represent a structurally and functionally diverse group of membrane proteins. These channels play an important role in determining the length of the cardiac action potential and are the targets for antiarrhythmic drugs. Many K+ channel genes have been cloned from human myocardium and functionally contribute to its electrical activity. One of these channels, Kv1.5, is one of the more cardiovascular-specific K+ channel isoforms identified to date and forms the molecular basis for an ultra-rapid delayed rectifier K+ current found in human atrium. Thus, the blocker of hKv1.5 is expected to be an ideal antiarrhythmic drug for atrial fibrillation. In the present study, we examined the effect of the extracts from many kinds of plants on the hKv1.5 current expressed in Ltk-cells using whole cell mode of patch clamp techniques. We found out that chelidonine isolated from Chelidonium majus inhibited the hKv1.5 current expressing predominantly in human atrium without affecting the HERG current expressing mainly in ventricle. Additionally, chelidonine prolonged the action potential durations of atrial, ventricular myocytes and Purkinje fibers in a dose-dependent manner. The effect of chelidonine on atrial APD was frequency-dependent whereas the effect of chelidonine on the APDs of ventricular myocytes and Purkinje fibers was not frequency-dependnet. In contrast, a well-known antiarrhythmic drug, dofetilide, prolonged the APDs slightly in frequency-independent manner. These results strongly suggest that chelidonine could be an ideal drug for atrial fibrillation.

[PA1-5] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Prevalence of resistance to macrolide, lincosamide, streptogramin and ketolide antibiotics against Gram-positive bacteria in Korea

Lim JungA°, Yoon EungJeong, Kim Sunghoon, Choi SungSook, Choi EungChil

College of Pharmacy, Seoul National University, 151-742, Seoul

The purpose of this study is to investigate the prevalence of resistance to macrolide, lincosamide, streptogramin and ketolide antibiotics in Korea. The antibiotic susceptibility test was performed to the macrolide erythromycin, clarithromycin, azithromycin, josamycin, the lincosamide clindamycin, the streptogramin synercid and the ketolide ABT-773 against 337 clinical Staphylococcus aureus(SAU), Coagulase-negative Staphylococci (CNS) and Enterococci isolates exhibited an average percentage of 64%, 56%, and 81% of resistance to erythromycin, respectively.

[PA1-6] [04/17/2003 (Thr) 14:00 - 17:00 / Hall P]

Metabolism of Rutaecarpine by Rat Liver Microsomes

Lee SangKyu°, *Lee Jaeick, Jahng Yourngdong, Chang HyeunWook, Lee Eung-Seok, *Kim DongHyun, Jeong TaeCheon

College of Pharmacy, Yeungnam University, Kyungsan, *Bioanalysis and Biotransformation Research Center, KIST

Rutaecarpine is an alkaloid originally isolated from the unripe fruit of Evodia rutaecarpa. In addition to its traditional use in treatment of gastrointestinal disorders, rutaecarpine has recently been characterized to have anti-inflammatory activity through cyclooxygenase-2 inhibition. More recently, to develop rutaecarpine as an anti-inflammatory agent, total synthesis of rutaecarpine has successfully been established in our group. In the present study, metabolic fate and cytochrome P450s involved in the metabolism of rutaecarpine was partially investigated in rat liver microsomes. When rutaecarpine was incubated with rat microsomes, 5 major peaks were detected on an LC/MS/MS. Two peaks (M1/M2) were believed to be a metabolte hydroxylated on

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

Lim DongYoon°, Kang MooJin

Department of Pharmacology, College of Medicine, Chosun University, Gwangju501-759, Korea

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]