (56 mM), DMPP (100 uM for 2 min), McN-A-343 (100 uM for 2 min), cyclopiazonic acid (10 uM for 4 min) and Bay-K-8644 (10 uM for 4 min). Also, under the presence of minoxidil (100 uM), which is also known to be a potassium channel activator, CA secretory responses evoked by ACh, high potassium, DMPP, McN-A-343, Bay-K-8644 and cyclopiazonic acid were also significantly depressed. However, in adrenal glands preloaded with pinacidil (100 uM) under the presence of glibenclamide (1 uM), an antidiabetic sulfonylurea that has been shown to be a specific blocker of ATP-regulated

potassium channels (for 20 min), CA secretory responses evoked by ACh, high potassium, DMPP, McN-A-343, Bay-K-8644 and cyclopiazonic acid were considerably recovered to a considerable extent of the normal release as compared to that of pinacidil only.

These results, taken together, suggest that pinacidil cause the marked inhibition of CA secretion evoked by stimulation of cholinergic (both nicotinic and muscarinic) receptors as well as by membrane depolarization, indicating strongly that this effect may be mediated by inhibiting influx of extracellular calcium and release in intracellular calcium in the rat adrenomedullary chromaffin cells. Furthermore, these findings suggest strongly that these potassium channel openers-sensitive membrane potassium channels also play an important role in regulating CA secretion.