



Chapter 4

Results

Effect of biliary obstruction on plasma bilirubin concentration comparing between sham control group (group I) and biliary obstruction without indomethacin treated group (group IV)

Table I and Figure 1 show the plasma concentration of bilirubin. The plasma total and direct bilirubin were 4.13 ± 1.63 and 2.76 ± 1.13 mg/100 ml in biliary obstructed rats (group IV), whereas in sham control rats (group I) were 0.1 ± 0.05 and 0.04 ± 0.03 mg/100 ml, respectively.

Effect of biliary obstruction on general circulation

Data of general circulation from 5 groups of rats are shown in Table II and Figure 2. In 5 groups of rats, mean arterial blood pressure (MABP) and heart rate (HR) were not different. Hematocrit (Hct) was decreased significantly in sham control with vehicle treated groups (group II), sham control with indomethacin treated group (group III) and biliary obstruction with indomethacin treated group in comparing with sham control group (group I). The Hct value in biliary obstructed group (group IV) was not significantly different from sham control group.

Effect of biliary obstruction and indomethacin on renal hemodynamics

Renal hemodynamics changes are shown in Table III and Figures 3-10. The glomerular filtration rate (GFR), effective renal plasma

flow (ERPF), effective renal blood flow (ERBF) and renal vascular resistance (RVR) were not significantly different among group I, II, III and V. Only group IV was shown a significant enhance of GFR, ERPF, ERBF and fall in RVR in comparing with group I. The GFR, ERPF and ERBF in group IV were approximately 52.5%, 63.1% and 62.6%, respectively, greater than group I, whereas RVR was significantly decreased to 55.5% in comparing with group I. Filtration fraction (FF) calculated as $GFR/ERPF$ in 5 groups was not significantly different.

Effect of biliary obstruction and indomethacin on plasma concentration of electrolytes

Table IV shows the plasma concentration of sodium (Na), potassium (K), chloride (Cl) and calcium (Ca) in 5 groups of rats. There was no significant difference in plasma concentration of Na, K, Cl and Ca between group I and group IV. The plasma Na and Ca concentration in group II, III and V increased significantly as compared to that of group I and group IV (Figures 11,13). Inversely, the plasma K concentration in group III and V decreased significantly as compared to that of group I, II and IV which were not significantly different (Figure 12). Furthermore, the plasma Cl concentration in 5 groups were not significantly different.

Effect of biliary obstruction and indomethacin on urine flow rate, urea nitrogen clearance, osmolar clearance and free water clearance

The urine flow rate (V), urea nitrogen clearance (C_{UN}), osmolar clearance (C_{OSM}) and free water clearance (C_{H_2O}) were shown in Table V. No significant difference was found in them between group

I and group IV. The values of V , C_{UN} and C_{OSM} in group II, III and V significantly increased as compared to that of group I and IV (Figures 14, 15, 16). On the other hand, C_{H_2O} in group II, III and V significantly decreased in comparing with group I and IV (Figure 17).

Effect of biliary obstruction and indomethacin on excretion rate of electrolytes

The results are shown in Table VI and Figures 18 - 21. Excretion rate of sodium ($U_{Na}V$), potassium (U_KV), chloride ($U_{Cl}V$) and calcium ($U_{Ca}V$) between group I and IV were not significantly different. The values of $U_{Na}V$, U_KV , $U_{Cl}V$ and $U_{Ca}V$ in group II, III and V significantly increased as compared to those values of group I and IV.

Effect of biliary obstruction and indomethacin on fractional excretion of electrolytes

Table VII and Figures 22-25 show the results of fractional excretion of electrolytes. Fractional excretion of sodium (FE_{Na}), potassium (FE_K), chloride (FE_{Cl}) and calcium (FE_{Ca}) in group I and IV were not significantly different. The values of $U_{Na}V$, U_KV , $U_{Cl}V$ and $U_{Ca}V$ in group II, III and V were high while the GFR of them were unchanged, reflected a marked rise in FE_{Na} , FE_K , FE_{Cl} and FE_{Ca} which were significantly different from group I and IV.

Table I Plasma total and direct bilirubin in sham control and 5 days biliary obstructed rats.

	group I Sham control (n=14)	group IV Biliary obstruction (n=5)
Plasma total bilirubin, mg/100 ml	0.10 \pm 0.05	4.13 ^{***} \pm 1.63
Plasma direct bilirubin, mg/100 ml	0.04 \pm 0.03	2.76 ^{***} \pm 1.13

Values are means \pm S.D.

Significant difference using unpaired t-test is indicated by

* $p < 0.05$; ** $p < 0.025$; *** $p < 0.001$.

ศูนย์วิทยุทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Table II Effect of biliary obstruction and indomethacin on general circulation.

	Sham control			Biliary obstruction	
	-	+Vehicle	+Indomethacin	-	+Indomethacin
	group I	group II	group III	group IV	group V
	(n=14)	(n=5)	(n=11)	(n=11)	(n=10)
MABP,	137	137	140	125	134
mmHg	<u>+21</u>	<u>+26</u>	<u>+10</u>	<u>+20</u>	<u>+21</u>
HR,	395	432	421	390	393
beat/min	<u>+43</u>	<u>+30</u>	<u>+20</u>	<u>+34</u>	<u>+33</u>
Hct, %	45.8	40.2 ^{**}	42.1 ^{**}	43.6	40.6 ^{**}
	<u>+3.0</u>	<u>+3.9</u>	<u>+2.1</u>	<u>+4.4</u>	<u>+3.1</u>

Values are means \pm S.D.

Significant difference from group I using unpaired t-test is indicated by * $p < 0.05$; ** $p < 0.025$; *** $p < 0.001$.

ศูนย์แพทย์ทหารอากาศ
จุฬาลงกรณ์มหาวิทยาลัย

Table III Effect of biliary obstruction and indomethacin on renal hemodynamics.

	Sham control			Biliary obstruction	
	-	+Vehicle	+Indomethacin	-	+Indomethacin
	group I	group II	group III	group IV	group V
	(n=14)	(n=5)	(n=11)	(n=11)	(n=10)
GFR,	1.736	1.729	1.852	2.648 ^{**}	2.109 ^r
ml/min	± 0.637	± 0.379	± 0.394	± 0.640	± 0.410
ERPF,	5.254	3.878	5.153	8.571 ^{**}	6.535 ^r
ml/min	± 2.921	± 0.364	± 1.092	± 2.405	± 1.956
ERBF,	9.710	6.485	8.866	15.791 ^{**}	11.016 ^{rr}
ml/min	± 5.176	± 0.566	± 1.659	± 3.945	± 3.263
RVR, 10^3 dyne	1538.2	1689.6	1262.9	684.1 ^{**}	1060.0 ^{rr}
-sec/cm ⁵	± 1057.9	± 550.1	± 238.8	± 225.4	± 358.0
FF, %	38.7	44.6	36.7	33.0	34.5
	± 14.5	± 9.6	± 7.7	± 12.0	± 7.0

Values are means \pm S.D.

Significant difference from group I using unpaired t-test is

indicated by * $p < 0.05$; ** $p < 0.025$; *** $p < 0.001$.

r $p < 0.05$; rr $p < 0.025$; rrr $p < 0.001$, as compared to the biliary obstruction without indomethacin-treated rats (group IV).

Table IV Effect of biliary obstruction and indomethacin on plasma concentration of electrolytes.

	Sham control			Biliary obstruction	
	-	+Vehicle	+Indomethacin	-	+Indomethacin
	group I	group II	group III	group IV	group V
	(n=14)	(n=5)	(n=11)	(n=11)	(n=10)
P_{Na} , mEq/L	139.4 \pm 5.6	146.2 ^{**} \pm 3.7	144.3 ^{**} \pm 2.5	143.5 \pm 6.5	145.3 ^{**} \pm 2.7
P_K , mEq/L	4.3 \pm 0.5	3.8 \pm 0.2	3.7 ^{**} \pm 0.2	4.3 \pm 0.4	3.6 ^{**rrr} \pm 0.2
P_{Cl} , mEq/L	107.9 \pm 4.9	104.6 \pm 3.9	106.5 \pm 2.6	105.6 \pm 4.6	105.6 \pm 2.4
P_{Ca} , mg/100ml	7.2 \pm 1.1	8.9 ^{**} \pm 0.6	8.3 ^{**} \pm 0.8	7.9 \pm 1.7	8.5 ^{**} \pm 0.7

Values are means \pm S.D.

Significant difference from group I using unpaired t-test is indicated by * $p < 0.05$; ** $p < 0.025$; *** $p < 0.001$.

r $p < 0.05$; rr $p < 0.025$; rrr $p < 0.001$, as compared to the biliary obstruction without indomethacin-treated rats (group IV).

Table V Effect of biliary obstruction and indomethacin on urine flow rate, urea nitrogen clearance, osmolar clearance and free water clearance.

	Sham control			Biliary obstruction	
	-	+Vehicle	+Indomethacin	-	+Indomethacin
	group I (n=14)	group II (n=5)	group III (n=11)	group IV (n=11)	group V (n=10)
V, ml/min	0.0381 ± 0.064	0.1117** ± 0.055	0.1129** ± 0.051	0.0311 ± 0.023	0.1159**rrr ± 0.044
C _{UN} , ml/min	1.150 ± 0.665	1.705** ± 0.493	2.485*** ± 0.331	1.206 ± 0.616	1.775**r ± 0.449
C _{osm} , ml/min	0.065 ± 0.032	0.190*** ± 0.044	0.221*** ± 0.053	0.069 ± 0.038	0.226***rrr ± 0.065
C _{H₂O} , ml/min	-0.026 ± 0.056	-0.103*** ± 0.019	-0.108*** ± 0.017	-0.038 ± 0.019	-0.110***rrr ± 0.031

Values are means \pm S.D.

Significant difference from group I using unpaired t-test is indicated by * $p < 0.05$; ** $p < 0.025$; *** $p < 0.001$.

r $p < 0.05$; rr $p < 0.025$; rrr $p < 0.001$, as compared to the biliary obstruction without indomethacin-treated rats (group IV).

Table VI Effect of biliary obstruction and indomethacin on excretion rate of electrolytes.

	Sham control			Biliary obstruction	
	-	+Vehicle	+Indomethacin	-	+Indomethacin
	group I	group II	group III	group IV	group V
	(n=14)	(n=5)	(n=11)	(n=11)	(n=10)
$U_{Na}V$, mEq/min	2.146 ± 2.087	16.124 ^{***} ± 7.493	22.358 ^{***} ± 7.584	3.062 ± 3.705	21.395 ^{***rrr} ± 9.150
$U_{K}V$ mEq/min	1.929 ± 1.079	3.561 ^{***} ± 0.584	4.860 ^{***} ± 1.190	1.960 ± 0.913	4.240 ^{***rrr} ± 1.305
$U_{Cl}V$, mEq/min	3.165 ± 2.826	15.714 ^{***} ± 7.226	21.957 ^{***} ± 6.689	4.140 ± 4.761	19.550 ^{***rrr} ± 7.509
$U_{Ca}V$, mg/min	0.161 ± 0.110	0.534 ^{**} ± 0.273	0.721 ^{**} ± 0.478	0.168 ± 0.056	0.543 ^{***rrr} ± 0.207

Values are means \pm S.D.

Significant difference from group I using unpaired t-test is indicated by * $p < 0.05$; ** $p < 0.025$; *** $p < 0.001$.

r $p < 0.05$; rr $p < 0.025$; rrr $p < 0.001$, as compared to the biliary obstruction without indomethacin-treated rats (group IV).

Table VII Effect of biliary obstruction and indomethacin on fractional excretion of electrolytes.

	Sham control			Biliary obstruction	
	- group I (n=14)	+Vehicle group II (n=5)	+Indomethacin group III (n=11)	- group IV (n=11)	+Indomethacin group V (n=10)
FE _{Na} '	0.858	6.534 ^{***}	8.297 ^{***}	0.784	6.991 ^{***rrr}
%	<u>+0.903</u>	<u>+1.945</u>	<u>+2.423</u>	<u>+0.907</u>	<u>+2.727</u>
FE _K '	27.098	58.655 ^{***}	72.684 ^{***}	17.462	56.000 ^{***rrr}
%	<u>+15.463</u>	<u>+6.324</u>	<u>+12.478</u>	<u>+7.105</u>	<u>+16.351</u>
FE _{Cl} '	1.635	8.913 ^{***}	11.085 ^{***}	1.455	8.928 ^{***rrr}
%	<u>+1.437</u>	<u>+2.583</u>	<u>+2.955</u>	<u>+1.615</u>	<u>+2.990</u>
FE _{Ca} '	1.311	3.525 ^{**}	4.360 ^{***}	0.749	2.969 ^{**}
%	<u>+1.029</u>	<u>+1.300</u>	<u>+2.252</u>	<u>+0.218</u>	<u>+1.124</u>

Values are means \pm S.D.

Significant difference from group I using unpaired t-test is indicated by * $p < 0.05$; ** $p < 0.025$; *** $p < 0.001$.

r $p < 0.05$; rr $p < 0.025$; rrr $p < 0.001$, as compared to the biliary obstruction without indomethacin-treated rats (group IV).

Figure 1 Plasma total and direct bilirubin in sham control and five days biliary obstruction. Value are mean \pm S.D.

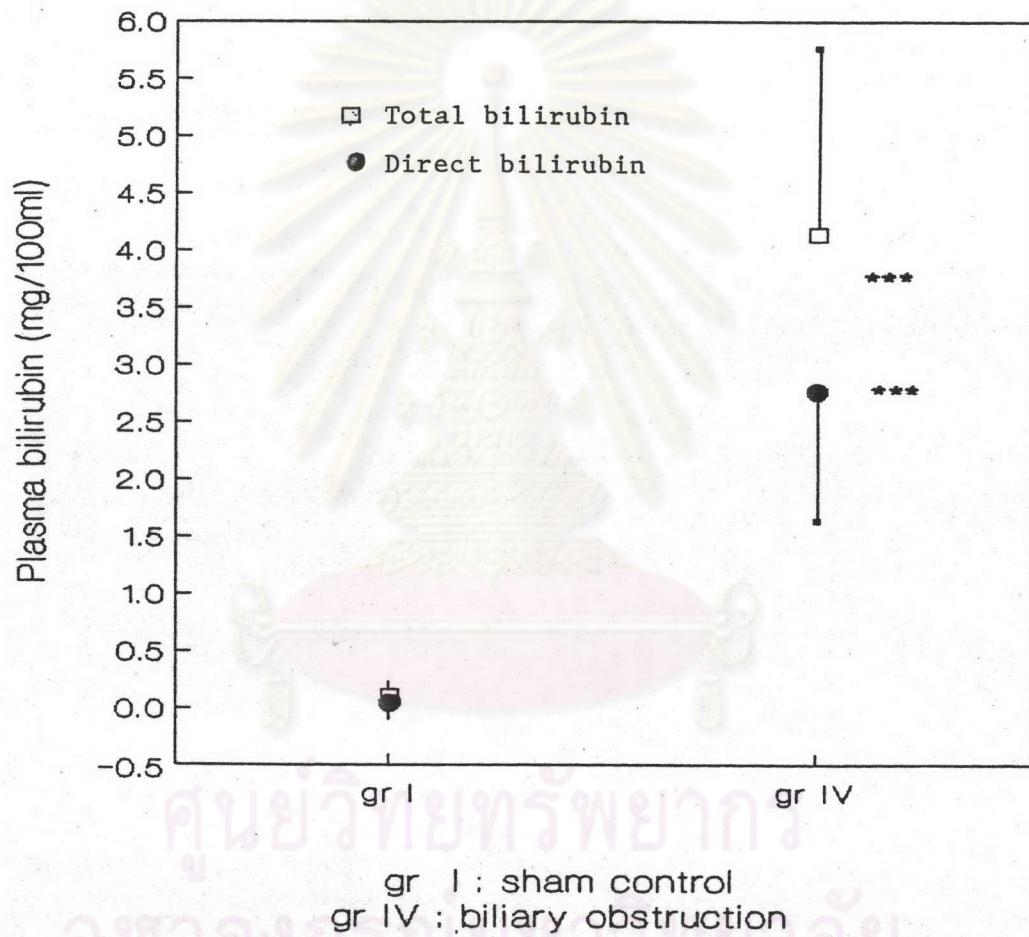
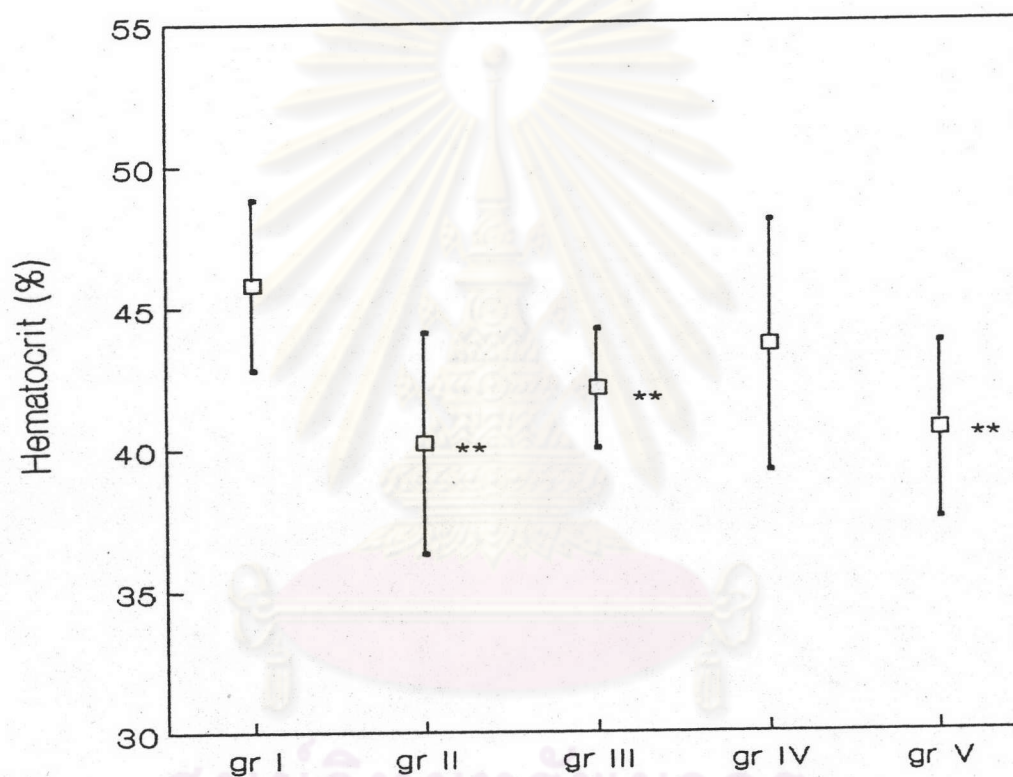
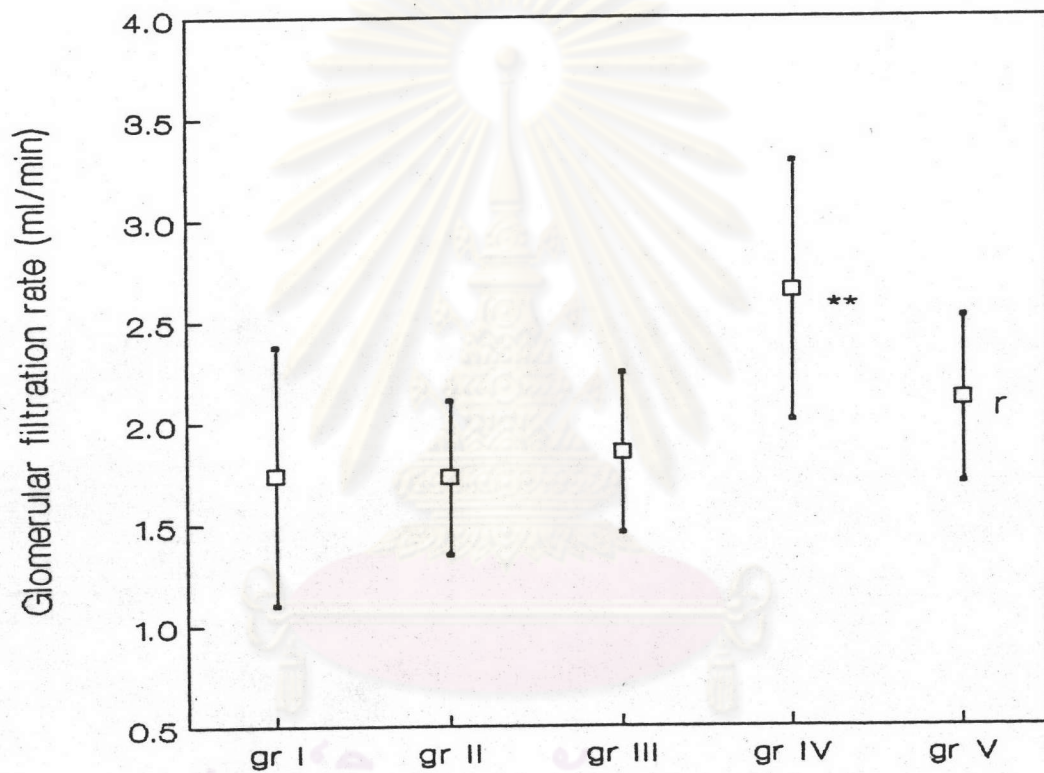


Figure 2 Comparison of hematocrit (Hct) in five groups of rats. Values are mean \pm S.D.



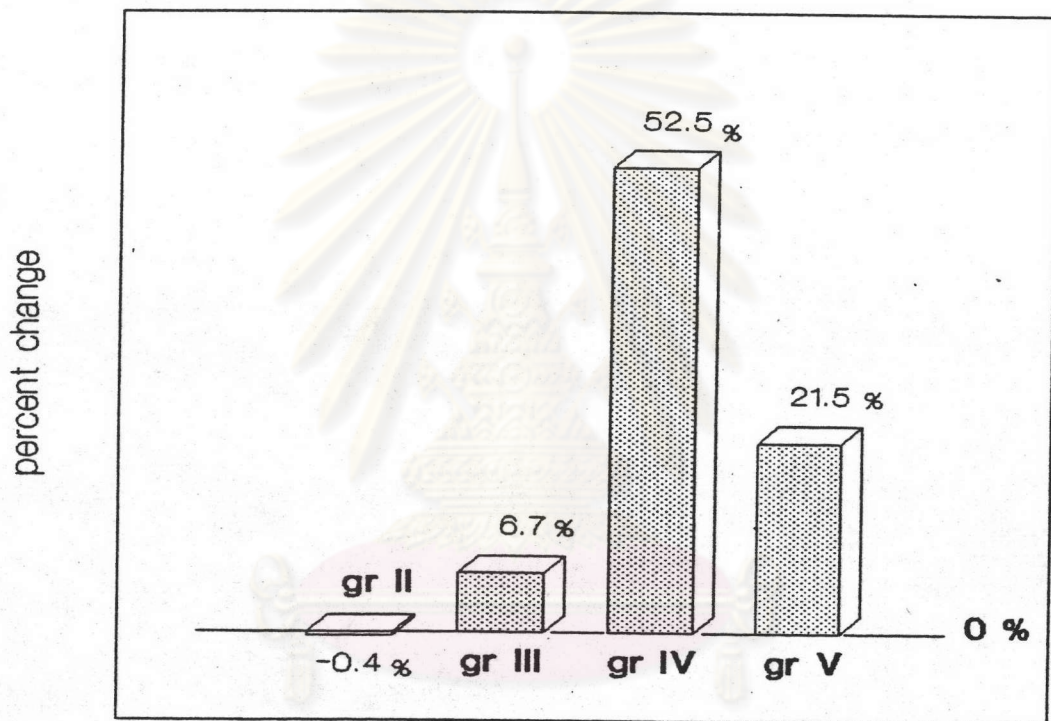
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 3 Comparison of glomerular filtration rate (GFR) in five groups of rats. Values are mean \pm S.D.



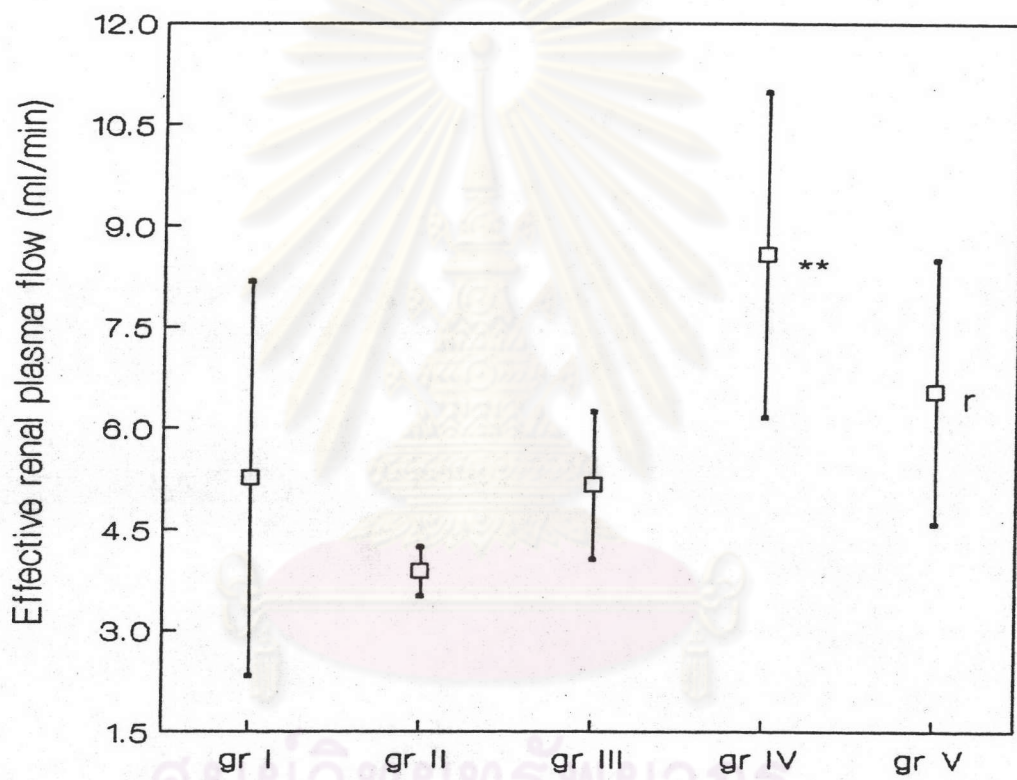
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 4 Percent change in glomerular filtration rate(GFR) of group II,III,IV, and V as compared to group I.



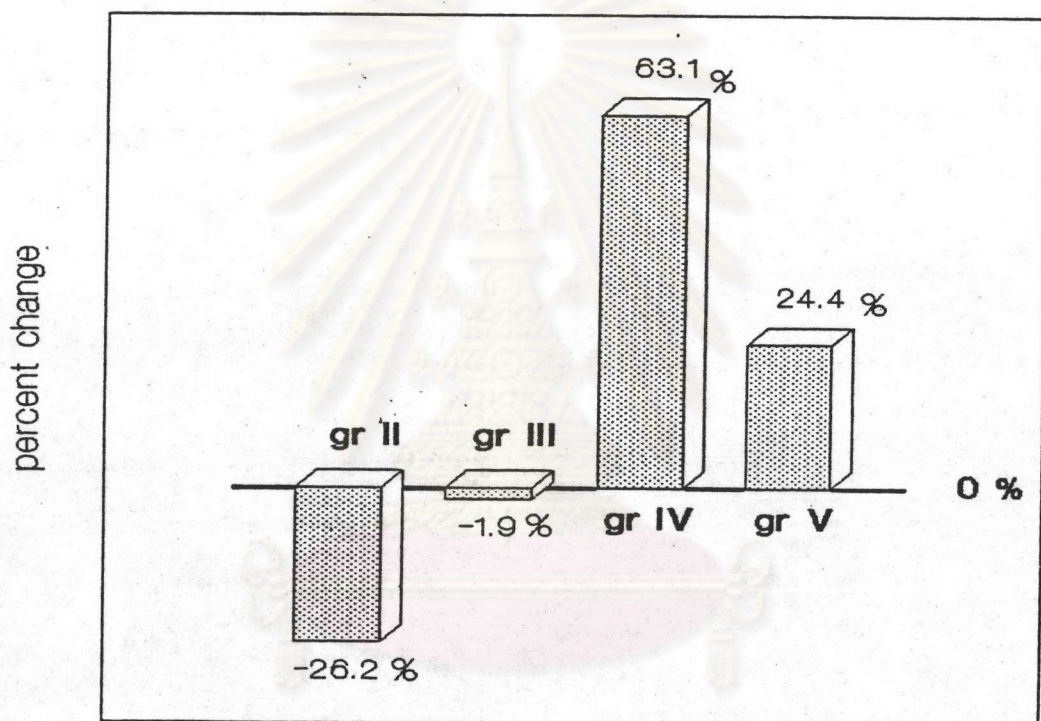
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 5 Comparison of effective renal plasma flow (ERPF) in five groups of rats. Values are mean \pm S.D.



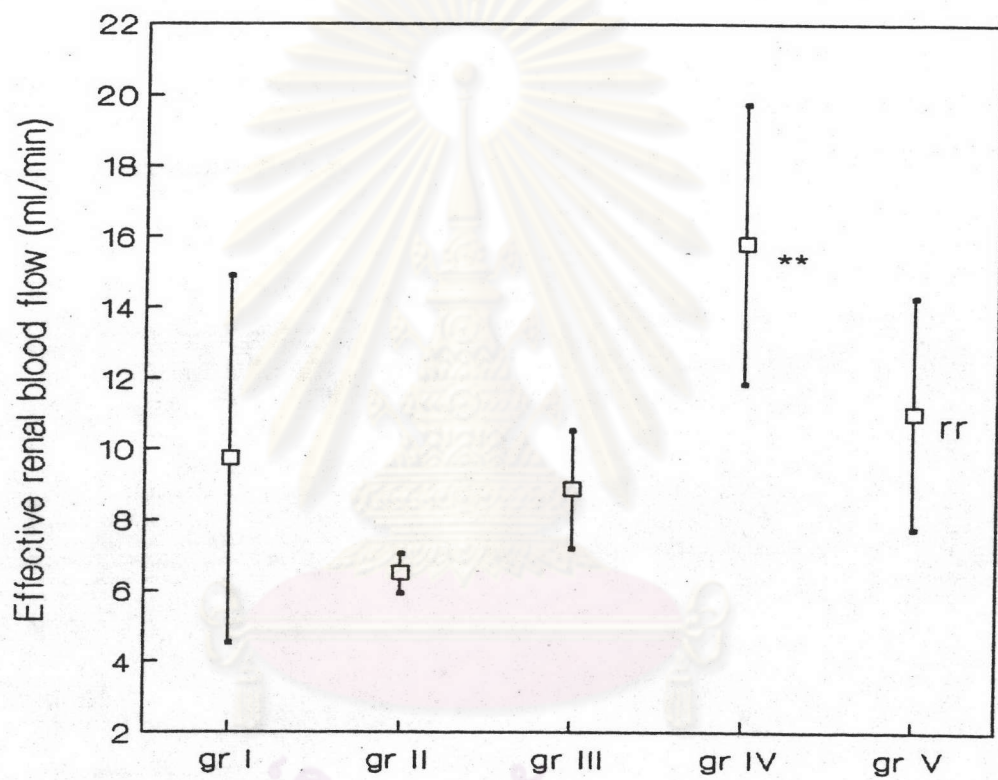
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 6 Percent change in effective renal plasma flow(ERPF) of group II,III, IV and V as compared to group I.



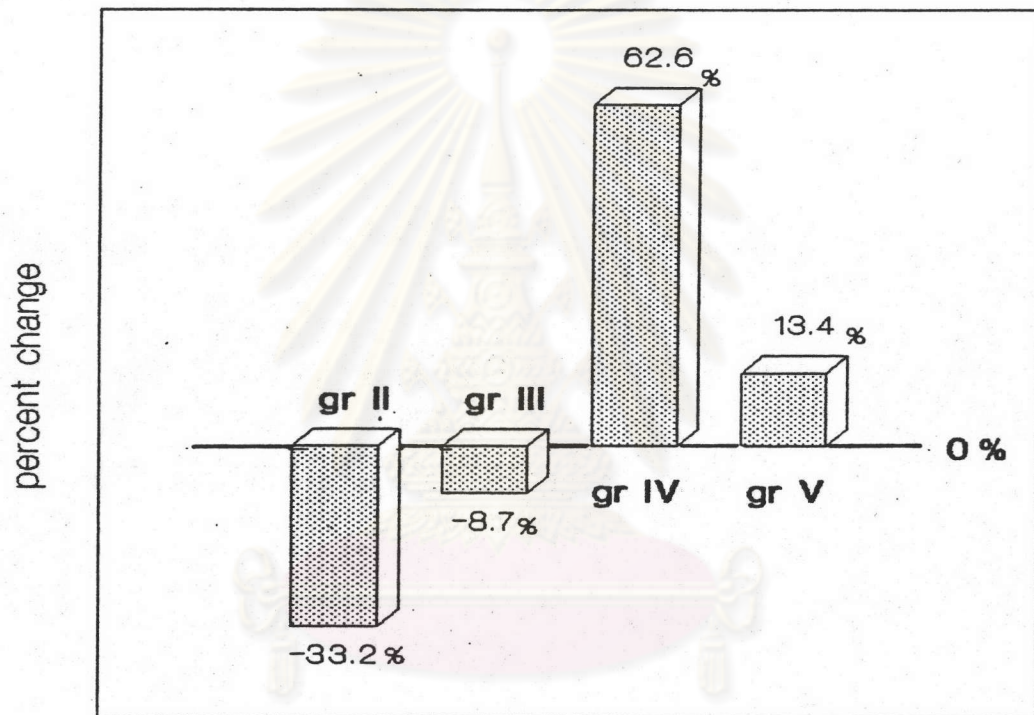
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 7 Comparison of effective renal blood flow (ERBF) in five groups of rats. Values are mean \pm S.D.



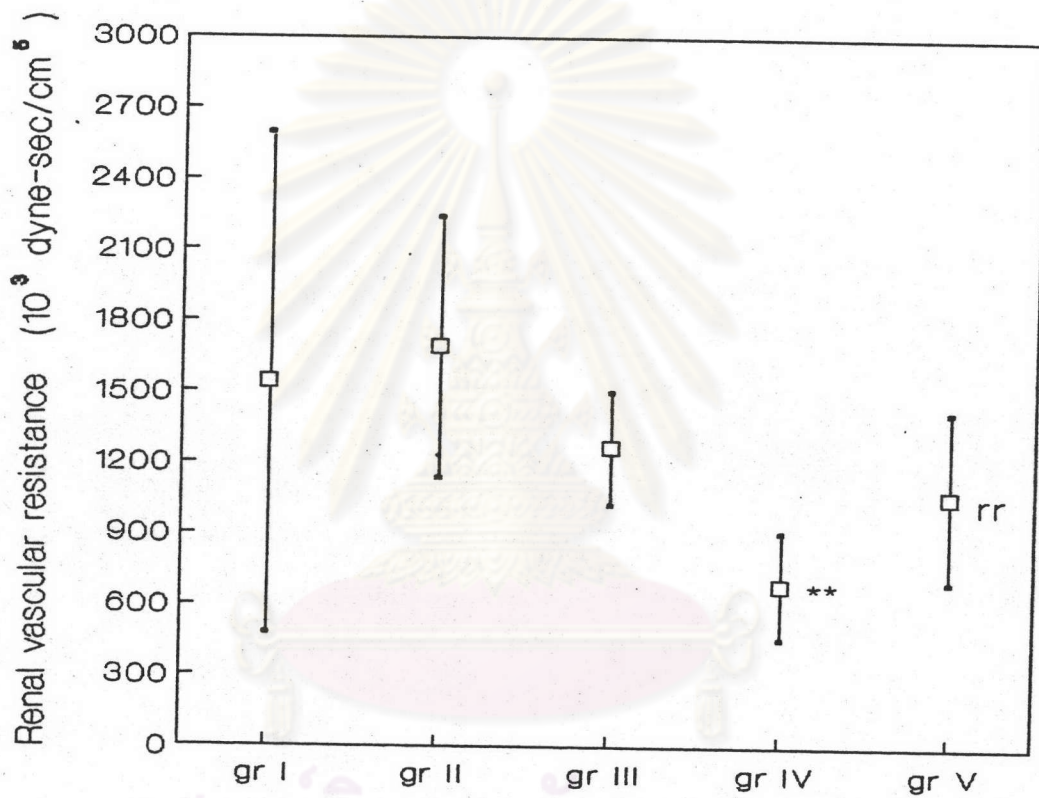
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 8 Percent change in effective renal blood flow (ERBF) of group II,III, IV and V as compared to group I.



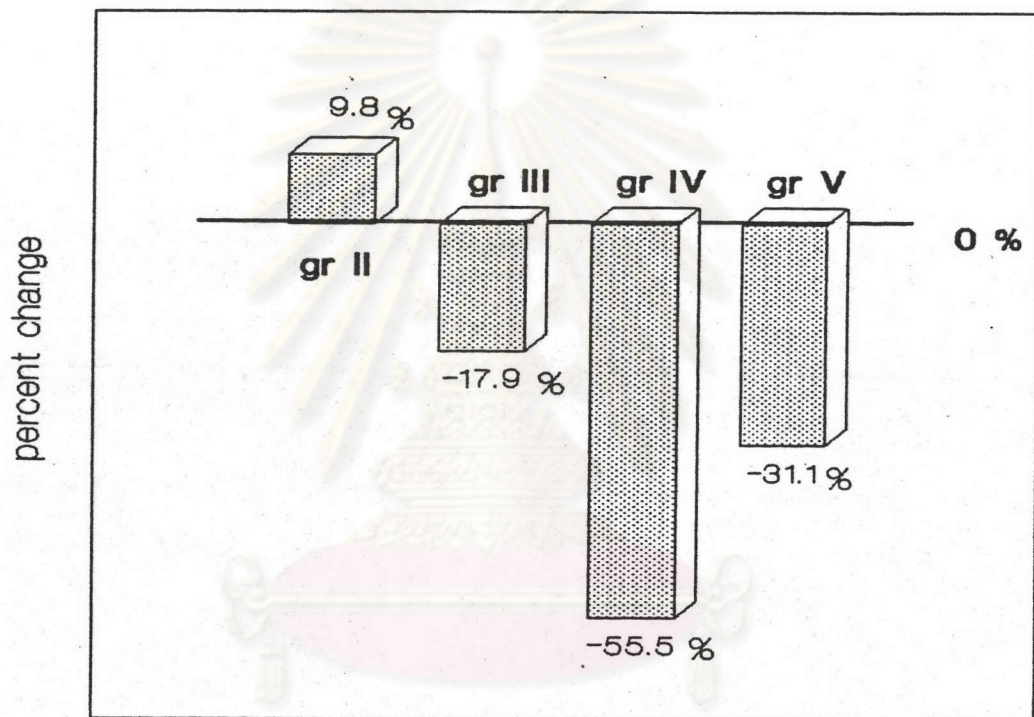
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 9 Comparison of renal vascular resistance (RVR) in five groups of rats. Values are mean \pm S.D.



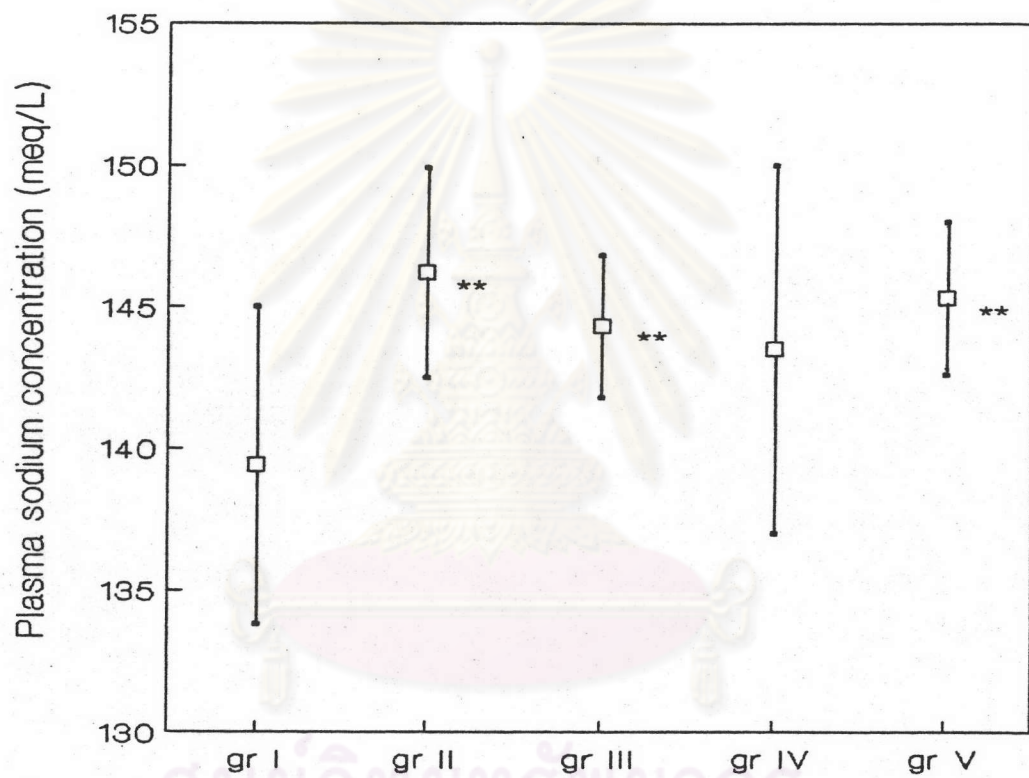
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 10 Percent change in renal vascular resistance (RVR) of group II, III, IV and V as compared to group I.



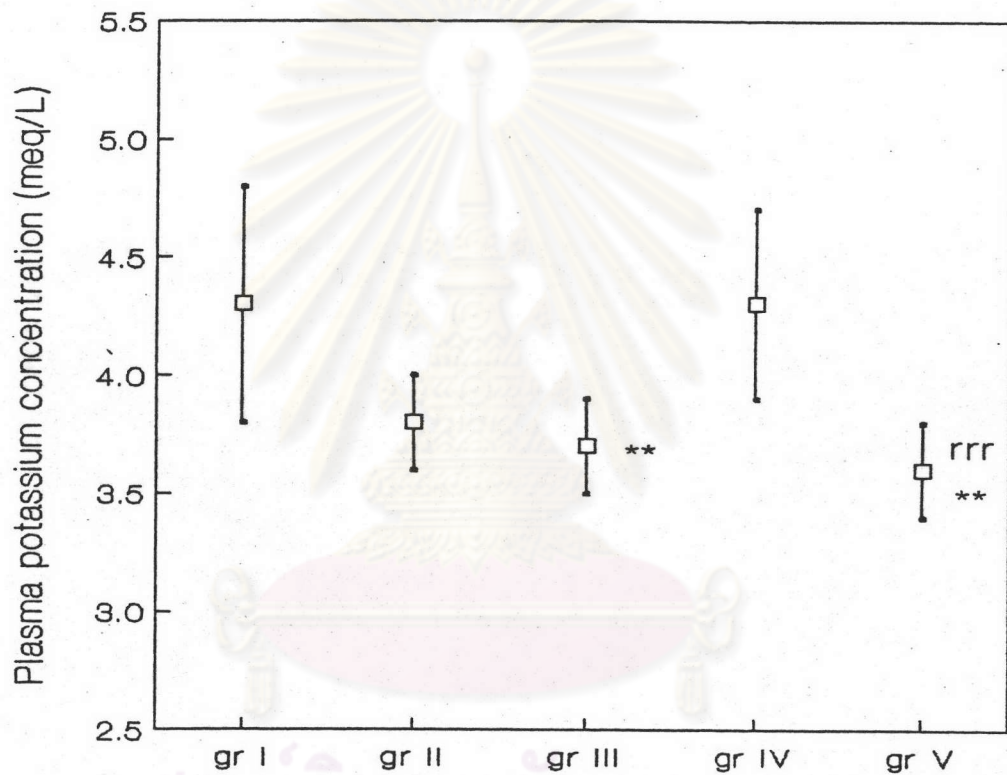
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 11 Comparison of plasma sodium concentration (P_{Na}) in five groups of rats. The values are mean \pm S.D.



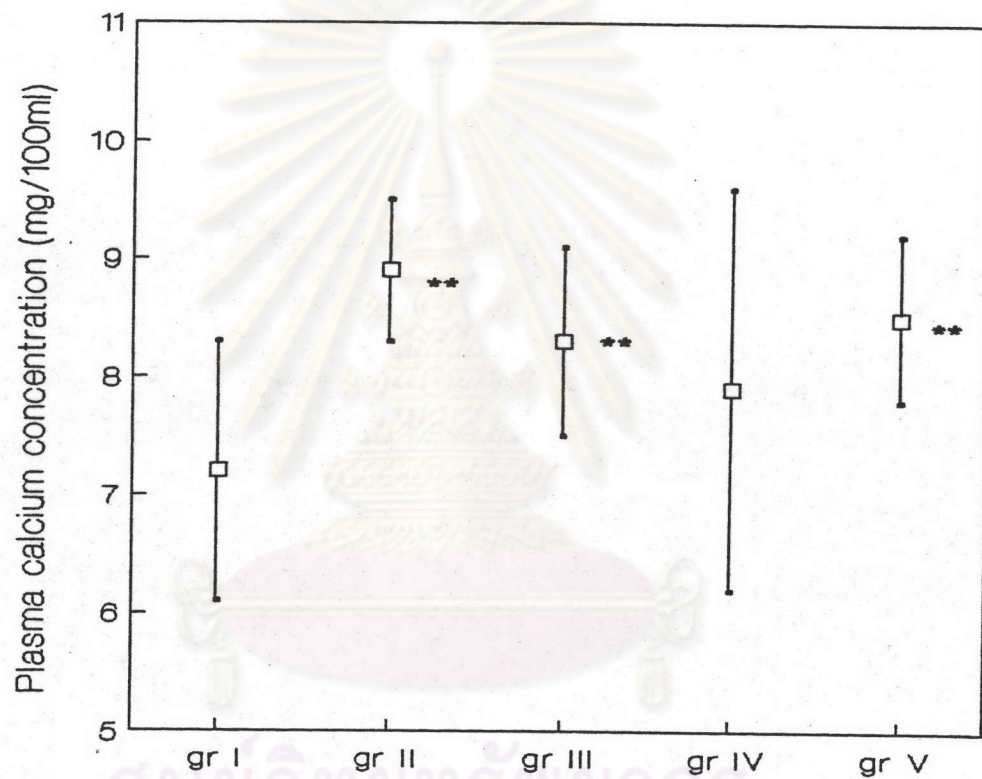
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst. gr V : biliary obst.+indomethacin

Figure 12 Comparison of plasma potassium concentration (P_K) in five groups of rats. Values are mean \pm S.D.



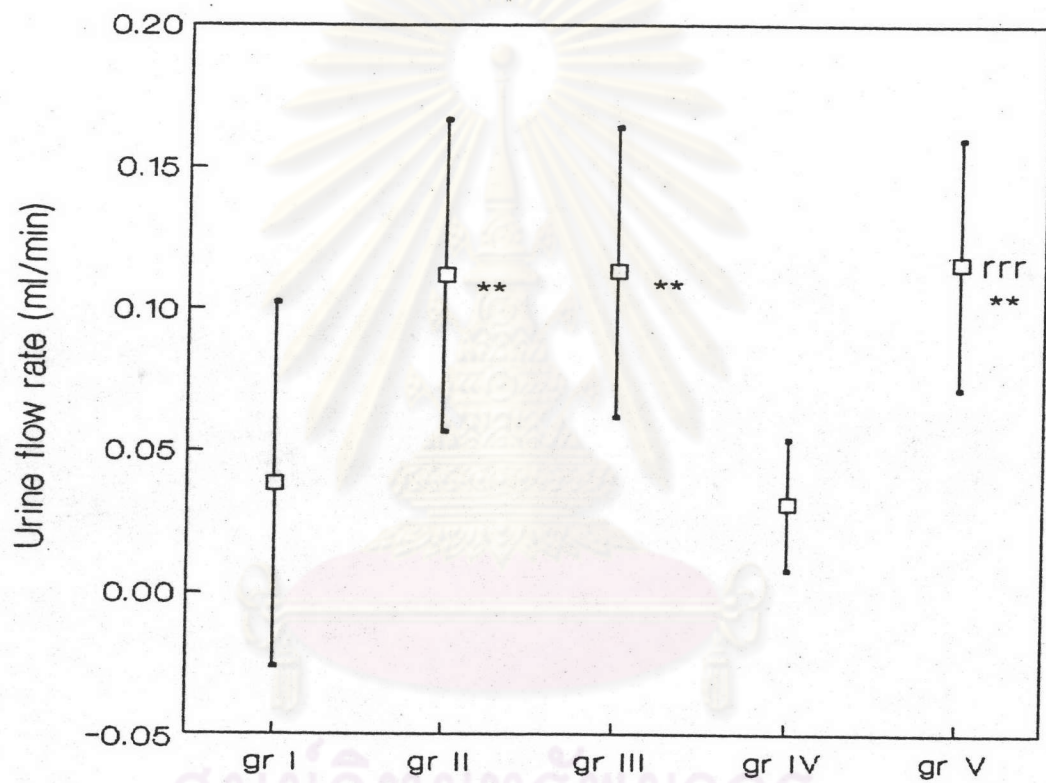
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 13 Comparison of plasma calcium concentration (P_{Ca}) in five groups of rats. The values are mean \pm S.D.



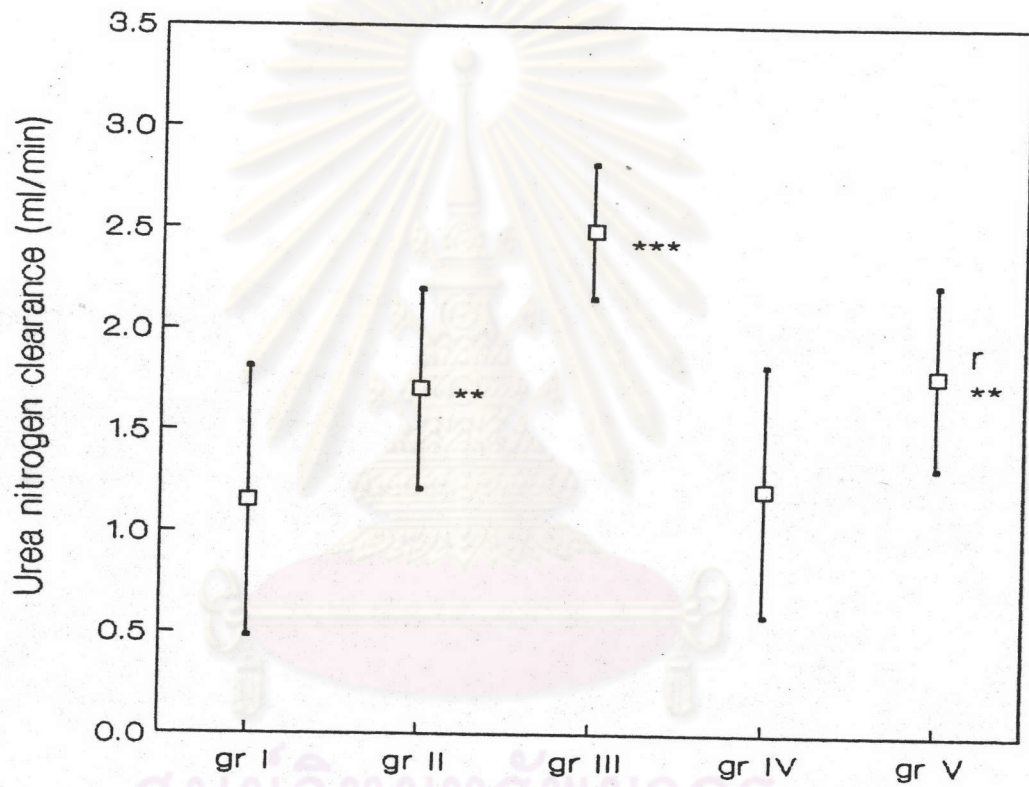
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 14 Comparison of urine flow rate (V) in five groups of rats. The values are mean \pm S.D.



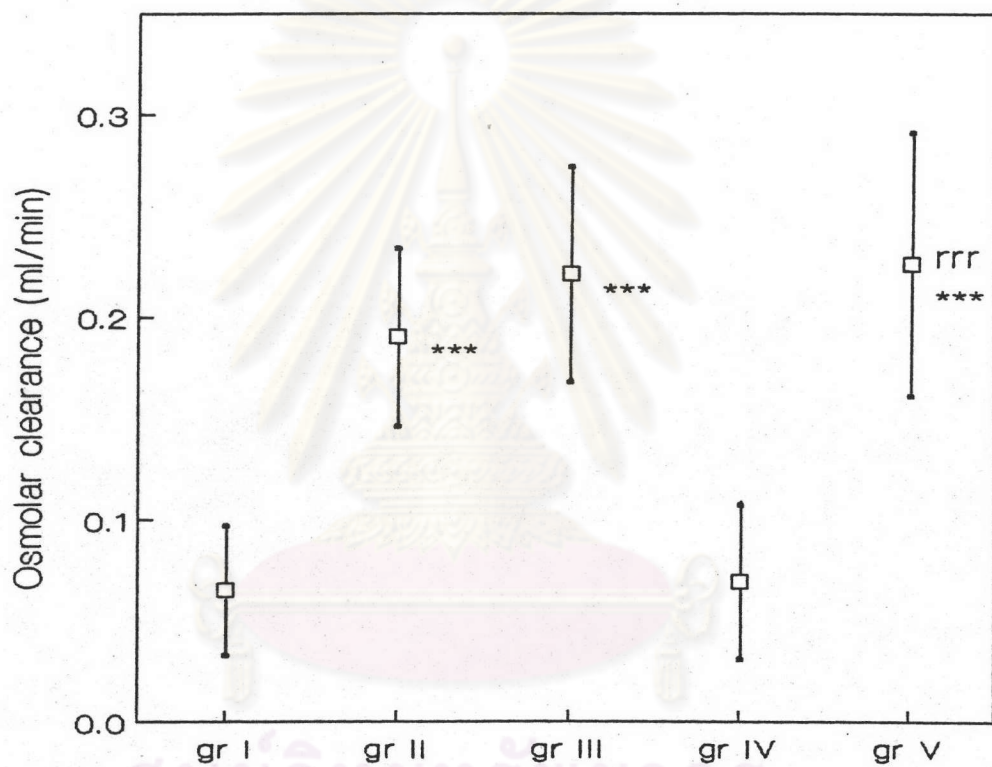
gr I : sham control, gr II : sham+vehicle,
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 15 Comparison of urea nitrogen clearance (C_{UN}) in five groups of rats. The values are mean \pm S.D.



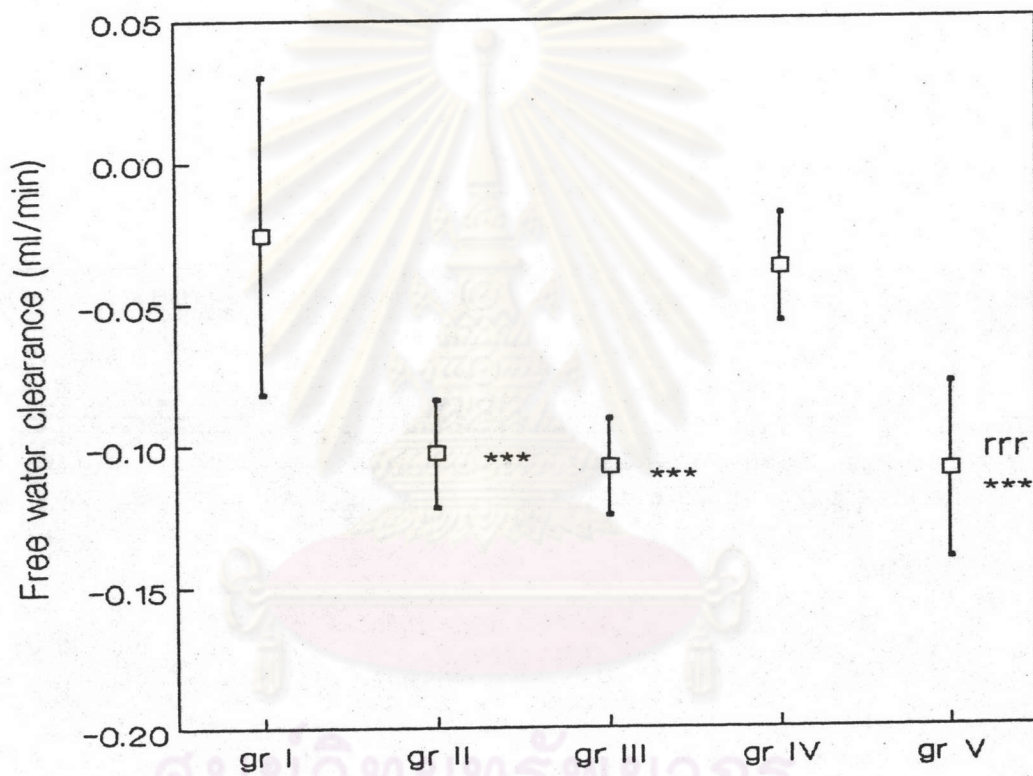
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 16 Comparison of osmolar clearance (C_{Osm}) in five groups of rats. Values are mean \pm S.D.



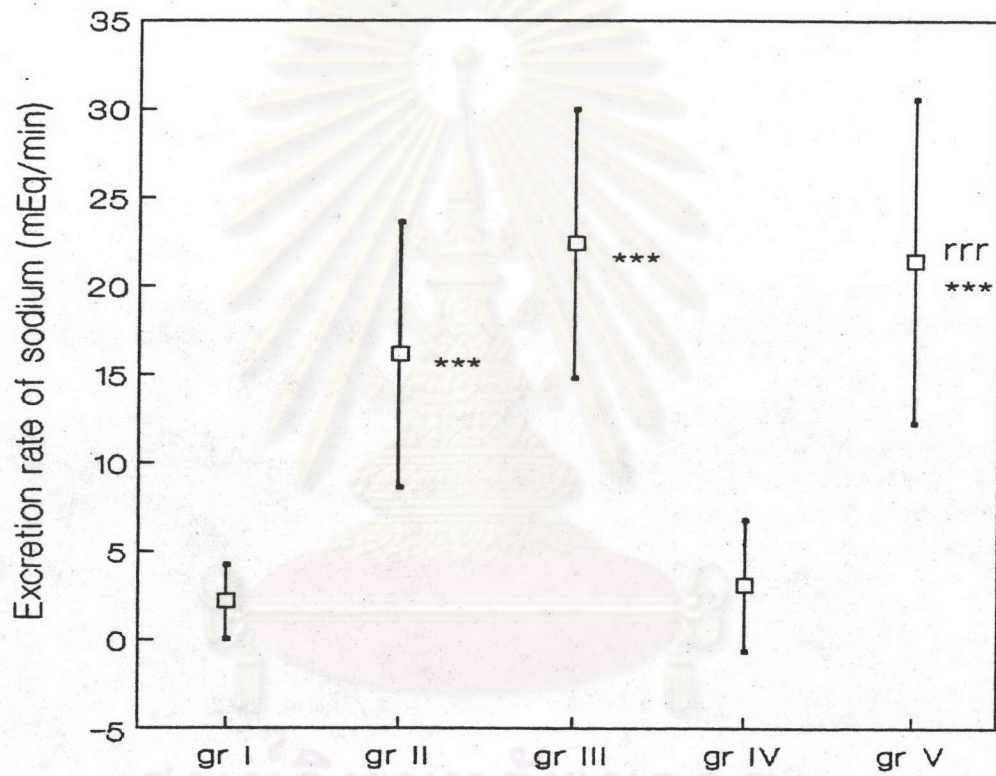
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 17 Comparison of free water clearance (C_{H_2O}) in five groups of rats. The values are mean \pm S.D.



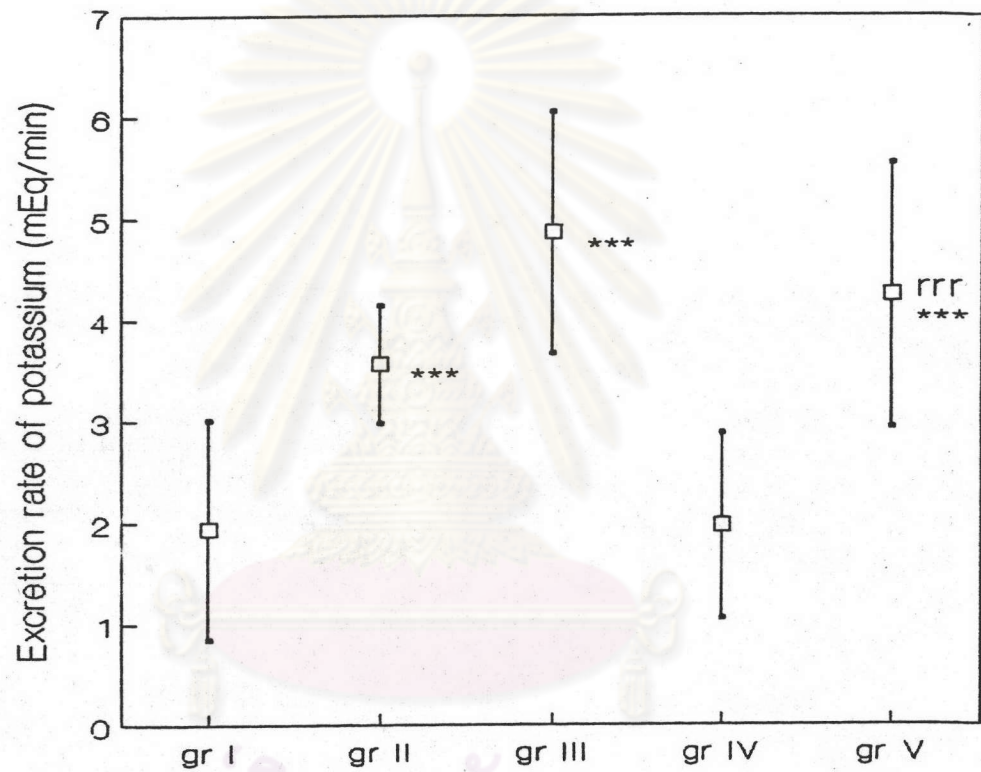
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 18 Comparison of excretion rate of sodium ($U_{Na} V$) in five groups of rats. The values are mean \pm S.D.



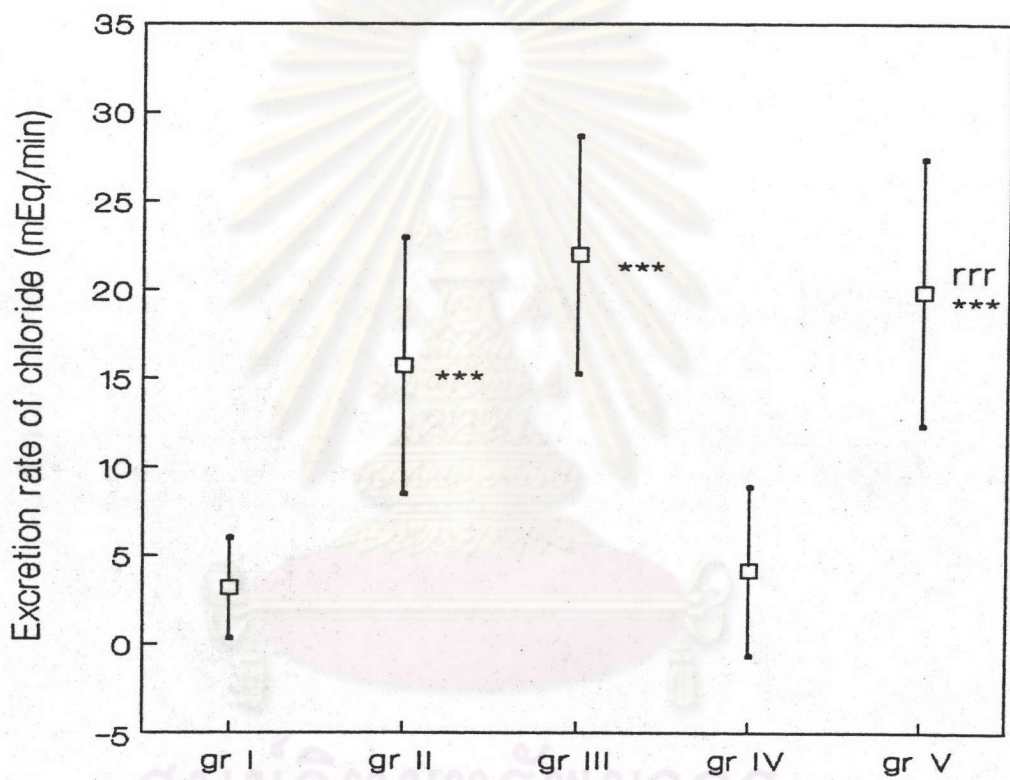
gr I : sham control, gr II : sham+vehicle
 gr III : sham+indomethacin, gr IV : biliary
 obst., gr V : biliary obst.+indomethacin

Figure 19 Comparison of excretion rate of potassium ($U_{K V}$) in five groups of rats. Values are mean \pm S.D.



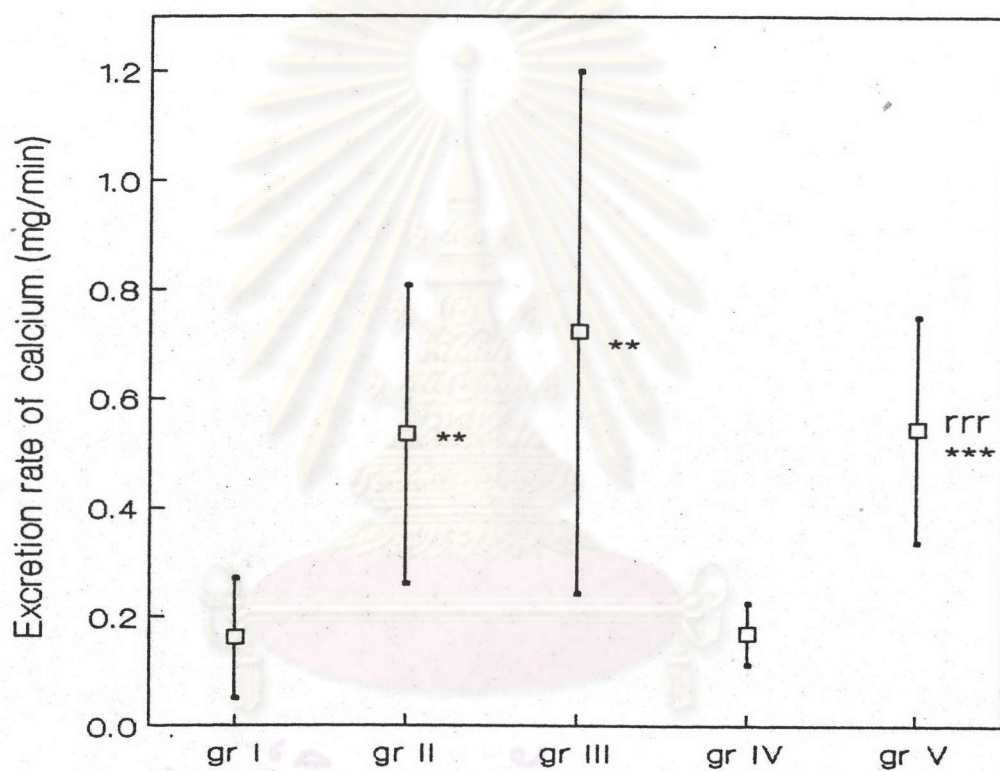
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 20 Comparison of excretion rate of chloride ($U_{Cl} V$) in five groups of rats. Values are mean \pm S.D.



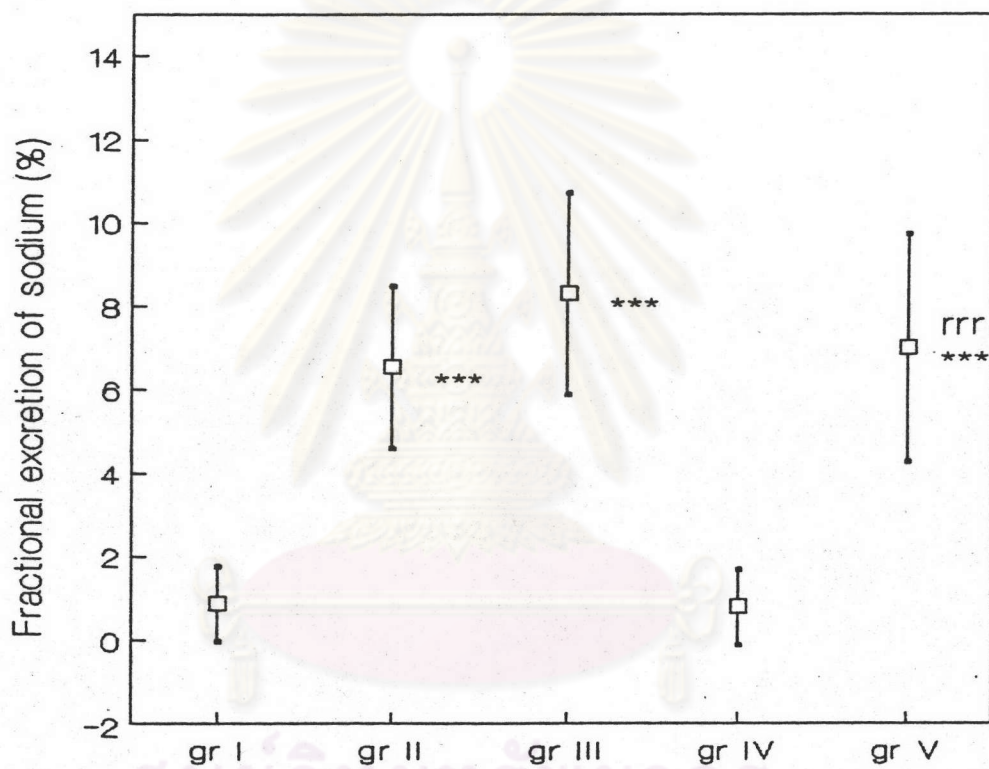
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 21 Comparison of excretion rate of calcium ($U_{Ca}V$) in five groups of rats. Values are mean \pm S.D.



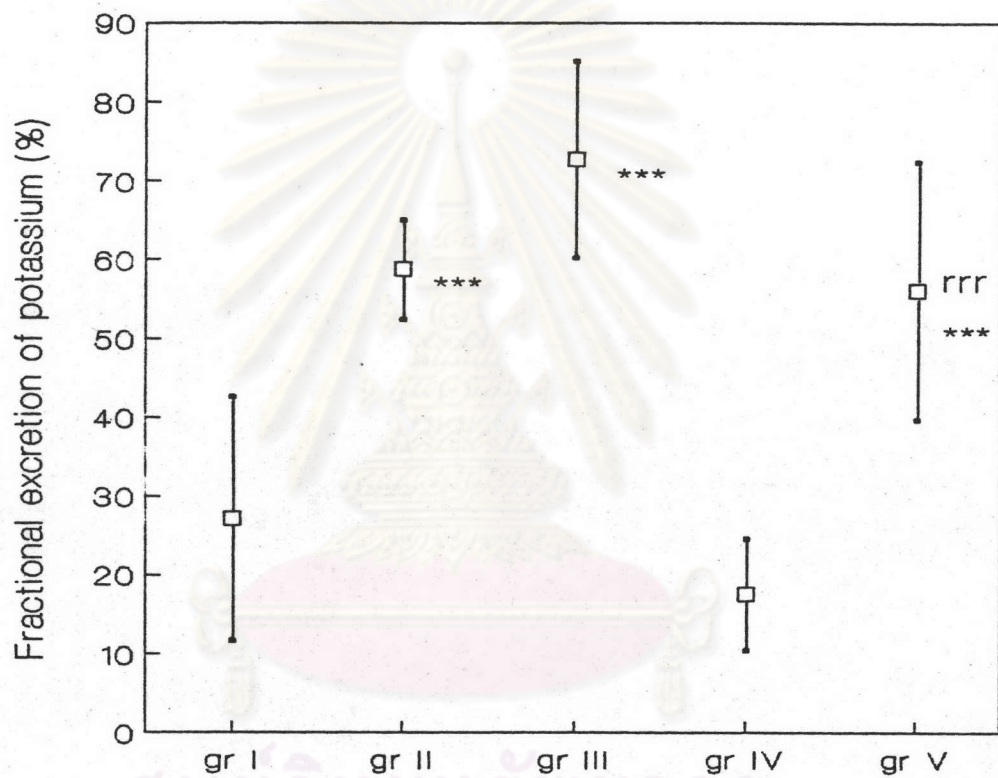
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 22 Comparison of fractional excretion of sodium (FE_{Na}) in five groups of rats. Values are mean \pm S.D.



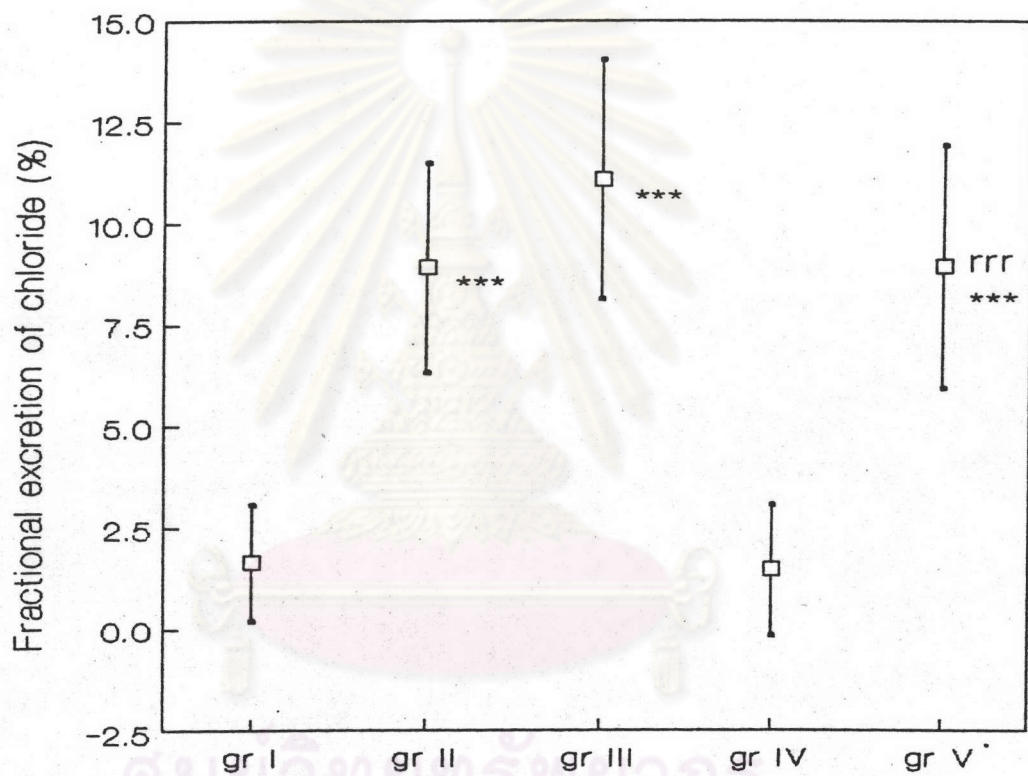
gr I : sham control, gr II : sham+vehicle
gr III : sham+indomethacin, gr IV : biliary
obst., gr V : biliary obst.+indomethacin

Figure 23 Comparison of fractional excretion of potassium (FE_K) in five groups of rats. Values are mean \pm S.D.



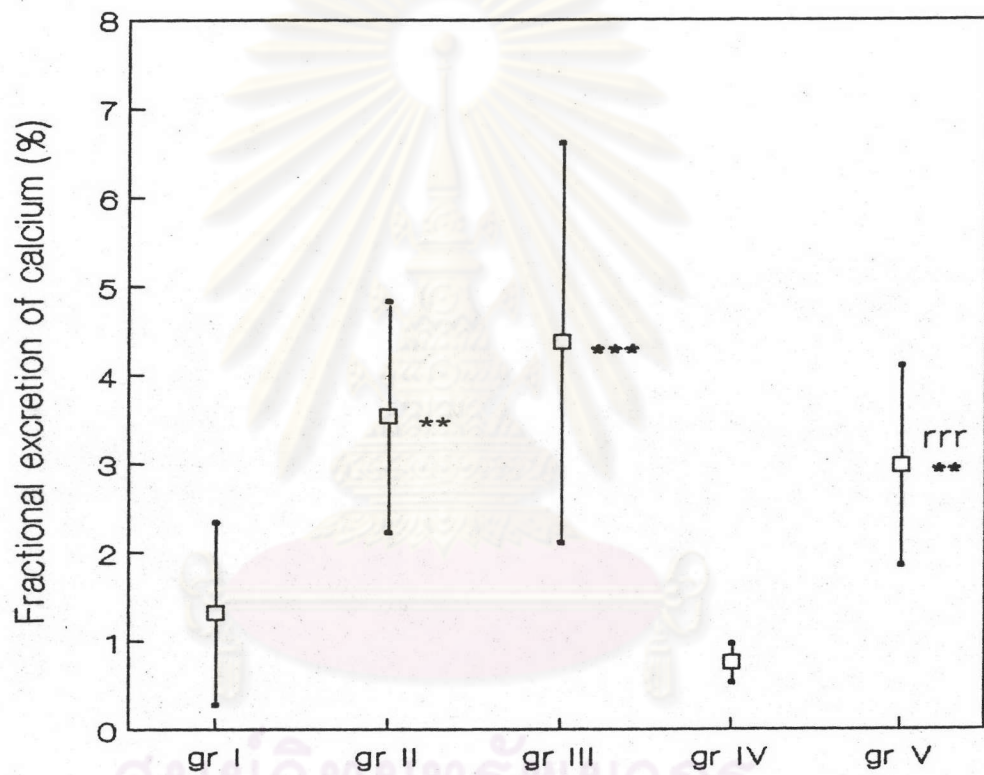
gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin

Figure 24 Comparison of fractional excretion of chloride (FE_{Cl}) in five groups of rats. Values are mean \pm S.D.



gr I :sham control, gr II :sham+vehicle
 gr III :sham+indomethacin, gr IV :biliary
 obst., gr V :biliary obst.+indomethacin

Figure 25 Comparison of fractional excretion of calcium (FE_{Ca}) in five groups of rats. Values are mean \pm S.D.



gr I :sham control, gr II :sham+vehicle
gr III :sham+indomethacin, gr IV :biliary
obst., gr V :biliary obst.+indomethacin