the C-ring , two peaks (M3/M4) were believed to be a metabolite hydroxylated on the A-ring and last peak (M5) to be a metabolte hydroxylated on the phenyl moiety of E-ring. Using enriched rat liver microsomes, the anticipated isoforms of cytochrome P450s in the metabolism of rutaecarpine were partially characterized. The phenobarbital-induced microsomes greatly increased in the formation of the metabolic M1 and M5. The 3-methylcholanthrene-induced microsomes increased in the formation of metabolites M2, M3 and M5. Therefore, it was concluded that rutaecarpine would be metabolized by more than one isozyme of cytochrome P450 in rat liver microsomes. (Supported by a grant of the Korea Research Foundation supporting the Institute for Drug Research, Yeungnam University)

[PA1-7] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

INFLUENCE OF BRADYKININ ON CATECHOLAMINE SECRETION FROM THE ISOLATED PERFUSED RAT ADRENAL GLAND

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Bradykinin modulates the sympathetic system in various ways. It can stimulate sympathetic neurotransmission directly through presynaptic receptors (Llona et al., 1991) and indirectly via its hypotensive or nociceptive effects which activate central and ganglionic mechanisms (Kuo and Keeton, 1991; Dray et al., 1988). However, it has been found that bradykinin can also liberate prostaglandins in peripheral tissues, thereby attenuating the release of catecholamines (Starke et al., 1977). The adrenal medulla may in particular be a prominent target for the actions of angiotensin II and bradykinin, since both peptides have been shown to produce catecholamine release from this organ (Feldberg and Lewis 1964; Staszewska-Barczak and Vane 1967). Therefore, the aim of the present study was to investigate the effect of bradykinin on secretion of catecholamines (CA) evoked by stimulation of cholinergic nicotininc and muscarinic receptors, and membrane depolarization from the isolated perfused model of the rat adrenal glands and to elucidate its mechanism of action. Bradykinin (3 x 10-8 M) alone produced a weak secretory response of the CA. however, the perfusion with bradykinin (3 x 10-8 M) into an adrenal vein of the rat adrenal gland for 90 min enhanced markedly the secretory responses of CA evoked by ACh (5.32 x 10-3 M), excess K+ (5.6 x 10-2 M, a membrane depolarizer), DMPP (10-4 M, a selective neuronal nicotinic agonist) and McN-A-343 (10-4 M, a selective M1-muscarinic agonist). Moreover, bradykinin (3 x 10-8 M) in to an adrenal vein for 90 min also augmented the CA release evoked by BAY-K-8644, an activator of the dihydropyridine L-type Ca2+ channels. However, in the presence of (N-Methyl-D-Phe7)-bradykinin trifluoroacetate salt (3 x 10-8 M), an antagonist of BK2-bradykinin receptor, bradykinin no longer enhanced the CA secretion evoked by Ach and high potassium whereas the pretreatment with Lys-(des-Arg9, Leu8)-bradykinin trifluoroacetate salt (3 x 10-8 M), an antagonist of BK1-bradykinin receptor did fail to affect them. Furthermore, the perfusion with bradykinin (3 x 10-6 M) into an adrenal vein of the rabbit adrenal gland for 90 min enhanced markedly the secretory responses of CA evoked by excess K+ (5.6 x 10-2 M).

Collectively, these experimental results suggest that bradykinin enhances the CA secretion from the rat adrenal medulla evoked by cholinergic stimulation (both nicotininc and muscarinic receptors) and membrane depolarization through the activation of B2-bradykinin receptors. It seems that this facilitatory effect of bradykinin may be associated to the increased Ca2+ influx through the activation of the dihydropyridine L-type Ca2+ channels, and there is no species difference in action of BK on CA release between the rat and rabbit.

[PA1-8] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]