Korean J. of Pharmacology
Vol. 24, No.1, pp.135-145, 1988

Influence of Intracerebroventricular Domperidone on Rabbit Renal Function

Young Soo Kim

Department of Internal Medicine Chung-Ang University Medical College Seoul, Korea

ABSTRACT

Dopamine when given icv induces antidiuresis along with transient natriuretic tendency, and it has been suggested that both subtypes of central dopamine receptors may influence renal function differentially. This study was undertaken to delineate the role of central D_2 receptors employing domperidone (DOM), a selective D_2 antagonist. DOM icv elicited antidiuresis and antinatriuresis in doses ranging from 15 to 135 μg/kg. GFR and RPF as well as sodium excretion decreased. Systemic blood pressure increased slightly. Intravenous DOM did not elicit significant changes in sodium excretion. Denervation of the kidney abolished the hemodynamic change induced by icv DOM, but sodium excretion decreased on both innervated and denervated kidneys. No diuretic tendency was uncovered by the denervation. Dopamine, 150μg/kg icv, produced antidiuresis along with decreases in hemodynamics.

These effects were not affected by DOM-pretreatment, and no natriuretic tendency was unveiled. Bromocriptine, a D_2 receptor agonist, 200μg/kg icv, elicited marked diuresis and natriuresis, which were completely abolished by DOM-pretreatment. Apomorphine, another prototype of D_2 agonist, 150μg/kg icv, produced diuresis and natrituresis with increases in renal hemdoynamics, followed by decreases in all parameters. DOM-pretreatment did not affect the renal hemodynamic effects, wherease the increases in urine flow and sodium excretion were markedly reduced by DOM. Present study suggests that central D_2 receptors mediate natriuretic and diuretic influence to the kidney, possibly through mediation of natriuretic humoral factor, and provide further evidence supporting the hypothesis that central D_1 receptors mediate antidiuretic influence via nerve pathway, whereas natriuresis are brought about through mediation of central D_2 receptors.

Key Words: Domperidone, Renal function, Central D_2 receptor.

Abbreviations: RPF, renal plasma flow; GFR, glomerular filtration rate; icv, intracerebroventricular; DA, dopamine; DOM, domperidone; BRC, bromocriptine; APO, apomorphine.

INTRODUCTION

The central nervous system (CNS) regulates the excretory function of the kidney either through secretion of humoral agents (Verney, 1947; DeWardener, 1973) or via neural pathways, in which the sympathoadrenal system plays the most important roles(Gottschalk, 1979; Kim *et al*, 1980; Kook *et al*. 1984; Beers *et al*, 1986). Recently it has been shown that dopamine (DA), the most abundant catecholamine in the brain, and its receptors in the CNS also have a role in the regulation of renal function. DA, when administered directly into a lateral ventricle (icv) of rabbit brain, elicits antidiuresis and decreases in renal hemodynamics in a dose-dependent manner (Choi, 1974; Kim *et al*. 1982). Large doses of haloperidol, a DA antagonist, induce diuresis and natriuresis when given icv in rabbits (Kim *et al*, 1982), suggesting a physiological role of central dopaminergic system.

However, it has also been noted that the influence of central DA on the renal function is not so simple as it has first been assumed, as certain agonists of DA receptors produced natriuresis and diuresis when given icv. Bromocriptine icv elicited marked natriuresis and diuresis in spite of decreases in glomerular filtraion and renal blood flow (Kook *et al,* 1985), and apomophine icv also produced diuresis and natriuresis followed by antidiuresis (Cho, 1983). Also, DA itself can elicit natriuresis under certain circumstances, such as the pretreatment with yohimbine (Kook *et al,* 1986). Thus, all the evidence led to the hypothesis that the central DA system influences the renal function in dual ways, i.e., antidiuresis resulting from decreased renal hemodynamics and diuresis mediated by some natriuretic humoral factor, and that the former influence ordinarily predominates in the overall effects whereas the latter may be apparent only when the hemodynamic effects has been removed (Kim, 1984; Kook *et al,* 1984). And it has been further suggested that the DA receptors involved in the natriuresis may of D_2 type, whereas D_1 receptors might mediate the hemodynamic effects (Kim, 1984; Kook *et al,* 1986).

Domperidone, a benzimidazoline, has been reported to be a specific ligand for D_2 binding sites in the CNS (Lazareno and Nohorski, 1982), while it is practically inactive toward DA senstive adenylate cyclase(Laduron and Leysen, 1979). And it has also been found to be a highly selective antagonist of DA_2 receptors in the periphery (Kohli *et al,* 1983). Thus, it is thought to be a very useful tool in characterizing the subtypes of DA receptors (Stoof and Kebabina, 1984). It is therefore undertaken in this study to observe the effects of icv domperidone on the renal function in the rabbit and to delineate the receptors involved in the central dopaminergic regulation of renal function.

METHODS

Adult rabbits of either sex, weighing 1.8-2.3 kg, were anesthetized with 1 g/kg urethane s.c. Airway was kept free by inserting a T-tube into the trachea. Infusion of 0.3% NaCl and 3% glucose solution containing 45 mg% of para-amino-hippuric acid (PAH) and 250 mg% of creatinine (cr) was given into an ear vein at a rate of 0.5 ml/min. Through a small midline incision close to the symphysis, both ureters were cannulated with PE tubings for th collection of urine samples, and for obtaining blood samples a femoral artery was cannulated with PE tubing, which was then kept patent with heparin-saline(400 μ/ml). For intracerebroventricular (icv) administration of the agents a lateral ventricle of the cerebrum was cannulated. A hole was drilled on the skull at a point 1.5 cm rostral to the occiput tubercle and 0.5 cm lateral to the midline, and a cannula made PE tubing of 1.5 cm O.D. was introduced obliquely until clear cerebrospinal fluid appeared in the cannula, and then it was kept in place by cementing to the bone. The volume administered did not exceed 0.15 ml. At the end of each experiment the location of the cannula tip was checkd by dissection.

When urine flow rate became stable several hours after the initiation of the infusion, collection of clearance samples was started. After two 10-minute clearance periods the agent was administered, and then two 10-min and three 20-min clearance samples were collected. The blood samples were obtained at midpoint of each clearance period from a femoral artery and were immediately centrifuged to separate the plasma.

In denervation experiments the kidney was approached through a paravertebral incision and the renal pedicle was isolated from surrounding tissue, and the renal nerve was removed as thoroughly as possible under a magnifier, and the renal pedicle was wrapped with a cotton swab soaked with 10% phenol.

Quantitative analyses of creatinine were done by the method of Phillips (1944) and PAH by that of Smith et al (1945). Na and K concentrations were determined by flamephotometry, and the osmolality with osmometer. Statistical significance was assessed either with Student's t-test or with ANOVA with repeated measures on time (Winer, 1971). If significant differences were detected with ANOVA, further analyses as required were performed to determine which of the groups differed from the appropriate controls. For multiple group comparison Bonferroni's modified t-test was applied (Wallenstein *et al.,* 1980).

Dopamine and apomorphine hydrochloride were obtained from Sigma Co., and dissolved in 0.9 % NaCl solution immediately before

administration. Domperidone was obtained from Janssen Co. and dissolved in 30% ethanol-saline. Bromocriptine methane sulfonate was obtained from Sigma Co. and a stock solution of 8 mg/ml in 0.4 N acetic acid was diluted with distilled water before use.

RESULTS

Renal effects of intracerebroventricular domperidone

Domperidone (DOM) when administered into a lateral ventricle (icv) of rabbit brain elicited antidiuretic and antinatriuretic responses in doses ranging from 15 to 135μg/kg as shown in Table 1. Smaller doses induced only slight tendency towards antidiuresis. Fifteen ug(=33 nmoles)/kg icv tended to slightly depress renal plasma flow (RPF; $=C_{PAH}$) and sodium excretion as well as urine flow rate for the first 10-min period following the administration. And after 40 min, glomerular filtration rate (GFR;$=C_{cr}$) and renal perfusion significantly decreased by ca 10% and 20%, resp. Sodium excretion and urine flow rate also significantly decreased by 2/3 and 1/3, resp. The reabsorption of free water (TcH_2O) did not change significantly, and mean arterial pressure tended to increase slightly and transiently for the first 10-min period.

Increasing the doses three-fold to 45μg(= 100 nmoles)/kg icv produced greater antidiuretic response, most of the parameters reaching the nadir during the 20'-40' period after the administration. The renal hemodynamics significantly decreased by 1/4 to 1/3 of the control level, with the filtration fraction (FF) tending slightly to increase. Howevere, the excretory

Table 1. Effects of intracerebroventricular domperidone on rabbit renal function

	Control	0'–10'	10'–20'	20–'–40'	40'–60'	60'–80'
			15 ug/kg (6)			
Vol	0.325 ± 0.031	0.289 ± 0.040	0.310 ± 0.053	0.283 ± 0.063	0.215 ± 0.051*	0.187 ± 0.050*
C_{PAH}	16.4 ± 2.4	14.2 ± 1.8	15.9 ± 2.7	14.1 ± 2.6	13.5 ± 2.2*	12.1 ± 1.6
C_{cr}	6.16 ± 1.04	6.00 ± 1.05	6.36 ± 1.28	5.73 ± 1.17	5.61 ± 1.08*	5.27 ± 0.86*
$U_{Na}V$	9.33 ± 3.07	7.13 ± 2.49	8.03 ± 2.94	5.91 ± 2.13	3.34 ± 1.28*	1.95 ± 0.70
			45 ug/kg (6)			
Vol	0.269 ± 0.047	0.201 ± 0.036	0.159 ± 0.045	0.134 ± 0.036*	0.215 ± 0.030	0.209 ± 0.031
C_{PAH}	14.7 ± 1.5	11.8 ± 2.8	11.1 ± 3.2	10.3 ± 2.5*	13.7 ± 1.1	14.1 ± 1.4
C_{cr}	6.44 ± 0.69	5.63 ± 1.14	5.20 ± 1.46	4.92 ± 1.08*	6.11 ± 0.66	6.25 ± 0.60
$U_{Na}V$	4.18 ± 1.92	1.75 ± 0.76	0.59 ± 0.10	0.41 ± 0.08*	2.63 ± 1.55	3.13 ± 1.93
U_KV	4.85 ± 0.66	3.71 ± 0.65	3.43 ± 0.93	2.94 ± 0.81*	4.54 ± 0.33	4.66 ± 0.35
			135 ug/kg (6)			
Vol	0.173 ± 0.022	0.126 ± 0.019*	0.106 ± 0.017*	0.114 ± 0.025	0.112 ± 0.029	0.087 ± 0.016*
C_{PAH}	17.9 ± 1.9	14.2 ± 1.2	15.4 ± 1.6	16.3 ± 1.0	15.5 ± 1.5	14.1 ± 1.6*
C_{cr}	7.64 ± 1.16	6.29 ± 0.70	6.58 ± 0.36	6.92 ± 0.61	6.53 ± 0.60	6.33 ± 0.59
$U_{Na}V$	6.08 ± 1.79	4.70 ± 2.09	2.95 ± 0.49	4.66 ± 2.11	4.43 ± 2.17	1.95 ± 0.76
C_{osm}	0.290 ± 0.051	0.234 ± 0.050*	0.222 ± 0.046	0.239 ± 0.077	0.242 ± 0.042	0.219 ± 0.040
MAP	83 ± 5	106 ± 10*	104 ± 10	101 ± 8	96 ± 6	93 ± 6
RVR	4.9 ± 0.6	7.5 ± 0.5*	7.5 ± 1.5	6.3 ± 0.7	6.6 ± 1.0	7.2 ± 1.3

Mean ± SEM from number of experiments in parentheses. Vol represents urine flow rate in ml/min ; C_{PAH}, C_{cr} and C_{osm} are clearances of *p-aminohippuric acid, creatinine and osmolar substances, resp., in ml/min* ; $U_{Na}V$ and U_KV are excretory rates of sodium and potassium, resp., in uEq/min ; T^cH_2O is rate of free-water reabsorption in ml/min; MAP denotes mean arterial pressure in mmHg ; and RVR stands for renal vascular resistance, as calculated from MAP/C_{PAH}. Significance of paired difference from control periods were tested with Student's t-test. Significant differences were marked with asterisks ($P < 0.05$).

function declined more markedly. Sodium excretion decreased to 1/10 and fractional sodium excretion (FE_{Na}) to 15% of the control levels. Potassium excretion as well as osmolar clearance decreased by 1/3. Urine flow rate decreased by half. Systemic arterial pressure also tended to increase slightly and transiently. Further increase of doses to 135μg (=300 nmoles)/kg icv tendend to elicit the antidiuretic response sooner, but the magnitude of responses did not further increase. Rather, the hemodynamic response became smaller. However, the systemic blood pressure increased by 23 mmHg and renal vascular resistance by 53%. Further increasing the doses was not feasible because of low solubility of the agent. The vehicle of DOM did not produce any significant changes in renal function as shown in Fig. 1, which also compares the changes of some parameters of renal function after the icv administration of 45μg/kg DOM with those of the vehicle, 0.9% NaCl solution.

Overall, DOM given icv elicited antidiuretic and antinatriuretic responses, with 45μg/kg showing the peak effects, and no diuretic and natriuretic tendency was discernible with icv DOM.

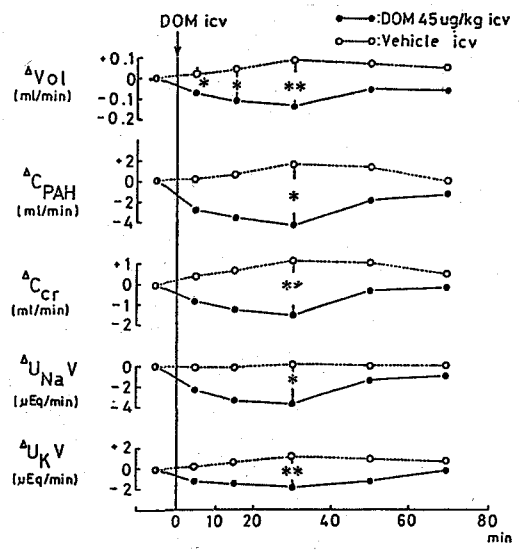

Fig. 1. Renal effects of 45 ug/kg domperidone icv. Mean changes from the control values with one S. E. (n=6, each group) are depicted. Significant differences from the corresponding values of the vehicle group as tested with ANOVA and Newman-Keuls test are marked with asterisks.

Renal effects of intravenous domperidone

To test the possibility that the icv administered DOM might have reached into the general circulation from the site of administration and exerted its effect directly on the kidney, DOM was administered intravenously. When 45μg/kg was given iv, no significant changes in renal function as well as in blood pressure were noted, except transient tendency of decreases in GFR and urine flow rate during the first 10-minute period. Table 2 shows the effects of 135μg/kg DOM iv. Urine flow rate and GFR decreased by about 20 percent in the first two 10-minute periods, but no significant changes were noted in sodium excretion and blood pressure. After 20 minutes these changes returned to pre-administration levels. Thus it is unlikely that icv DOM might have acted directly on the kidney.

Influence of denervation on the effects of domperidone

To see whether the icv DOM effects are mediated by neural pathway and to find out whether there exists a hidden natriuretic ten-

Table 2. Effects of domperidone, 135 ug/kg iv, on rabbit renal function

	Control	0'–10'	10'–20'	20'–40'	40'–60'	60'–80'
Vol	0.189 ± 0.017	0.155 ± 0.015*	0.164 ± 0.018	0.272 ± 0.045	0.244 ± 0.029	0.259 ± 0.036
C_{PAH}	11.47 ± 1.72	9.66 ± 2.41	10.12 ± 2.39	12.11 ± 1.72	10.34 ± 1.62	10.21 ± 1.53
C_{cr}	6.23 ± 1.09	5.04 ± 1.30	4.83 ± 1.19*	5.52 ± 1.07	5.16 ± 0.99	5.16 ± 0.80*
$U_{Na}V$	4.44 ± 1.49	3.59 ± 1.42	3.77 ± 1.31	5.53 ± 1.48	4.66 ± 1.38	4.60 ± 1.18
MAP	95.2 ± 5.0	94.2 ± 4.9	95.2 ± 4.2	96.5 ± 4.6	96.5 ± 4.4	95.0 ± 4.8

Mean ± SEM from 6 experiments. Legends as in Table 1.

Table 3. Influence of denervation on the renal effects of icv domperidone

		Control	0'–10'	10'–20'	20'–40'	40'–60'	60'–80'
Vol	D..	0.317 ± 0.040	0.280 ± 0.044	0.291 ± 0.043	0.321 ± 0.035	0.280 ± 0.039	0.213 ± 0.030
	I.	0.072 ± 0.012	0.036 ± 0.010**	0.009 ± 0.003**	0.009 ± 0.004**	0.043 ± 0.006*	0.067 ± 0.011
C_{PAH}	D.	9.39 ± 0.63	9.22 ± 0.95	8.76 ± 0.75	7.92 ± 0.77*	7.27 ± 0.66**	6.28 ± 0.61**
	I.	5.20 ± 0.69	2.64 ± 0.77**	0.64 ± 0.22***	0.66 ± 0.31**	3.98 ± 0.61	5.43 ± 0.64
C_{cr}	D.	4.17 ± 0.43	3.41 ± 0.22	3.44 ± 0.34*	2.92 ± 0.42*	2.71 ± 0.36**	3.01 ± 0.21**
	I.	2.72 ± 0.48	1.34 ± 0.36*	0.40 ± 0.14**	0.39 ± 0.16**	1.50 ± 0.24*	1.88 ± 0.14
$U_{Na}V$	D.	20.20 ± 4.05	17.90 ± 5.12	19.82 ± 5.04	17.14 ± 3.85	12.44 ± 3.78**	10.25 ± 3.22**
	I.	0.52 ± 0.11	0.18 ± 0.03*	0.07 ± 0.02**	0.06 ± 0.02**	0.30 ± 0.12*	0.76 ± 0.25
FE_{Na}	D.	3.28 ± 0.43	3.68 ± 1.09	3.83 ± 0.77	4.02 ± 0.55	3.26 ± 0.74	2.24 ± 0.54*
	I.	0.13 ± 0.03	0.13 ± 0.05	0.14 ± 0.06	0.17 ± 0.04	0.15 ± 0.05	0.27 ± 0.08

Mean ± SEM from 6 experiments. Domperidone 45 ug/kg was given icv at 0 time. "D" stands for the denervated kidney, "I" the innervated control kidney. FE_{Na} is fractional excretion of sodium, Other legends are as in Table 1.

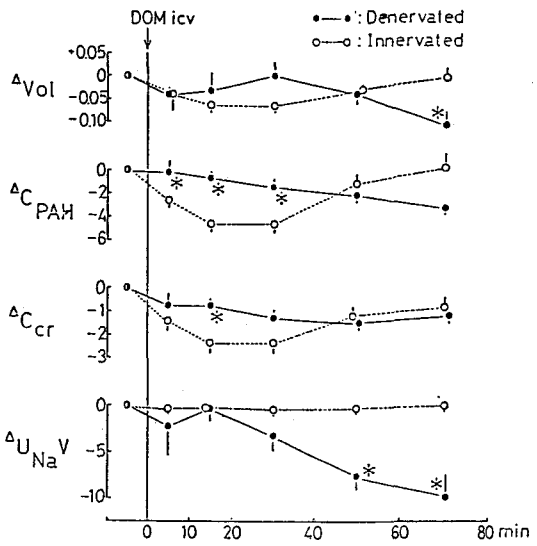

Fig. 2. Influence of denervation on the renal effects of icv DOM. Domperidone 45 ug/kg icv was given at 0 time. Mean changes from the control values with one S. E. (n=6) are shown. Asterisks indicate significant differences between both kidneys as tested by ANOVA and Newman-Keuls test.

dency masked by the neural influence, the renal responses to icv DOM were observed in the rabbits in which one kidney was denervated and the other served as control. Table 3 summarizes the data from 6 such experiments with 45μg/kg DOM icv.

In the control periods, the denervated kidney is clearly undergoing "denervation diuresis", while the innervated control kidney is subjected to severe antidiuresis which presumably results from reflexively increased sympathetic influence. The RPF and GFR in the denervated side exceeded the control side by 80 % and 50%, resp., and sodium excretion outweighed about 40 times, while urine flow rate surpassed by more than 4 times. Upon adminstration of DOM the innervated side responded with prominent antidiuresis even if it had been already undergoing severe antidiuresis. Decreases in all the parameters of renal function seemed to be exaggerated than in the control experiments. The denervated kidney also responded with decreases in renal hemodynamics. However, the magnitude of decreases is significantly less in the denervated kidney, indicating that the hemodynamic effects of icv DOM is largely dependent on the renal nerve activity. The decreases in sodium excretion in the denervated side were of greater magnitude than in the innervated kidney, but it may be due to the larger control values. But when calculated as percent decreases, the response in the denervated side was smaller. The FE did not signifcantly differ from the control period in both kidneys. Thus, no diuretic and natriuretic responses were observed in the denervated kidney.

Table 4. Influence of domperidone pretreatment on the dopamine action

	Control	0'–10'	10'–20'	20'–30'	30'–40'	40'–60'	60'–80'
Vol.	0.312 ±0.049	0.242 ±0.044	0.179 ±0.052	0.195 ±0.057*	0.171 ±0.34*	0.201 ±0.043	0.224 ±0.042
C_{PAH}	10.76 ± 1.57	8.50 ± 1.59**	7.23 ± 2.08*	8.32 ± 2.96	7.97 ± 2.27	8.40 ± 2.02	8.53 ± 1.98
C_{cr}	4.89 ± 0.85	4.00 ± 0.97	3.51 ± 1.17	3.53 ± 1.28	3.45 ± 1.11*	3.17 ± 0.91***	3.24 ± 0.79**
$U_{Na}V$	9.47 ± 3.28	6.72 ± 2.39*	4.93 ± 2.16*	5.12 ± 1.94	3.10 ± 1.10	3.83 ± 1.29	3.94 ± 1.35
$U_{K}V$	5.16 ± 0.92	3.93 ± 0.81**	3.20 ± 0.93**	3.46 ± 1.30	3.10 ± 1.03*	2.80 ± 0.65**	2.86 ± 0.66**
$T^{c}H_2O$	0.151 ±0.021	0.123 ±0.023	0.104 ±0.031	0.104 ±0.040	0.094 ±0.038	0.059 ±0.033**	0.053 ±0.019**

Mean ± S.E. from 6 experiments. Domperidone 45 ug/kg icv was given at 0', followed by dopamine, 150 ug/kg icv at 20'. Paired difference from control values were test with Student's t-test. Significant differences were marked with asterisks. (*P < 0.05 ; ** P < 0.01 ; *** P < 0.001).

Influence of domperidone on the dopamine effects

As control experiments the effects of DA, 150 μg(=1 umole)/kg icv, which had been previously shown to elicit maximum effects, were observed in 6 experiments. During the first 10-min period after the administration sodium excretion and urine flow rate showed a slight tendency towards increases(3-4%) in spite of decreasing tendency of renal hemodynamics (2-3%). In the next 10-min period, however, the renal hemodynamics significantly decreased by about 1/4, and electrolyte excretion and osmolar clearance tended to decline correspondingly, while urine flow decreased significantly by about 30%. During the next 20-min period all the parameters of renal function except for the FF and TcH_2O highly significantly decreased, sodium excretion reaching to less than 1/3 and all other parameters to about 1/2 of the control levels. These changes did not recover until the end of the observation periods.

The data from 6 experiments in which DA, 150μg/kg icv, was given 20 min after the DOM administration are summarized in Table 4. Fig. 3 depicts the changes of several parameters of renal function from the control values, comparing three groups. As clearly seen here, the antidiuresis and antinatriuresis elicited by DOM persisted after DA adminsitration and all

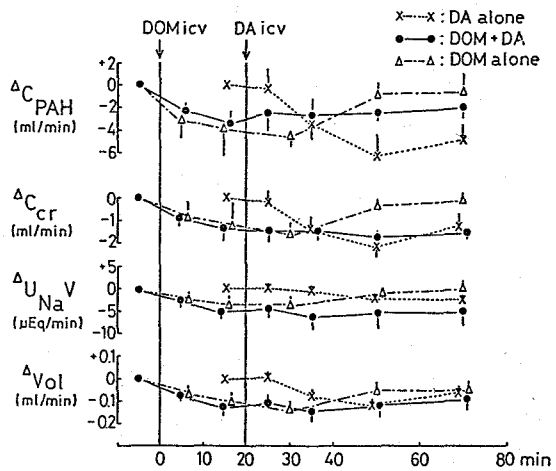

Fig. 3. Influence of DOM-pretreatment on the renal effects of icv dopamine. At DOM, domperidone 45 ug/kg icv was given, and at DA, dopamine 150 ug/kg icv was administered. Mean changes from 6 experiments with one S.E. are shown. No significant difference between the DA alone group and the DOM + DA group was noted.

the parameters remained depressed until the end of the experiments. No natriuresis and diuresis such as observed with DA after yohimbine-pretreatment (Kook *et al*, 1986) was noted. Thus, it seems obvious that DA can exert its antidiuretic effects unaffected by the pretreatment with DOM.

Influence of domperidone on the bromocriptine effects

Bromocriptine (BRC), 200μg/kg icv. produced marked diuresis and natriuresis lasting for an hour, confirming the observation by Kook et al(1985). Changes from the control values are shown in Fig. 4. The fractional excretion of Na increased eight-fold to 7.97% from the control level of 0.99%. This natriuretic effect took place in spite of decreases in renal hemodynamics, which has been shown to be induced by the vehicle (Kook *et al.*, 1985).

The influence of the DOM pretreatment on the BRC effects was observed in 6 rabbits and the changes from the control values are depicted in Fig. 4. As clearly seen here, upon BRC administration, the decreased renal perfusion and glomerular filtration returned to control levels. However, the urine flow rate as well as sodium excretion remained depressed and no natriuresis or diuresis ensued. It is thus evident that the natriuresis elicited by icv BRC is completely abolished by domperidone pretreatment.

Influence of domperidone on the apomorphine effects

As another prototype of DA agonist, apomorphine (APO) was employed. APO, 150μg/kg icv, produced increases in urine flow as well as in electrolyte excretion for twenty minutes, along with increases in renal hemodynamics, but all the parameters of renal function except for free water reabsorption decreased after 40 min. The changes from control values are depicted in Figure 5. The influence of the DOM pretreatment on the APO effects were observed in 6 rabbits. For the first 10-min period following APO, urine flow rate and elctrolyte excretion tended to increase slightly and then declined again, while the hemodynamics seemed to recover to a greater degree. And the later-stage antidiuresis seen in the APO-alone group was not evident in the DOM-pretreated animals. Fig. 5 shows changes of some parameters of renal function. The significance of difference between the APO-

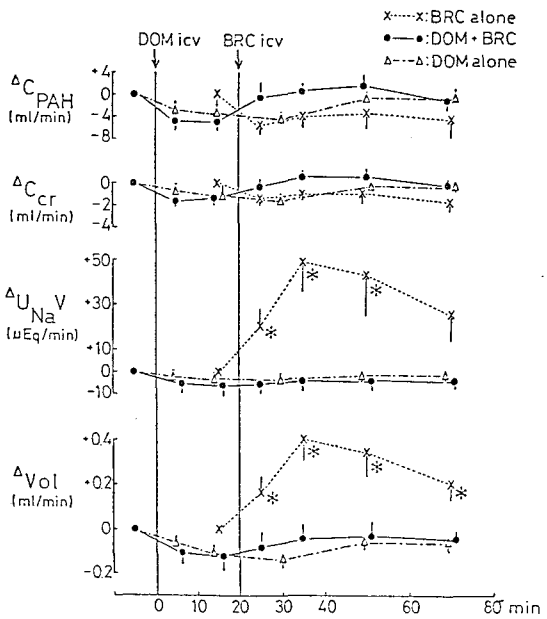

Fig. 4. Influence of DOM-pretreatment on the renal effects of icv bromocriptine. AT BRC, bromocriptine 200 ug/kg icv was given. Asterisks indicate significant differences between the BRC alone group and the DOM-BRC group (t-test). Other legends as in preceding figures.

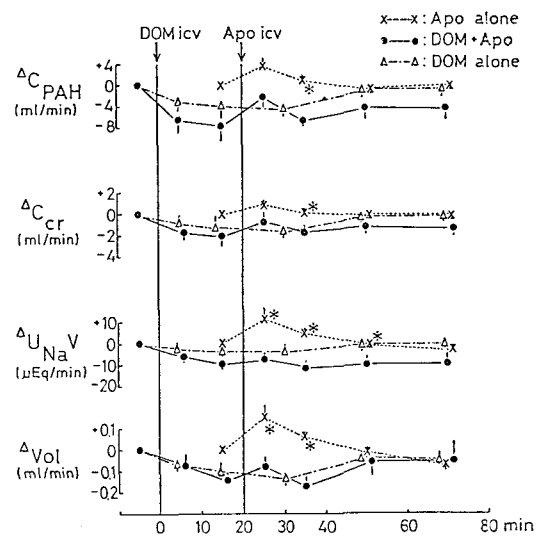

Fig. 5. Influence of DOM-pretreatment on the renal effects of icv apomorphine. At APO, apomorphine 150 ug/kg icv was given. Significant difference between the APO alone group and the DOM + APO group was marked with asterisks. Other legends as in preceding figures.

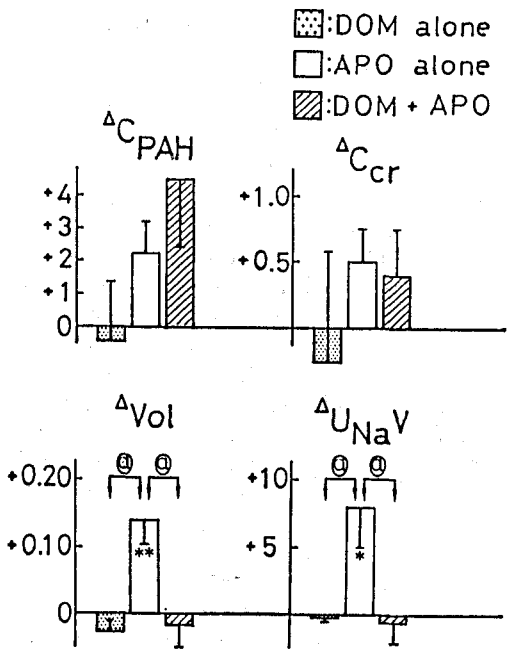

Fig. 6. *Comparison of changes of renal function* during 20 min following icv apomorphine. Data from preceding tables and figures. As the control group served the DOM (45 ug/kg icv) along group and the difference between values of the 20'–40' and 10'–20' periods after DOM administration. Significant changes from the control values are marked with asterisks, and significant differences between groups are marked with @.

alone group and the DOM-APO group are marked with @. Fig. 6 compares the three groups, in which the values for "DOM+APO" group were calculated as the differences between the after-APO value (mean of the 20' -30' value and the 30'-40') and the before-APO value (the 10'-20' value), and the values for the "DOM alone" group were the differences between the 20'-40' value and the 10'-20'. It was noted that DOM-pretreatment did not affect the hemodynamic changes by APO, while it reduced the excretory rates of electrolytes and urine flow.

DISCUSSION

Since the hypothesis that dopamine receptors exist in two subtypes, D_1 and D_2 dopamine receptors, in the CNS as well as in certain endocrine tissues was presented (Kebabian and Calne, 1979), two different kinds of dopamine receptors have been postulated also in the peripheral vascular tissues and designated as DA_1 and DA_2 (Goldberg and Kohli, 1979). In addition to various classifications by may groups, up to 4 different binding sites (D_1, D_2, D_3, and D_4) have also been postulated in the brain (Seeman, 1981), causing some confusion in the terminology. However, recent availability of selective agonists and antagonists capable of discriminating dopamine receptor subtypes led to the general acceptance of two categories of dopamine receptors and to the recognition that DA_1 and DA_2 receptors are virtually identical to D_1 and D_2 receptors, respectively (Hilditch *et al,* 1984; Stoof and Kebabian, 1984; Kebabian et al, 1986). SKF 38393 was found to be the most selective agonist of D_1 receptors (Stoff and Kebabian, 1984), whereas SCH 23390 is the most potent and specific antagonist of D_1 receptors (Hyttel, 1983; Kebabian *et al,* 1986). As for the D_2 subypes, quinpirol, pergolide and bromocriptine are the selective agonists, while (-)sulpiride and domperidone are the most selective antagonists found so far (Stoof and Kebabian, 1984).

Domperidone, a benzimidazoline derivative, has been found to possess potent anti-emetic activity while failing to cause certain behavioral as well as biochemical changes (Leysen *et al,* 1978; Laduron and Leysen, 1979), and reported to be a specific ligand for D_2 receptors in CNS (Lazareno and Nahorski, 1982). It also selectively blocks the peripheral DA_2 receptors (Kohli et al, 1983). Thus, it has become a very useful tool in characterizing the subtypes of DA receptors.

Our observations indicate that domperidone when injected directly into the cerebral ventricle of the rabbit elicits antidiuresis and antinatriuresis, along with decreases in renal hemodynamics. These responses seem most likely to be center-mediated, as the same amount of domperidone given intravenously produced no significant changes but only a slight tendency toward decreases in renal function. The slight and transient elevation in systemic blood pressure did not contribute to the icv domperidone effects, and it may reflect increases in peripheral vascular resistance. The

decrease in renal hemodynamics by icv domperidone was abolished by denervation, indicating that sympathetic tone to the kidney had been increase by icv DOM. However the excretory rates of sodium may not be entirely accounted for solely by the renal hemodynamic changes, as the denervated kidney also exhibited decrease in sodium excretion. These results can be interpreted as suggesting that D_2 receptors in the center had been exerting mitigating influence on the sympathetic tone to the kidney and D_2 receptors may have led to increased sympathetic tone, which is also evidenced by the increases in blood pressure. Presysnaptic dopamine receptors on both dopamine-and acetylcholine-containing nerve terminals were found to be of D_2 type (Starke, 1980; Langer, 1981), and also D_2 receptors occur postsynaptically on dopamine cell bodies (autoreceptors) and on the adrenergic neurons, and their stimulation leads to decreased transmitter release (Galzin, *et al.,* 1982; Jackish *et al,* 1985). D_2 receptor blockade with either domperidone or (-) sulpiride significantly increased norepinephrine release in *in vitro* superfused prepration of hippocampal tissue (Jackisch *et al.,* 1985). And stimulation of central D_1 receptors with SKF 38393 led to increased renal nervous tone and antidiuresis and antinatriuresis (Park, 1988). Thus, our data may be taken as in accordance with these evidence, and may be interpreted as follows: by blocking D_2 receptors (or dopamine autoreceptors) DOM brings about increased nervous influence to the kidney. Our results also suggest that D_2 receptors had been exerting at the same time natriuretic influence via some humoral pathway, and blocking the pathway may have led to decreased sodium excretion.

Dopamine when given icv produces antidiuresis and antinatriuresis following transient diuretic tendency (Choi, 1974; Kook *et al,* 1986), as confirmed in this study. It has also been shown that the natriuretic response to icv dopamine can be uncovered after D_1 blockade (Park, 1988), and it has been postulated that central D_1 receptors mediate antidiuresis via increased nerve tone, wherease D_2 receptors mediate natriuresis by way of certain humoral factor, but the former influence predominates when both pathways are stimulated simultaneously as in the case with icv dopamine (Kook *et al.,* 1986; Park, 1988). Our present observations show that the dopamin effects are not affected by pretreamtent with DOM, suggesting that the D_2 stimulation by dopamine may be antagonized, but the D_1 agonistic action of dopamine cannot manifest itself because DOM has already unfolded its antidiuretic action fully.

Bromocriptine has been shown to be a D_2 agonist (Kebabian and Calne, 1979; Sibley and Creese, 1983), and at the same time it is antagonsitic to D_1 receptors (Kebabian and Calne, 1979), and when given icv it produces marked natriuresis and diuresis, in spite of decreased renal perfusion and glomerular filtration, indicating humoral mechanism involved in it. The decreased renal hemodynamics was shown to be nonspecific and caused by the vehicle (Kook *et al.,* 1985). Present results confirm the renal effects of icv BRC and further show that DOM pretreatment completely abolishes the natriuresis produced by icv BRC, supporting the premises that D_2 receptors may have been involved in the natriuretic response. Apomorphine also known to be an agonist to D_2 receptors in nanomolar range, whereas D_1 receptors are affected in dual ways with micromolar concentrations of APO (Kebaian and Calne, 1979). The diuretic and natriuretic response followed by antidiuresis to icv APO (Cho, 1983) was confirmed in the present study, and it is further noted that the natriuretic response was antagonized by DOM-pretreatment, again supporting that D_2 receptors are involved in the center-mediated natriuresis.

Present observations present evidence supporting the hypothesis that both subtypes of DA receptors are involved in the regulation of renal function and that D_2 receptors elicit natriuresis and diuresis by way of humoral mechanism whereas D_1 receptors produce antidiuresis and antinatriuresis by increasing nervous influence to the kidney. To be verified is the release of a transferable natriuretic factor by the stimulation of D_2 receptors and the inhibition of its release by D_2 blockade, in order to further substantiate the hypothesis. However, Lim (1984) has reported that DA after yohimbine pretreatment produced natriuresis which is transferable to rats, rendering evidence of humoral mediation. Further investigations on the nature and origin of the factor should clarify whether it is related to the atrial natriuretic factors (DeBold *et al,* 1981; Currie *et*

al, 1984) or certain natriuretic hormone suggested to be dervied from central nervous system (De Wardener, 19739. Overall, present results indicate that central dopaminergic system plays an important role in the regulation of renal function.

ACKNOWLEDGEMENT

The author feels greatly indebted to Prof. Young Johng Kook, Department of Pharmacology, Chonnam University Medical School, Kwangju, Korea, for his invaluable advice and assistance, and wishes to express his cordial gratitude.

REFERENCES

Beers ET, Carroll RG, Young DB and Guyton AC: *Effects of graded changes in reflex renal nerve activity on renal function. Am J Physiol 250: F559-565, 1986*

Cho JB: *Influence of apomorphine on the renal function of the rabbit. Inaug. Dissertation, Chonnam University, 1983*

Choi KD: *Influence of intracerebroventricular administration of dopamine on the renal function of the rabbit. Chonnam Med J 11:655-662, 1974*

Currie MG, Geller DM, Cole BR, Soegel NR, Fok KF, Adams SB, Eubanks SR, Gallupi GR and Neeldeman P: *Purification and sequence analysis of bioactive atrial peptides (Atriopetins). Sci 223:67-69, 1984*

DeBold AJ, Borenstein HB, Veress AT and Sonnenberg H: *A potent and rapid natriuretic response to intravenous injection of atrial myocardial extracts in rats. Life Sci 28:89-94, 1981*

DeWardener HE: *The control of sodium excretion. In: Handbook of Physiology, Section 8, Renal physiology, American Physiological Soc, 1973, p677*

Galzin AM, Dubocovich ML and Langer SZ: *Presynaptic inhibition by dopamine receptor agonists of noradrenergic neurotransmission in the rabbit hypothalamus. J Pharmacol Exp Ther 221:461-471, 1982*

Goldberg LI and Kohi JD: *Peripheral pre-and postsynaptic dopamine receptors. Are they different from dopamine receptors in the central nervous system?, Commun Psychopharmacol 3:447-456, 1979*

Gottschalk CW: *Renal nerves and sodium excretion. Ann Rev Physiol 41:229-240, 1979*

Hilditch A, Drew GM and Naylor RJ: *SCH 23390 is a very potent and selective antagonist at vascular dopamine receptors. Eur J Pharmacol 97:333-334, 1984*

Kebabian JW, Agui T, van Oene JC, Shigematsu K and Saavedra JM: *The D_1 dopamine receptor: new perspectives. Trends Pharmacol Sci 7:96-99, 1986*

Kebabian JW and Calne DB: *Multiple receptors for dopamine. Nature 277:93-96, 1979*

Kim JK: *Interaction of several dopamine receptor agonits and antagonists on the central regulation of rabbit renal function. Inaug. Dissertation, Chonnam University, 1984*

Kim JK, Choi BK and Kook YJ: *Influence of intracerebroventriuclar haloperiol on the rabbit renal function. Kor J Pharmacol 18:103-117, 1982*

Kim JK, Linas S and Schrier RW: *Catecholamine and sodium transport in the kidney. Pharmacol Rev 31:160-178, 1980*

Kohli JD, Glock D and Goldberg LI: *Selective DA_2 versus DA antagonist activity of domperidone in the periphery. Eur J Pharmacol 89:137-141, 1983*

Kook YJ, Lee YH and Choi BK: *Influence of intracerebroventricular clonidine on the rabbit renal function. Kor J Pharmacol 21:59-71, 1984*

Kook YJ, Kim KK, Kim JP and Kim KH: *Renal effects of intracerebroventricular bromocriptine in the rabbit. Kor J Pharmacol 21:49-61, 1985*

Kook YJ, Kim KK, Cho KS and Min BK: *Influence of yohimbine on the central dopaminergic regulation of renal function. Kor J Pharmacol 23:71-87, 1986*

Laduron PM and Leysen JE: *Domperidone, a specific in vitro dopamine antagonist, devoid of in vivo central dopaminergic activity. Biochem Pharmacol 28:2161-2165, 1979*

Langer SZ: *Presynaptic regulation of the release of catecholamine. Pharmacol Rev 32:337-362, 1981*

Lazareno S and Nahorski SR: *Selective labelling of dopamine (D_2) receptors in rat striatum by [^{3}H] domperiodne but not by [^{3}H] spiperone. Eur J Pharmacol 81:273-285, 1982*

Lim JK: *Studies on the mechanism of natriuresis induced by intracerebroventricular dopamine in the rabbit. Inaug Dissertation, Chonnam Univ., 1984*

Park JO: *Influence of SCH 23390 on the central*

dopaminergic control of rabbit renal function. Inaug. Dissertation, Chonnam Univ., 1988

Phillips RA: *In: Quantitative Clinical Chemistry. Vol 2, Methods, Peters & Van Slyke (Eds), Williams & Wilkins, 1944*

Smith HW, Finkelstein N, Alimonosa L, Crawford B and Graber B: *The renal clearances of substituted hippuric acid derivative and other aromatic acids in dog and man. J Clin Invest 24:388-404, 1945*

Stoof JC and Kebabian JW: Two dopamine receptors: Biochemistry, Physiology and Pharmacology. Life Sci 35:2281-2296, 1984

Seeman P: *Brain dopamin receptors. Pharmacol Rev 32:229-313, 1981*

Sibley DR and Creese I: *Interactions of ergot alkaloids with anterior pitutitary D-2 receptors. Mol Pharamacol 23:585-593, 1983*

Starke K: *Presynaptic receptors. Ann Rev Pharmacol Toxicol 21:7-30, 1981*

Verney EB: *The antidiuretic hormone and the factors which determine its release. Proc Roy Soc London, Ser B 135:25-106, 1947.*

Wallenstein S, Zucker CL and Fleiss JL: *Some statistical methods used in circulation research. Circ Res 47:1-9, 1980*

Winer BJ: *Statistical principles in experimental design. 2nd ed, McGraw-Hill, New York, 1971*

=국문초록=

가토 신장기능에 미치는 뇌실내 Domperidone의 영향

중앙대학교 의과대학 내과학교실

김 영 수

Dopamine(DA)은 뇌실내 투여시에 항이뇨와 함께 Na 배설증가 경향을 보이며, D_1 및 D_2 두 종류의 중추 Dopamine 수용체가 신장기능에 서로 상반되는 영향을 미치고 있음이 시사된 바 있다. 본 연구에서는 선택적 D_2 길항제인 Domperidone(DOM)을 이용하여 중추 D_2 수용체의 역할을 구명코자 하였다.

DOM은 측뇌실내로 (icv)투여시 항이뇨 및 Na 배설감소를 초래하였으며 신혈류 및 사구체여과율도 감소하였다. 전신혈압은 약간 증가하였다. 정맥내투여시에는 Na 배설에 변동이 없었다. 신경을 제거한 신장에서는 icv DOM에 의한 신혈류역학적 변동은 제거되었으나 Na 배설은 제신경신장측에서도 정상신장측에서와 같이 감소하였다. DA icv의 항이뇨작용은 DOM 전처치에 의하여 영향받지 아니하였다. D_2 수용체 agonist인 Bromocriptine은 뇌실내 투여시 현저한 이뇨 및 Na 이뇨를 나타냈으나 이 작용은 DOM 전처치로 완전히 차단되었다. 또 다른 형의 D_2-agonist인 Apomorphine의 icv 투여는 일과성으로 신혈류역학의 증가와 함께 이뇨 및 Na 배설증가를 초래하였으며, DOM 전처치는 신혈류역학변동에 영향을 주지 못하였으나 뇨량 및 Na 배설증가는 DOM 전처치에 의하여 현저하게 감약시켰다. 본 연구는 중추 D_2 수용체가 어떤 체액성 natriuretic factor를 통하여 신장에 이뇨 및 Na 배설증가작용을 미치고 있음을 시사하였으며, 중추 D_1 수용체는 신경경로를 통하여 항이뇨적 영향을 미치고 중추 D_2 수용체는 Na 배설증가작용을 매개한다는 가설을 뒷받침하는 증거를 제시하였다.

大韓藥理學會 會員名單

가톨릭의대

(147-040) 서울특별시 서초구 반포동 505번지

Department of Pharmacology
Catholic University Medical College
505 Banpo-dong, Kangnam-gu, Seoul 147-040, Korea
Tel : (02)533-3200, 593-5141~9(교 1234)

曺圭喆	Cho Kyu-Chul	교 수	714-4689
李相馥	Lee Sang-Bok	교 수	717-3075
金玉女	Kim Ok-Nyu	부 교 수	
金寅順	Kim In-Soon	전임강사	
李權行	Lee Kweon-Haeng	전임강사	762-1949
李碩鎔	Lee Seok-Yong	전임강사	599-2925
金成允	Kim Seong-Yun	조 교	412-0849
成耆郁	Sung Ki-Wug	조 교	738-3856

경북의대

(700-422) 대구직할시 중구 동인동 2가 101번지

Department of Pharmacology
College of Medicine
Kyungpook National University
2-101 Dongindong, Jung-gu, Taegu 700-422, Korea
Tel : (053)422-1141(교 2850-2852)

金重暎	Kim Choong-Young	교 수	755-0408
李晩基	Lee Maan-Gee	조 교	632-1834
孫宜東	Sohn Uy-Dong	조 교	555-3138
崔秉周	Choi Byung-Ju	조 교	764-0691
金仁謙	Kim In-Kyeom	조 교	954-8988

경상의대

(660-280) 경상남도 진주시 칠암동 92

Department of Pharmacology
College of Medicine
Gyeongsang National University
92 Chilamdong, Jinju 660-280, Korea
Tel : (0591)52-0041(교 314)

張基哲	Chang Ki-Chul	조 교 수	42-1806
鄭壽蓮	Chung Soo-Youn		43-3693

경희의대

(030-701) 서울특별시 동대문구 회기동 1

Department of Pharmacology
School of Medicine, Kyung Hee University
1 Hoeki-dong Dongdaemun-gu, Seoul 030-701, Korea
Tel : (02)965-8000(교 2281, 2287, 2290, 2298)

韓大燮	Han Dae-Sup	명예교수	446-5782
高啓昌	Ko Kye-Chang	교 수	555-6585
鄭址昌	Jung Jee-Chang	교 수	967-1178
鄭柱浩	Jung Joo-Ho	전임강사	905-2843
박승준		조 교	883-2420 (인천)
李光載	Lee Kwang-Jae	대학원생	623-7264 (부산)
손치동		대학원생	2-2219 (당진)
徐東曄	Suh Dong-Yup	대학원생	568-6315
우장상		대학원생	413-0180
金明煥	Kim Myung-Hwan	대학원생	556-4763
안종국		대학원생	412-8024
나영설		대학원생	463-4583

고려의대

(110-522) 서울특별시 종로구 명륜동 2가 4번지

Department of Pharmacology
College of Medicine, Korea University
4-2 Myungryun-dong, Chongro-gu, Seoul 110-522, Korea
Tel : (02)762-5111(교 33)

申萬鍊	Shin Man-Ryun	명예교수	542-5413
千然淑	Cheon Yun-Sook	교 수	783-5881
全普權	Chun Boe-Gwun	부 교 수	372-0855
尹恒斌	Yun Hang-Bin	외래교수	253-3535
李敬熙	Lee Kyung-Hee	외래교수	763-3362
崔百熙	Choi Baik-Hi	외래교수	783-1428
李在鉉	Lee Jae-Hyun	조 교	763-7020
金梧允	Kim Oh-Yoon	조 교	603-2622

계명의대

(700-310) 대구직할시 중구 동산동 194번지

Department of Pharmacology
School of Medicine, Keimyung University
194 Dongsan-dong, Taegu 700-310, Korea
Tel : (053)252-5101~10(교 2476)

金秀京	Kim Soo-Kyung	조 교 수	252-510 1~10(교 2476)

고신의대

(602-030) 부산직할시 서구 암남동 34번지

Department of Pharmacology
Kosin Medical College
34 Amnam-dong, Suh-gu, Pusan 602-030, Korea
Tel : (051)26-5161~8(교 5110)

姜求一	Kang Koo-Il	부 교 수	622-1980
金思悅	Ghim Sa-Youl	조 교	26-5161
裵晟준	Bae Sung Jun	조 교	623-5633

동아의대

(600-020) 부산시 사하구 하단동 840번지

Department of Pharmacology
College of Medicine, Dong-A University
Hadan-dong 840, Pusan 600-020, Korea
Tel : (051)204-0171~0175

이강현	Lee Kang-Hyun	부 교 수	

부산의과대학

(602-739) 부산시 서구 아미동 1가 10번지

Department of Pharmacology
College of Medicine, Pusan National University
10 Ami-Dong 1-Ga, Seogu, Pusan 602-739, Korea
Tel : (051)256-0101, 0171 Ext. 681

洪起煥	Hong Ki-Whan	교 수	42-3433
林炳用	Rhim Byung-Yong	조 교 수	202-6727
李元石	Lee Won-Suk	전임강사	626-1592
金治大	Kim Chi-Dae	조 교	643-1547
鄭炳律	Jeong Byeong-Ryool	조 교	44-1278
鄭賢玉	Jeong Hyun-Ok	시간강사	243-3218

부산약대

(602-739) 부산시 서구 아미동 1가

Department of Pharmacology
College of Pharmacy, Pusan National University
Ami-dong 1 ga, Seo-gu, Pusan 602-739, Korea
Tel : (051)26-0171

홍승철	Hong Seong-Chul	교 수	

부산치대

(602-739) 부산시 서구 아미동 1가

Department of Pharmacology,
College of Dentistry, Pusan National University
Ami-dong 1 ga, Seo gu, Pusan 602-739, Korea
Tel : (051)26-0717(교 733)

윤 일	Yun Il	부 교 수	56-4893
이은주	Lee Eun-Ju		
손의동	Soon Eui-Dong	조 교	27-4706

삼육약대

(132-242) 서울시 도봉구 공릉 2동 233번지

Department of Pharmacy
Sahmyook University
Kongneung 2-dong, Dobong-gu, Seoul 132-242, Korea
Tel : (02)972-3606

이종화	Lee Jong-Hwa	교 수	

서울대 수의과대

(440-744) 경기도 수원시 서둔동 103번지

Department of Pharmacology and Toxicology
College of veternary Medicine, Seoul National University
103 Seodun-dong, Suwon 440-744, Korea
Tel : (0331)44-2120

이장락	Lee Jang-Nag	교 수	842-3497
이창업	Lee Chang-Eop	교 수	5-4885 (수원)
이문한	Lee Mun-Han	교 수	7-0230 (수원)
이영재	Lee Young-Jae	조 교	46-0816 (수원)
성하정	Sung Ha-Jeong	대학원생	
홍충만	Hong Choong-Man	대학원생	
오구택	Oh Goo-Tag	대학원생	

서울대 생약연구소

(110-460) 서울특별시 종로구 연건동 28

Natural Products Research Institute
Seoul National University
28 Yonkeun-dong, Chongno-gu, Seoul 110-460,

Korea
Tel : (02)762-8320

이은방	Lee Eun-Bang	교 수	784-2711
장일무	Chang Il-Moo	교 수	593-7827

서울의대

(110-460) 서울특별시 종로구 연건동 28

Department of Pharmacology
College of medicine, Seoul National University
28 Yonkeun-dong, Chongro-gu, Seoul 110-460, Korea
Tel : (02)762-5300~9(교 268), 7601-3391

吳鎭燮	Oh Jin-Sup	명예교수	
林定圭	Lim Jung-Kyoo	교 수	447-1585
朴贊雄	Park Chan-Woong	교 수	783-3920
金明石	Kim Myung-Suk	부 교 수	543-1421
鄭明熙	Chung Myung-Hee	부 교 수	591-9437
徐維憲	Suh Yoo-Hun	부 교 수	690-3718
申相久	Shin Sang-Goo	조 교 수	533-0597
金龍植	Kim Yong-Sik	조 교 수	502-5602
金奉基	Kim Bong-Ki	연구교수	712-3929
朴鍾完	Park Jong-Wan	조 교	032)64-7301
金憲植	Kim Hun-Sik	조 교	795-2303
李潤松	Lee Yun-Song	조 교	798-1841
金星秀	Kim Seoung-Su	조 교	903-8996
全陽淑	Chun Yang-Sook	조 교	032)64-7031
許星五	Huh Sung-Oh	조 교	978-7199
張仁鎭	Jang In-Jin	조 교	965-7289
申載國	Shin Jae-Gook	조 교	978-0700
李東律	Yi Dong-Ryool	조 교	(0551) 3-1685
柳昊陳	You Ho-Jin	조 교	(062)-222-8975 (광주)

서울약대

(151) 서울특별시 관악구 신림동 산 56-1

Department of Pharmacology
College of Pharmacy, Seoul National University
San 56-1 Shinrim-dong, Kwanak-gu, Seoul 151, Korea
Tel : (02)886-0101(교 2816, 2202)

金洛斗	Kim Nak-Doo	교 수	
高光浩	Ko Kwang-Ho	부 교 수	
李明杰	Lee Myung-Gull	조 교 수	
李相奉	Lee Sang-Bong	조 교	
高鴻淑	Ko Hong-Sook	대학원생	
金娟兌	Kim Yun-Tai	대학원생	
金源起	Kim Won-Ki	대학원생	
宋善權	Song Sun-Gwon	대학원생	
元善美	Won Sun-Me	대학원생	
兪重根	Yoo Jong-Keun	대학원생	
李富淵	Lee Bu-Yean	대학원생	
張洪媛	Jang Hong-Weon	대학원생	
鄭相穆	Chung Sang-Mock	대학원생	
鄭□炅	Chung Hyeone-Gyeong	대학원생	
崔榮文	Choi Young-Moon	대학원생	
金運子	Kim Oon-Ja	대학원생	
朴允珠	Park Yun-Joo	대학원생	
尹銀晶	Yun Eun-Jeong	대학원생	
李允淑	Lee Yun-Suk	대학원생	
趙晟恩	Cho Seong-Eun	대학원생	

서울치대

(110-460) 서울특별시 종로구 연건동 28-2

Department of Pharmacology and Dental Therapeutics
College of Dentistry, Seoul National University
28-2 Yeon-Kun Dong, Chong-Ro Ku, Seoul 110-460, Korea
Tel : (02)745-6701, ext. 381, 382

丁東均	Cheong Dong-Kyun	교 수	741-3193
金寬植	Kim Gwan-Shik	조 교 수	743-0311
金正根	Kim Jung-Keun	조 교	
金明洙	Kim Myung-Soo	조 교	
金世源	Kim Se-Won	조 교	
金亨龍	Kim Hyung-Yong	조 교	
李仁錫	Lee In-Seog	조 교	

성균관약대

(440-746) 경기도 수원시 천천동 300

Department of Pharmacology
School of Pharmacy, Sung Kyun Kwan University
300 Chunchoeon-dong, Suwon 440-746, Korea
Tel : (0331)44-2161

趙台淳 Cho Tai-Soon 교 수 599-7251
李香雨 Lee Hyang-Woo 교 수 648-0101
崔承珍 Choi Seung-Jin 조 교 962-8715
趙成益 Cho Sung-Ik 대학원생 695-9444

순천향의대

(330-100) 충남 천안시 봉명동 23-20

Department of Pharmacology
College of Medicine, Soonchunhyang University,
Chun-an 330-100, Korea
Tel : (0417)565-3711(교 840)

趙炳憲 Cho Byung-Heon 교 수 교)841
朴永鉉 Park Young-Hyun 전임강사 교)842
李鍾和 Lee Jong-Hwoa 조 교 교)840
權俊澤 Kwan Jun-Tack 조 교 교)840
崔圭□ Choi Kyu-Hong 대학원생 교)840

연세의대

(120-749) 서울특별시 서대문구 신촌동 134

Department of Pharmacology
Yonsei University College of Medicine
C.P.O. Box 8044, Seoul 120-749, Korea
Tel : (02)392-0161(교 3080-3086)

李宇柱 Lee Woo-Choo 명예교수 334-6612
洪思奭 Hong Sa-Suk 교 수 362-5661
柳京子 Ryu Kyung-Za 교 수 542-3236
金景煥 Kim Kyung-Hwan 교 수 648-3432
安英秀 Ahn Young-Soo 부 교 수 648-5357
金東龜 Kim Dong-Goo 조 교 수 305-3924
李善美 Lee Sun Mee 연구강사 555-1980
崔宰源 Choi Jae-Won 연구강사 356-2065
金禮植 Kim Ye Sik 조 교 542-1113
崔賢圭 Choi Hyon Kyoo 조 교 392-6572
崔珠英 Choi Joo Young 조 교 783-0987
朱一路 Jou Ilo 조 교 737-3212
李胤郎 Lee Yoon-Tae 조 교 712-7865
李京恩 Lee Kyung-Eun 조 교 671-7163

영남의대

(705-032) 대구시 남구 대명동 317-1

Department of Pharmacology
College of Medicine, Yeungnam University
317-1 Daemyung-dong, Namgu, Taegu 705-032,
Korea
Tel : (053)623-8001(교 3651), 33-0823

金源准 Kim Won-Joon 교 수
李光潤 Lee Kwang-Youn 조 교 수 756-7026
河貞姬 Ha Jeoung-Hee 연 구 원 67-0842
權五哲 Kwon O-Cheol 조 교 633-3577

원광의대

(570-180) 전북 이리시 신용동 344-2

Department of Pharmacology
School of Medicine, Won Kwang University
344-2 Shinyong-dong, Iri 570-180, Korea
Tel : (0653)2-6041

최봉규 Choi Bong-Kyu 조 교 수

이화의대

(120-750) 서울특별시 서대문구 대현동 11

Department of Pharmacology
School of Medicine, Ewha Woman's University
11 Daehyun-dong, Seodaemoon-gu, Seoul 120-750,
Korea
Tel : 362-6151~70

裵玲淑 Pae Young-Sook 부 교 수 (02)362-6151 交 575, 583

이화약대

(120-750) 서울시 서대문구 대현동

Department of Pharmacology
College of Pharmacy, Ewha Woman's University
11 Daehyun-dong, Seodaemoon-gu Seoul 120-750,
Korea
Tel : (02)362-6151(교 600)

윤재순 Yun Jae-Soon 교 수 783-2277
최신규 Choi Shin-Kyu 조 교 수 905-9009

인제의대

(614-112) 부산직할시 부산진구 개금동 633-165

Department of Pharmacology
Inje Medical College
Gaekum-dong, Pusanjin-gu, Pusan 614-112, Korea
Tel : (051)93-3421

車仁俊 Cha In-June 부 교 수 85-6033

인하의대

(402-751) 인천직할시 남구 용현동 253

Department of Pharmacology and Toxicology
Inha University College of Medicine
Tel : (032)862-0077(교 3053)

車英男 Cha Young-Nam 교 수
河銀珠 Ha Eun-Ju 연구교수

전남의대

(501-190) 광주직할시 동구 학동 5

Department of Pharmacology
College of Medicine, Chonnam National University
5 Hak-dong, Dong-ku, Kwanju 501-190, Korea
Tel : (062)232-1244

金永寅	Kim Yung-In	교 수	22-4557
鞠永棕	Kook Young-Johng	교 수	672-1124
백영홍	Baik Young-Hong	부 교 수	673-2948
김재하	Kim Jae-Ha	전임강사	66-6885
김종근	Kim Jong-Kun	전임강사	27-4296
김경근	Kim Kyung-Kun	전임강사	55-7658
임영채	Lim Young-Chai	조 교	232-1244

전북의대

(560-756) 전라북도 전주시 금암동 산 20

Department of Pharmacology
College of Medicine, Chonbuk National University
San 20 Kumamdong, Chonju 560-756, Korea
Tel : (0652)70-3087

曺圭朴	Cho Kyu-Park	교 수	2-3236
蔡洙完	Choi Soo-Wan	전임강사	72-2005
金基元	Kim Kee-Won	전임강사	74-0260
林定勳	Lim Jung Hwn	조 교	74-9822

전북치대

(520-020) 전라북도 전주시 경원동 3가 14

Department of Pharmacology
College of Dentistry, Chonbuk National University
San 20 Kumamdong, Chonju 520-020, Korea
Tel : (0652)85-1110

吳貴玉	Oh Kwi-Ok	조 교 수	762-5107 (서울)

전주우석대학교 약학대학

(565-800) 전라북도 완주군 삼례읍 후정리

Tel : (0652)73-8001

殷載淳	Eun Jae-Soon		74-7391

조선의대

(501-759) 광주직할시 동구 서석동 375

Department of Pharmacology
College of Medicine, Chosun University
375 Seoseok-dong, Dong-gu, Kwangju 501-759, Korea
Tel : (062)232-6301~5

林東潤	Lim Dong-Yoon	부 교 수	34-2005
柳昊陳	Yoo Ho-Jin	조 교	222-8975
吳眞希	Oh Jin-Hee	조 교	222-0333
崔哲熙	Choi Cheol-Hee	조 교	55-9981

조선약대

(501-759) 광주시 동구 서석 2동 375번지

Department of Pharmacology
College of Pharmacy, Chosun University
375 Seoseok-dong, Dong-gu, Kwangju 501-759, Korea
Tel : (062)22-9214

고석태	Ko Suk-Tai	교 수	33-9512

중앙의대

(156-756) 서울시 동작구 흑석동 221

Department of Pharmacology
College of Medicine, Chung-Ang University
221 Heuksuk-dong, Dongjak-gu, Seoul 156-756, Korea
Tel : 815-5031~7

李光秀	Lee Kwang-Soo	교 수	532-6167
李延秀	Lee Chung-Soo	조 교 수	675-0617
申龍圭	Shin Yong Kyoo	조 교	535-9626

충남의대

(301-131) 충남 대전시 중구 문화 1동 6

Department of Pharmacology
College of Medicine, Chungnam National University
6 Munwha-1-dong, Daejeon 301-131, Korea
Tel : (042)524-4601

李載欣	Lee Jae-Heun	조 교 수	44-6624
昔廷鎬	Seok Jeong-Ho	조 교 수	46-4603
林鍾鎬	Lim Jong-Ho	조 교	526-4722

충남약대

(302-764) 충청남도 대전시 서구 궁동

Department of Pharmacology
College of Pharmacy, Chungnam National University

충북약대

(360-763) 충북 청주시 개신동 산 48

Department of Pharmacology
College of Pharmacy, Chungbuk National University
San 48 Gaesin-dong, Cheongju 360-763, Korea

金學成	Kim Hack-Seang	교 수	(0431)2-5497
李明求	Lee Myung-Koo	조 교 수	(0431)55-5771

한림의대

(200-010) 강원도 춘천시 옥천동 1번지

Department of Pharmacology
College of Medicine, Hallym University
1 Okchon-dong, Chunchon 200-010, Korea
Tel : (0361)54-7431

金永姬	Kim Yung-Hi	교 수	53-5181
宋東根	Song Dong-Keun	전 강	51-5606
魏明復	Wie Myung-Bok	조 교	53-1298
姜秉兌	Kang Byung-Tae	조 교	51-4157

한양의대

(133-791) 서울특별시 성동구 행당동 17

Department of Pharmacology
College of Medicine, Hanyang University
17 Haengdang-dong, Seongdong-ku, Seoul 133, Korea
Tel : (02)293-3111(교 2670~2674), 292-3111(교 2660~2663)

徐大圭	Suh Tae-Kyu	교 수	292-6686
申仁澈	Shin In-Chul	조 교 수	
孫東烈	Sohn Dong-Ryul	전임강사	군복무중
姜柱燮	Kang Ju-Seob		

화학연구소

안전성 연구실

(302-343) 충남 대전시 서구 장동

Tel : (042)822-7001(교 607)
Korea Research Institute of Chemical Toxicology
Center Technology

김은주

<특별회원 명단>

일화(주)

경기도 구리시 수택동 505

433-6141~7

제일약품 주식회사

서울 서초구 반포동 745-5

549-7451

제일제당 주식회사

경기도 이천군 마장면 덕평리 산 522-1 제일제당 종합연구소

(02)234-2978

부광약품공업(주)

서울 동작구 대방동 398-1(156-020)

812-3253~4

동영과학 주식회사

서울특별시 강남구 논현동 210-1

547-1758

녹십자의학공업 주식회사

경기도 용인군 기흥면 구갈리 227(170-73)

(0331)8-3224~5

일동제약 주식회사

서울 동대문구 신설동 45
(동대문사 78, 청량리私 116)

93-0081~5, 94-9221~5

청계약품 주식회사

서울 영등포구 영등포동 94-69
영등포 CPO Box 229

677-2828

유한양행
서울 동작구 대방동 49-6
(중앙사서함 98, 1136 영등포 22)
815-0181, 815-9721

한독약품공업 주식회사
서울 동대문구 상봉동 344
(중앙사서함 30, 청량리 120)
433-3131~9, 433-0151~9

한국쉐링 주식회사
서울 은평구 응암동 103-16(CPO 3141)
388-0141~5

선진의기상사
서울 중구 태평로 1가 76-3
(오양수산빌딩 317호)