

CHAPTER IV

RESULTS

The effects of intrarenal arterial administration of Sch28080 on general circulation :-

The results are shown in Figure 1 and Table 1. After Sch 28080 administration, arterial blood pressure (MAP) significantly increased in control dogs (group I) ($P < 0.01$) and hypokalemic dogs (group II) ($P < 0.01$) but it did not significantly change in both groups of adrenalectomized dogs (group III and IV) when compared to the period given dimethyl sulfoxide (DMSO). However, significant increases of MAP ($P < 0.01$) were observed in group II and III after given Sch28080 when compared to the control period. Heart rate (HR) did not significantly change after given Sch28080 in all groups when compared to the period given DMSO, whereas a significant increase of hematocrit (Hct) ($P < 0.05$) was seen in hypokalemic adrenalectomized dogs (group IV).

The effects of intrarenal arterial administration of Sch28080 on renal hemodynamics:-

The effects of Sch28080 administration on renal hemodynamics are shown in Table 2, 3 and Figure 2,3 and 4. It was found that within 40 min. after given Sch28080 in group I and II exhibited significant reductions of glomerular filtration rate (GFR) by 26% and 34% ($P < 0.05$) respectively; effective renal plasma flow (ERPF) by 25% ($P < 0.05$) and 40% ($P < 0.01$) respectively when compared to the period given DMSO. Nonsignificant reduction of GFR was noted but significant decreases in ERPF ($P < 0.05$) and ERBF ($P < 0.05$) were observed in group III. Urine flow rate (V) significantly decreased in group II and III ($P < 0.05$) but nonsignificantly decreased in group I given Sch28080 when compared to the

pretreated period. Filtration fraction (FF) of animals in group I and II did not alter while it tended to increase in group III. Renal vascular resistance (RVR) significantly increased by 44% ($P<0.05$) and 214% ($P<0.05$) after Sch28080 administration in group I and II respectively. While nonsignificant increases in group III and IV were recorded when compared to the pretreated period.

In group IV showed no changes of GFR, ERPF, ERBF and RVR while V and FF significantly increased ($P<0.05$) after given Sch28080.

The effects of intrarenal arterial administration of Sch28080 on urinary electrolyte excretion :-

Changes of urinary electrolyte excretion in animals treated with Sch28080 were shown in Table 4,5 and 6. It was noted in group II that plasma sodium concentration (Plasma Na^+) significantly increased ($P<0.01$) in DMSO treated period when compared to the control period and more significantly increased after given Sch28080 ($P<0.001$). This change was not apparent in other groups. Filterload of sodium showed significant fall in group I, II ($P<0.05$) and tended to decrease in group III. A significant reduction of urinary sodium excretion ($U_{\text{Na}}V$) was seen in group II and III ($P<0.05$) while fractional sodium excretion (FE_{Na}) significantly elevated in group II ($P<0.05$) and but not for in group III after given Sch28080. There were no changes in plasma Na^+ and filterload of Na in group IV while a significant increase of $U_{\text{Na}}V$ ($P<0.05$) was observed after Sch28080 administration (Figure 5) when compared to DMSO treated period.

Plasma potassium concentration (Plasma K^+) of group II significantly increased ($P<0.01$) with a significant decrease in urinary potassium excretion ($U_{\text{K}}V$) ($P<0.01$) and fractional excretion (FE_{K}) ($P<0.05$) after given Sch28080. However, the rise of plasma K^+ in group II was apparent with a reduction in filterload of K and a marked reduction in urinary potassium excretion ($U_{\text{K}}V$) ($P<0.01$). In group I, II and III showed decreases in filterload of K^+ and $U_{\text{K}}V$ while FE_{K} increased after Sch28080 injection. By contrast, significant decreases of plasma K^+ , while no change in filterload of K, $U_{\text{K}}V$ and FE_{K} were noted in group IV.

After given Sch28080, plasma chloride concentration (plasma Cl^-) did not alter in all groups when compared to the period given DMSO. In group I and II showed significant decrease in filterload of chloride ion but no change in urinary chloride excretion ($U_{\text{Cl}}V$) from pretreated period was noted. However, fractional chloride excretion (FE_{Cl}) significantly increased in group I but not for animals in group III after Sch28080 administration. In group IV, a significant increase of $U_{\text{Cl}}V$ ($P < 0.01$) coincided with increases in filterload of Cl^- and FE_{Cl} after Sch28080 administration.

The effects of intrarenal arterial administration of Sch28080 on urinary acid-base excretion :-

It was noted that the levels of blood pH, plasma bicarbonate concentration (plasma HCO_3^-) and base excess were high in furosemide-induced hypokalemic animals (Table 7). It was found that after intrarenal arterial injection of Sch28080, blood pH, plasma HCO_3^- and base excess did not alter in all groups. A decrease of urinary acid excretion (UAE) was observed in group I, II and III after Sch28080 injection. In group II and III showed significant reductions of urinary titratable acid excretion ($U_{\text{TA}}V$) by 23% and 52% respectively, urinary ammonium excretion ($U_{\text{NH}_4}V$) by 25% and 50% respectively and decreases in UAE by 24% and 51% respectively (Table 8 and Figure 6).

Observation in group IV showed that intrarenal arterial injection of Sch28080 did not affect on $U_{\text{TA}}V$, $U_{\text{NH}_4}V$ and UAE throughout the experimental period.

The effects of intrarenal arterial administration of Sch28080 on urinary water excretion :-

After intrarenal arterial injection of Sch28080, plasma osmolality (Posm) did not change within 40 min in all groups. However, significant increases of plasma and urine osmolality ($P < 0.05$) were seen at 60 min after Sch28080 injection in group II. Osmolar clearance (Cosm) significantly decreased in group I ($P < 0.05$) and tended to decrease in group II and III but significantly elevated in group IV when compared

to the period given DMSO after Sch28080 injection (Table 9). Fractional water excretion (FE_{H_2O}) showed no significant changes in all groups. However, a reduction of free water reabsorption was occurred in group I, II and III while it significantly elevated in group II ($P < 0.05$) after Sch28080 injection (Table 10).

Table 1 The effect of intrarenal arterial injection of Sch28080 on mean arterial pressure, heart rate and hematocrit.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Mean arterial pressure (mmHg)						
Control	127.0±8.4	123.0±9.0	128.0±9.0 ^{††}	135.7±11.8 [†]	137.7±10.5 ^{††}	130.7±10.1
Hypo K	100.8±9.1	104.2±9.7	108.6±8.3 ^{**}	110.3±8.6 ^{*††}	108.1±7.3 [*]	105.5±7.3
ADX	105.3±10.2	110.2±12.1	117.0±9.4 ^{**}	120.7±8.4 ^{**}	129.7±3.0 [*]	122.3±4.9
Hypo K+ADX	99.3±11.6	100.7±11.6	105.0±10.8	101.3±12.0	96.7±9.6	88.7±10.3 [†]
Heart rate (beats/min)						
Control	153±11	147±13	150±12	144±10 ^{**}	153±14	154±15
Hypo K	137±9	139±9	147±11	145±11	143±11	142±11
ADX	142±4	148±2	154±9	146±10	147±12	138±11
Hypo K+ADX	162±14	166±13	178±11	175±11	170±9	161±8
Hematocrit (%)						
Control	26.8±2.6	27.5±2.4	28.0±2.4	27.6±2.7	27.0±2.8	26.5±2.6
Hypo K	34.3±2.2	34.4±2.3	35.9±1.9	35.2±1.9	34.7±1.8	34.7±2.2
ADX	21.8±3.5	21.9±3.6	22.7±3.5	22.1±3.4	21.8±3.4	20.9±3.2
Hypo K+ADX	19.2±5.2	19.5±5.0	19.8±5.0 [†]	20.0±5.0 ^{††}	20.0±5.0 [*]	19.2±5.2

Values are mean±SEM. Hypo K, hypokalemic dogs ; ADX, adrenalectomized dogs ; Hypo K + ADX, hypokalemic adrenalectomized dogs ; DMSO, dimethyl sulfoxide.

Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; [†] P <0.05, ^{††} <0.01 compared with the period given DMSO .

Table 2 The effect of intrarenal arterial injection of Sch28080 on GFR, ERPF and ERBF.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Glomerular filtration rate (ml/min/kg.bw)						
Control	1.56±0.10	1.87±0.13 ^{***}	1.38±0.20 [†]	1.32±0.27	1.43±0.29	1.42±0.13 ^{††}
Hypo K	0.68±0.08	0.79±0.11	0.50±0.05 [†]	0.51±0.06	0.53±0.03 [†]	0.57±0.04 [†]
ADX	1.80±0.11	1.80±0.06	1.10±0.22 [*]	1.25±0.34	1.23±0.23 [*]	1.32±0.28
Hypo K+ADX	1.34±0.27	1.40±0.23	1.55±0.37	1.49±0.28	1.63±0.31	1.46±0.23
Renal plasma flow (ml/min/kg.bw)						
Control	4.31±0.90	4.53±0.84	3.30±0.58 ^{*†}	3.92±1.20	3.85±0.86	3.04±0.47 [†]
Hypo K	2.90±0.30	2.75±0.34	1.59±0.21 ^{***††}	1.62±0.26	1.63±0.13 ^{***†}	1.70±0.18 [*]
ADX	8.91±1.00	8.83±1.08	3.90±0.92 ^{*†}	5.70±1.62 [*]	5.78±1.20 ^{***†}	5.31±0.95 ^{***†}
Hypo K+ADX	7.89±1.92	8.31±2.0	7.56±1.58	6.10±2.02	7.51±1.88	7.96±1.99
Renal blood flow (ml/min/kg.bw)						
Control	5.84±1.09	6.20±1.07 [*]	4.61±0.79 ^{*†}	5.39±1.57	5.33±1.19	4.12±0.58 ^{*†}
Hypo K	4.38±0.33	4.19±0.50	2.50±0.34 ^{***††}	2.56±0.47 [*]	2.51±0.21 ^{***†}	2.63±0.31 [*]
ADX	11.11±1.75	11.43±1.46	5.10±1.24 ^{*†}	7.66±2.38 [*]	7.63±1.75 ^{*†}	6.89±1.43 ^{***†}
Hypo K+ADX	9.82±2.51	10.53±2.86	9.37±1.88	7.36±2.18	9.55±2.61	10.03±2.75

Values are mean±SEM. Hypo K, hypokalemic dogs ; ADX, adrenalectomize dogs ; Hypo K + ADX, hypokalemic adrenalectomized dogs;

GFR, glomerular filtration rate ; ERPF, effective renal plasma flow ; ERBF, effective renal blood flow ; DMSO, dimethyl sulfoxide.

Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; † P <0.05, †† P <0.01 compared with the period given DMSO .

Table 3 The effect of intrarenal arterial injection of Sch28080 on V, FF and RVR.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Urine flow rate ($\mu\text{l}/\text{min}/\text{kg}.\text{bw}$)						
Control	33 \pm 4	51 \pm 7 [*]	37 \pm 7	44 \pm 14	45 \pm 19	42 \pm 12
Hypo K	105 \pm 23	110 \pm 26	82 \pm 18 ^{*†}	92 \pm 15	108 \pm 25	84 \pm 17
ADX	36 \pm 9	40 \pm 7	29 \pm 8 [†]	34 \pm 4	38 \pm 3	34 \pm 6
Hypo K+ADX	69 \pm 24	73 \pm 20	75 \pm 18	99 \pm 20 [†]	108 \pm 27	91 \pm 28
Filtration fraction (%)						
Control	40.74 \pm 5.72	45.41 \pm 6.01	44.30 \pm 6.41	37.15 \pm 3.75	39.75 \pm 5.09	48.70 \pm 3.64
Hypo K	23.59 \pm 1.32	29.27 \pm 2.13 ^{**}	32.30 \pm 2.70 ^{**}	34.30 \pm 4.49 [*]	33.10 \pm 2.96 [*]	36.83 \pm 6.62
ADX	20.66 \pm 1.56	21.84 \pm 2.34	29.98 \pm 4.78	26.17 \pm 6.02	23.03 \pm 3.04	26.06 \pm 3.63
Hypo K+ADX	24.53 \pm 9.32	21.37 \pm 5.77	23.41 \pm 5.26	32.01 \pm 6.62	25.80 \pm 5.22 [†]	26.50 \pm 10.48
Renal vascular resistance (mmHg.min. kg.bw/ml)						
Control	25.56 \pm 5.25	22.89 \pm 4.38	32.68 \pm 7.26 [†]	33.99 \pm 9.11	32.99 \pm 9.29	35.78 \pm 7.63 [†]
Hypo K	25.86 \pm 3.93	28.87 \pm 7.50	48.44 \pm 8.40 ^{**†}	50.83 \pm 9.91	44.89 \pm 5.24 ^{**}	43.17 \pm 5.62
ADX	9.88 \pm 1.22	10.17 \pm 1.03	28.39 \pm 6.94	24.62 \pm 8.20	22.52 \pm 6.63	21.14 \pm 4.30
Hypo K+ADX	17.18 \pm 8.42	14.55 \pm 5.81	15.24 \pm 5.75	22.11 \pm 8.94	14.84 \pm 5.48	14.66 \pm 6.96

Values are mean \pm SEM. Hypo K, hypokalemic dogs ; ADX, adrenalectomized dogs ; Hypo K + ADX, hypokalemic adrenalectomized dogs ;

V, urine flow rate ; FF, filtration fraction ; RVR, renal vascular resistance ; DMSO, dimethyl sulfoxide.

Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; [†] P <0.05, ^{††} P <0.01 compared with the period given DMSO .

Table 4 The effect of intrarenal arterial injection of Sch28080 on sodium excretion.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Plasma sodium concentration (mEq/L)						
Control	139.4±2.1	137.7±3.3	137.0±2.8	138.4±2.8	138.8±2.9	139.4±3.1
Hypo K	132.3±1.5	134.3±1.3**	136.0±1.4***†	133.2±2.4	136.5±1.9*	136.5±1.9***†
ADX	129.4±2.6	130.6±2.5	130.0±2.2	129.6±2.1	130.2±3.2	131.0±1.5
Hypo K+ADX	136.2±2.6	137.6±2.8**	136.6±3.6	138.0±2.3**	138.2±1.9	137.4±2.7
Filterload of sodium (µEq/min/kg.bw)						
Control	217.3±12.7	256.1±14.7**	189.1±27.4†	182.2±38.5	198.7±41.6	198.1±20.2††
Hypo K	84.5±6.7	100.4±13.0	62.5±5.9†	66.7±9.8	67.9±4.9†	74.9±5.1†
ADX	232.8±15.5	235.7±11.4	141.3±27.7*	163.3±46.7	162.6±33.2*	173.2±38.1
Hypo K+ADX	183.0±37.3	192.8±32.7	213.8±51.5	205.9±38.6	226.1±42.8	201.2±31.6
Urinary sodium excretion (µEq/min/kg.bw)						
Control	4.61±1.12	6.44±1.39*	5.28±1.63	6.43±2.36	5.84±2.30	4.61±0.81
Hypo K	7.02±1.52	8.52±2.56	6.48±2.20†	8.18±1.56	10.02±2.90†	6.67±1.67
ADX	4.87±0.77	5.74±0.50	3.82±0.61†	4.82±0.34	5.22±0.41	4.62±0.93
Hypo K+ADX	5.60±3.06	6.26±2.65	5.91±1.50	10.62±2.60*†	12.64±3.84*†	8.72±2.47
Fractional sodium excretion (%)						
Control	2.09±0.45	2.45±0.44	2.66±0.53	3.14±0.69*	2.56±0.47	2.28±0.18
Hypo K	8.29±2.06	8.77±2.73	9.75±3.05	13.63±3.75†	14.73±4.59†	9.14±2.75
ADX	2.17±0.24	2.45±0.21	2.84±0.29	3.60±0.68	3.65±0.70	2.78±0.44
Hypo K+ADX	2.72±1.10	3.00±0.93	2.72±0.35	5.29±1.14	5.45±1.04	4.25±0.84

Values are mean±SEM. Hypo K, hypokalemic dogs; ADX, adrenalectomized dogs; Hypo K + ADX, hypokalemic adrenalectomized dogs; DMSO, dimethyl sulfoxide. Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; † P <0.05, †† P <0.01 compared with the period given DMSO .

Table 5 The effect of intrarenal arterial injection of Sch28080 on potassium excretion.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Plasma potassium concentration (mEq/L)						
Control	3.4±0.2	3.4±0.2	3.5±0.2	3.6±0.1	3.5±0.2	3.7±0.1 [†]
Hypo K	1.7±0.2	1.7±0.2	1.8±0.2	1.8±0.2 ^{††}	1.8±0.2	1.9±0.2
ADX	3.6±0.1	3.6±0.1	3.8±0.1	3.6±0.1	3.8±0.1	3.9±0.2
Hypo K+ADX	2.2±0.2	2.1±0.2	1.9±0.2	1.9±0.2 [†]	2.0±0.3	2.1±0.3
Filterload of potassium (μEq/min/kg.bw)						
Control	5.33±0.36	6.34±0.38 ^{***}	4.70±0.60 [†]	4.77±1.00	5.06±1.03	5.22±0.52 [†]
Hypo K	1.14±0.14	1.18±0.20	0.85±0.11	0.97±0.20	0.95±0.15	1.06±0.16
ADX	6.49±0.49	6.51±0.21	4.14±0.84 [*]	4.53±1.22	4.73±0.93 [*]	5.21±1.15
Hypo K+ADX	3.18±0.97	3.09±0.79	3.23±1.17	3.09±0.93	3.29±0.79	3.11±0.69
Urinary potassium excretion (μEq/min/kg.bw)						
Control	1.09±0.18	1.32±0.23	1.10±0.05	1.21±0.18	1.14±0.16	1.18±0.14
Hypo K	0.62±0.07	0.66±0.08	0.46±0.07 ^{††}	0.59±0.11	0.62±0.08	0.56±0.09
ADX	1.64±0.44	1.57±0.29	1.09±0.33	1.60±0.35	1.51±0.28	1.27±0.23
Hypo K+ADX	0.97±0.29	1.03±0.28	0.81±0.19	1.03±0.24	1.04±0.22	0.78±0.15
Fractional potassium excretion (%)						
Control	20.99±4.01	21.43±4.19	25.16±3.55	21.44±4.65	24.52±3.88	23.63±3.61
Hypo K	58.61±10.71	60.48±12.95	62.68±14.02	69.36±13.31 [†]	72.75±13.12 [†]	56.51±10.18
ADX	24.25±6.49	24.12±4.75	27.36±5.39	38.20±8.91	32.85±5.98	27.31±7.16
Hypo K+ADX	33.30±7.05	34.52±6.67	28.96±5.08	36.64±5.84	33.85±4.64	27.27±4.79

Values are mean±SEM. Hypo K, hypokalemic dogs; ADX, adrenalectomized dogs; Hypo K + ADX, hypokalemic adrenalectomized dogs; DMSO, dimethyl sulfoxide. Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period; [†] P<0.05, ^{††} P<0.01 compared with the period given DMSO.

Table 6 The effect of intrarenal arterial injection of Sch28080 on chloride excretion.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Plasma chloride concentration (mEq/L)						
Control	115.6±1.6	116.0±2.0	116.8±0.4	116.2±1.1	116.6±1.4	120.4±1.0*
Hypo K	99.2±2.0	100.2±1.3	99.2±3.2	104.0±1.9	103.3±2.7	106.2±1.6*†
ADX	108.6±4.9	104.6±5.3*	103.6±2.9	105.8±4.9	106.4±4.0	106.4±3.9
Hypo K+ADX	105.8±3.3	104.3±2.9	103.0±2.1	104.8±3.1	105.6±2.8	106.4±3.3
Filterload of chloride (µEq/min/kg.bw)						
Control	180.5±11.1	216.3±14.2**	161.4±23.6†	153.4±32.8	166.1±33.5	170.7±15.9†
Hypo K	67.6±7.5	79.7±11.2	48.6±4.0†	53.8±7.1	54.2±2.8	60.5±4.0
ADX	195.2±14.0	195.1±15.4	122.4±25.5	140.5±29.0	129.8±24.8**	137.3±27.6
Hypo K+ADX	142.1±28.7	146.3±25.2	159.6±37.2	156.1±29.2	171.3±29.7	155.3±23.3
Urinary chloride excretion (µEq/min/kg.bw)						
Control	3.09±0.73	4.30±1.03	3.27±0.84	4.30±2.08	4.14±2.10	3.71±1.08
Hypo K	5.90±1.91	6.79±2.32	5.11±1.71	6.43±1.59	8.07±2.51*†	5.19±1.31
ADX	3.98±0.52	4.87±0.58	3.55±0.56	4.02±0.62	4.68±0.48	4.52±0.91
Hypo K+ADX	4.47±3.27	5.08±2.94	6.16±2.93	9.17±3.12***††	11.41±4.52*†	9.97±4.75
Fractional chloride excretion (%)						
Control	1.71±0.38	1.96±0.40	2.09±0.42	2.41±0.57*	2.17±0.60	2.17±0.50
Hypo K	8.88±2.70	9.59±3.37	11.02±3.62	13.98±4.48†	15.90±5.39	9.17±2.83
ADX	2.07±0.29	2.38±0.32	3.14±0.46	2.92±0.47	4.09±0.82*	3.73±0.55*
Hypo K+ADX	2.51±1.64	3.08±1.58**	3.49±1.39	5.90±1.78*	6.04±1.50*†	5.73±2.03

Values are mean±SEM. Hypo K, hypokalemic dogs; ADX, adrenalectomized dogs; Hypo K + ADX, hypokalemic adrenalectomized dogs; DMSO, dimethyl sulfoxide. Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; † P <0.05, †† P <0.01 compared with the period given DMSO .

Table 7 The effect of intrarenal arterial injection of Sch28080 on blood pH, plasma bicarbonate and base excess.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Blood pH						
Control	7.32±0.01	7.29±0.02	7.29±0.01	7.30±0.01	7.29±0.01	7.29±0.02
Hypo K	7.39±0.03	7.38±0.03	7.37±0.03	7.37±0.03	7.37±0.02	7.34±0.03
ADX	7.31±0.03	7.29±0.04	7.30±0.02	7.30±0.03	7.29±0.04	7.30±0.04
Hypo K+ADX	7.37±0.02	7.37±0.02	7.37±0.01	7.35±0.02	7.34±0.02	7.34±0.01
Plasma bicarbonate (mmol/L)						
Control	18.4±0.8	17.9±0.6	17.5±0.7 [*]	17.4±0.7	17.3±0.5	16.2±0.7 [*]
Hypo K	22.8±1.1	22.6±1.0	22.1±1.0	21.8±1.2	21.2±1.1 [*]	21.3±1.0
ADX	19.1±1.4	20.2±1.5 [*]	19.5±1.6	19.5±1.6	19.0±1.6	18.8±1.7
Hypo K+ADX	20.1±2.7	20.1±2.6	18.9±2.1	19.1±2.1	19.2±2.4	19.3±2.2
Base excess (mmol/L)						
Control	-6.6±0.8	-7.5±0.7 ^{**}	-7.9±0.7 ^{**}	-7.8±0.7 [*]	-8.0±0.5 [*]	-9.1±0.6 ^{**}
Hypo K	-1.3±1.5	-1.2±1.4	-2.0±1.1	-2.5±1.3	-3.0±1.2 [*]	-3.5±1.0
ADX	-5.6±1.6	-5.4±1.5	-5.8±1.5	-5.7±1.5	-6.6±1.4	-6.6±1.4
Hypo K+ADX	-4.2±2.4	-4.3±2.4	-5.4±2.0	-5.4±1.9	-5.5±2.3	-5.5±2.1

Values are mean±SEM. Hypo K, hypokalemic dogs ; ADX, adrenalectomized dogs ; Hypo K + ADX, hypokalemic adrenalectomized dogs ; DMSO, dimethyl sulfoxide.

Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; † P <0.05 compared with the period given DMSO .

Table 8 The effect of intrarenal arterial injection of Sch28080 on $U_{TA,V}$, $U_{NH_4 V}$ and UAE

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Urinary titratable acid excretion ($\mu\text{Eq}/\text{min}/\text{kg}.\text{bw}$)						
Control	0.65±0.10	0.65±0.11	0.61±0.16	0.64±0.12	0.60±0.11	0.77±0.21
Hypo K	0.42±0.07	0.45±0.06	0.33±0.05	0.38±0.03	0.44±0.05	0.48±0.06
ADX	1.06±0.17	1.06±0.17	0.67±0.28	0.54±0.21 ^{**††}	0.57±0.20 ^{**††}	0.71±0.26
Hypo K+ADX	0.72±0.18	0.67±0.15	0.58±0.09	0.55±0.08	0.66±0.10	0.83±0.09
Urinary ammonium excretion ($\mu\text{Eq}/\text{min}/\text{kg}.\text{bw}$)						
Control	0.70±0.13	0.77±0.13	0.63±0.19	0.54±0.15	0.65±0.21	0.75±0.16
Hypo K	0.51±0.09	0.56±0.11	0.39±0.07 ^{*†}	0.45±0.05	0.48±0.10	0.49±0.05
ADX	1.10±0.16	1.13±0.15	0.73±0.18	0.55±0.14 ^{*†}	0.61±0.14 ^{*†}	0.72±0.18
Hypo K+ADX	0.70±0.15	0.69±0.13	0.67±0.12	0.66±0.07	0.77±0.15	0.78±0.24
Urinary acid excretion ($\mu\text{Eq}/\text{min}/\text{kg}.\text{bw}$)						
Control	1.35±0.22	1.42±0.22	1.24±0.36	1.18±0.25	1.25±0.30	1.52±0.36
Hypo K	0.93±0.14	1.01±0.16	0.72±0.11 [†]	0.83±0.07	0.92±0.15	0.97±0.09
ADX	2.15±0.27	2.17±0.28	1.40±0.45	1.09±0.34 ^{*†}	1.18±0.34 ^{*†}	1.43±0.42
Hypo K+ADX	1.42±0.31	1.36±0.25	1.25±0.20	1.20±0.14	1.43±0.23	1.61±0.32

Values are mean±SEM. Hypo K, hypokalemic dogs ; ADX, adrenalectomized dogs ; Hypo K + ADX, hypokalemic adrenalectomized dogs; DMSO, dimethyl sulfoxide., $U_{TA,V}$, Urinary titratable acid excretion, $U_{NH_4 V}$, Urinary ammonium excretion ; UAE, Urinary acid excretion Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; † P<0.05, †† P <0.01 compared with the period given DMSO .

Table 9 The effect of intrarenal arterial injection of Sch28080 on Posm Uosm and Cosm.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Plasma osmolality (mOsm/kg)						
Control	297±2	299±2	300±2	300±3	300±3	301±2 [*]
Hypo K	287±4	291±4 ^{**}	292±3	291±3	295±4 ^{***†}	296±3 ^{**††}
ADX	281±7	281±6	283±6	281±6	280±8	283±7
Hypo K+ADX	289±6	289±7	292±6	291±5	291±5	295±5 ^{*†}
Urine osmolality (mOsm/kg)						
Control	540±108	453±80	456±51	434±47	441±70	441±86
Hypo K	213±27	210±24	221±23	238±22	229±18 [†]	217±26
ADX	901±180	801±115	701±82	638±112	575±73	602±59
Hypo K+ADX	340±54	316±51	325±48	331±41	331±30	328±28
Osmolar clearance (µl/min/kg.bw)						
Control	58±10	74±14	58±14 [†]	64±19	59±18	53±8
Hypo K	108±31	150±68	107±43	134±61	128±44	113±52
ADX	100±16	103±7	70±19 [*]	76±14 ^{**}	78±12 ^{**}	73±16 ^{**}
Hypo K+ADX	80±32	80±26	85±25	111±25 [†]	126±37 [†]	107±39

Values are mean±SEM. Hypo K, hypokalemic dogs ; ADX, adrenalectomize dogs ; Hypo K + ADX, hypokalemic adrenalectomized dogs ; DMSO, dimethyl sulfoxide ; Posm, Plasma osmolality ; Uosm, Urine osmolality ; Cosm, Osmolar clearance .

Significant difference values using pair t-test, * P<0.05, ** P<0.01 compared with the control period ; † P <0.05, †† P <0.01 compared with the period given DMSO .

Table 10 The effect of intrarenal arterial injection of Sch28080 on FE_{H_2O} , C_{H_2O} and free water reabsorption.

	Control	DMSO	Sch28080 + DMSO			
			20 min	40 min	60 min	120 min
Fractional water excretion (%)						
Control	2.18±0.36	2.74±0.41*	2.73±0.36	3.09±0.32*	2.83±0.50	2.91±0.63
Hypo K	15.90±2.87	14.68±3.15	16.23±2.95	19.32±4.01	21.32±5.57	15.21±3.46
ADX	2.04±0.58	2.24±0.43	2.67±0.47	3.42±0.72	3.47±0.61	2.83±0.54
Hypo K+ADX	5.09±1.28	5.20±0.87	5.02±0.71	7.27±1.73	6.68±0.96	6.01±1.02
Free water clearance (µl/min/kg.bw)						
Control	-25±10	23±13	-21±9	-20±8	-14±7	-11±8
Hypo K	-2±26	-40±64	-26±42	-43±54	-20±39	-29±54
ADX	-63±6	-64±3	-41±12*	-42±13*	-40±10**	-40±11*
Hypo K+ADX	-11±11	-7±11	-9±11	-12±13	-18±13†	-16±11
Free water reabsorption (µl/min/kg.bw)						
Control	25±10	23±13	21±9	20±8	14±7	11±8
Hypo K	2±26	40±64	26±42	43±54	20±39	29±54
ADX	63±6	64±3	41±12*	42±13*	40±10**	40±11*
Hypo K+ADX	11±11	7±11	9±11	12±13	18±13†	16±11

Values are mean±SEM. Hypo K, hypokalemic dogs ; ADX, adrenalectomize dogs ; Hypo K + ADX, hypokalemic adrenalectomized dogs ; DMSO, dimethyl sulfoxide ; FE_{H_2O} , fractional water excretion ; C_{H_2O} , free water clearance.

Significant difference values using pair t-test, * $P < 0.05$, ** $P < 0.01$ compared with the control period ; † $P < 0.05$, compared with the period given DMSO .

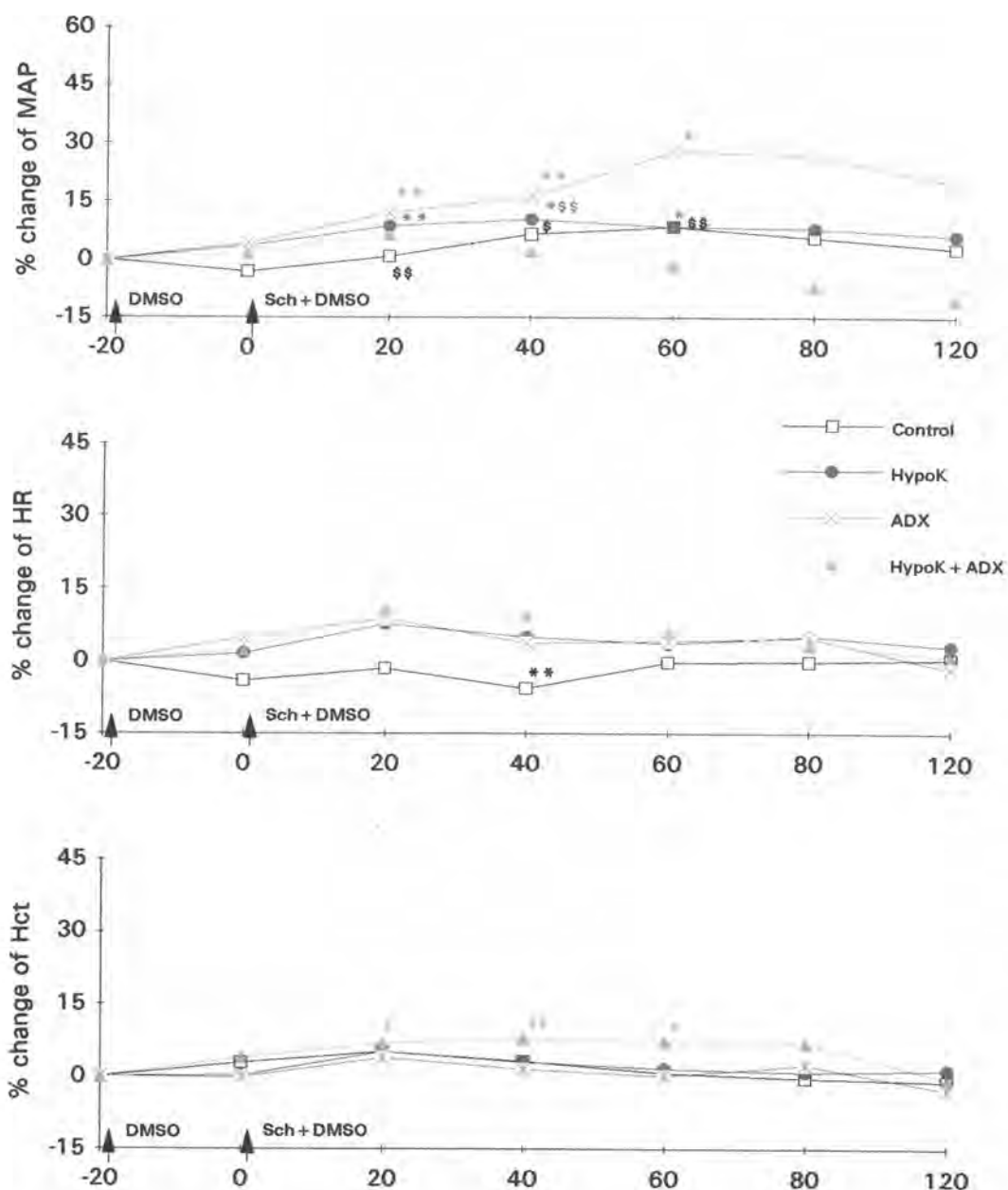


Figure 1 Percentage of changes of the mean arterial pressure (MAP), heart rate (HR) and hematocrit (Hct) after intrarenal arterial injection of Sch28080 in the control group, hypokalemic group (Hypo K), adrenalectomized group (ADX) and hypokalemic adrenalectomized group (Hypo K + ADX). Significant difference values using pair t-test * $P < 0.05$, ** $P < 0.01$, compared with the control period; \$ $P < 0.05$, compared with the period given dimethyl sulfoxide (DMSO).

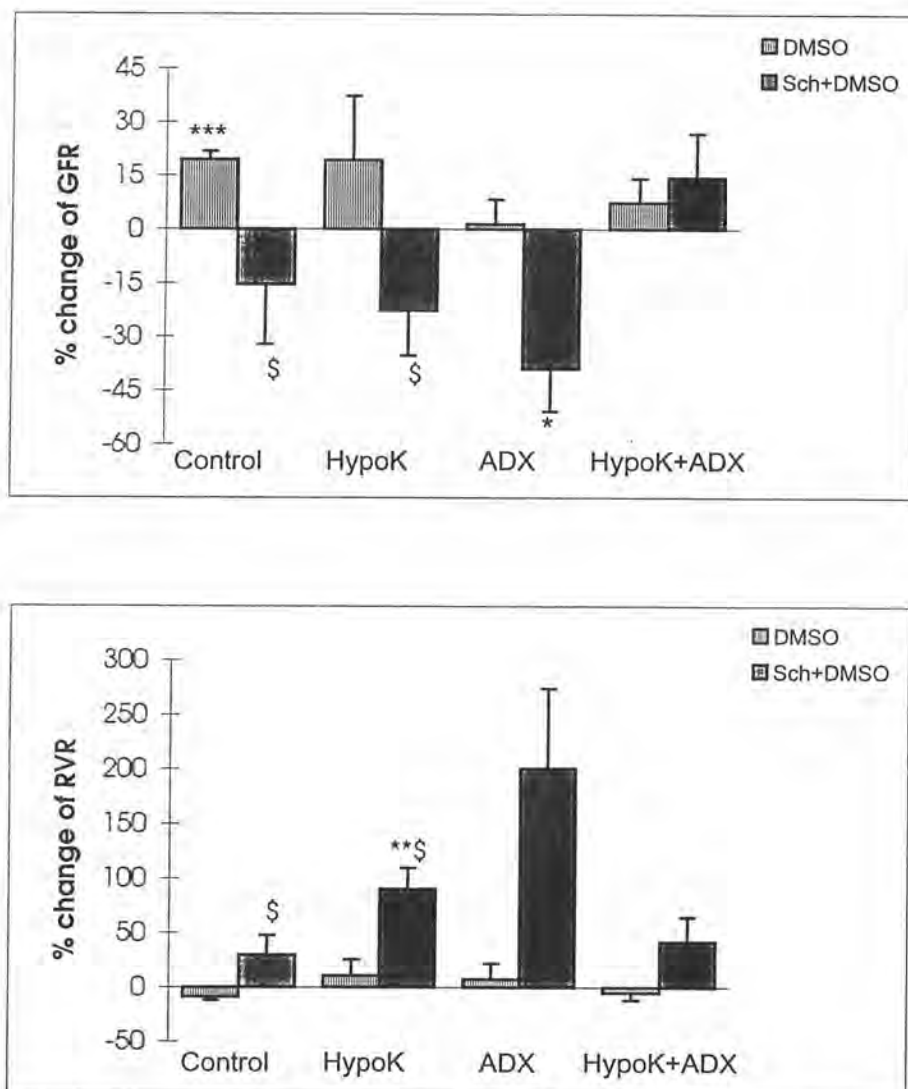


Figure 2 Percentage of changes of the glomerular filtration rate (GFR) and the renal vascular resistance within 40 min. after intrarenal arterial injection of Sch28080 in the control group, hypokalemic group (Hypo K), adrenalectomized group (ADX) and hypokalemic adrenalectomized group (Hypo K + ADX). Significant difference values using pair t-test * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ compared with the control period; \$ $P < 0.05$, compared with the period given dimethyl sulfoxide (DMSO).

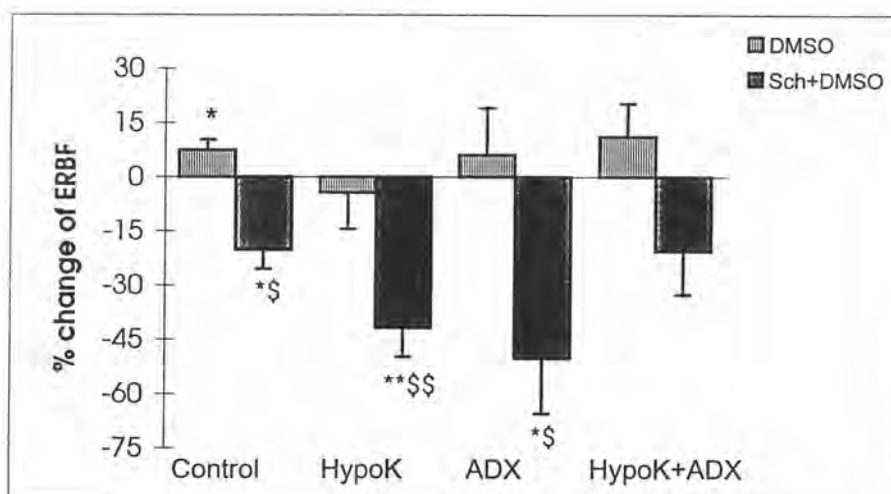
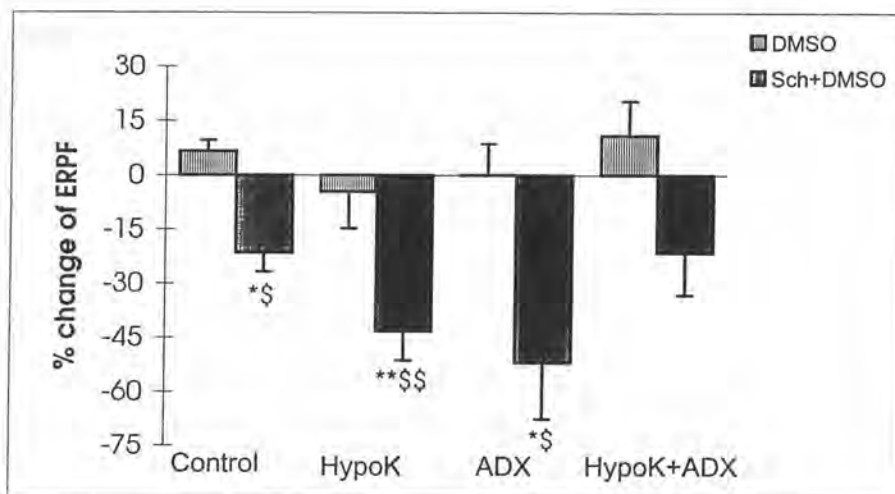


Figure 3 Percentage of changes of the effective renal plasma flow (ERPF) and effective renal blood flow within 40 min. after intrarenal arterial injection of Sch28080 in the control group, hypokalemic group (Hypo K), adrenalectomized group (ADX) and hypokalemic adrenalectomized group (Hypo K + ADX). Significant difference values using pair t-test * $P < 0.05$, ** $P < 0.01$, compared with the control period; $\$ P < 0.05$, $\$ \$ P < 0.01$ compared with the period given dimethyl sulfoxide (DMSO).

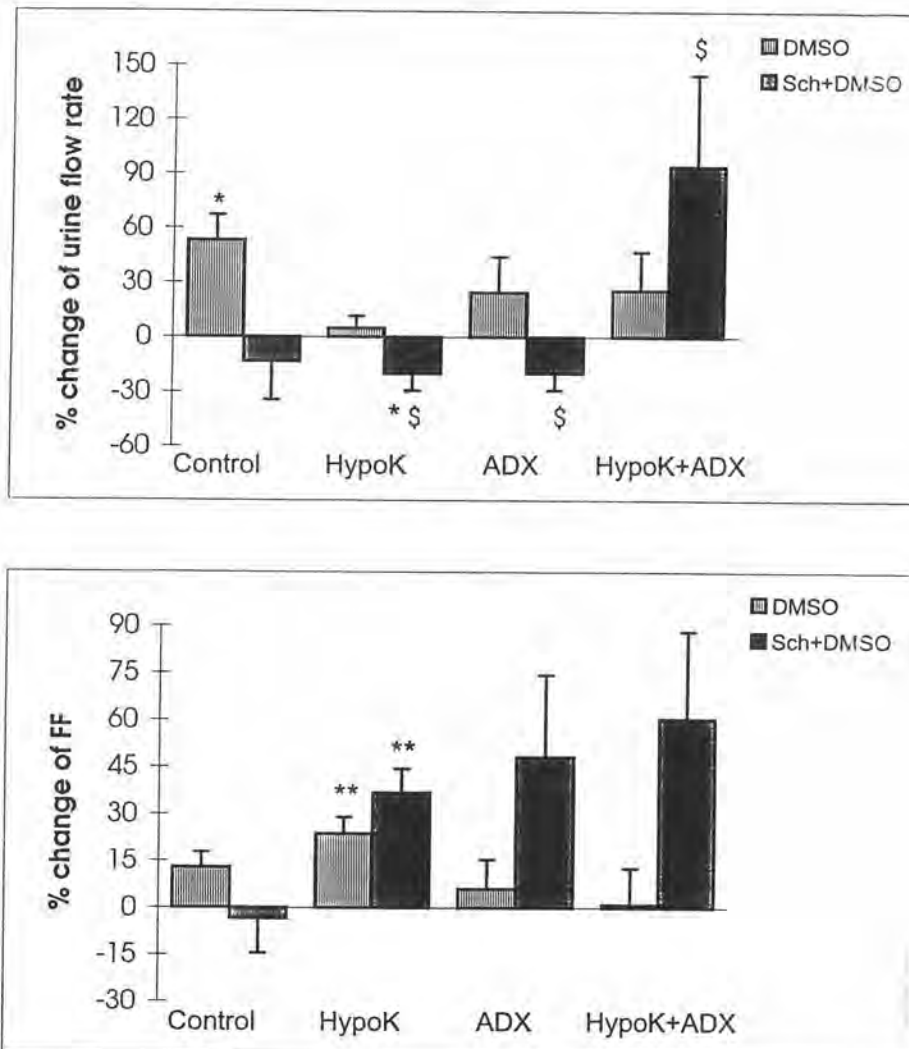


Figure 4 Percentage of changes of urine flow rate (V) and filtration fraction (FF) within 40 min. after intrarenal arterial injection of Sch28080 in control group, hypokalemic group (Hypo K), adrenalectomized group (ADX) and hypokalemic adrenalectomized group (Hypo K + ADX). Significant difference values using pair t-test * $P < 0.05$, ** $P < 0.01$ compared with the control period; \$ $P < 0.05$, compared with the period given dimethyl sulfoxide (DMSO).

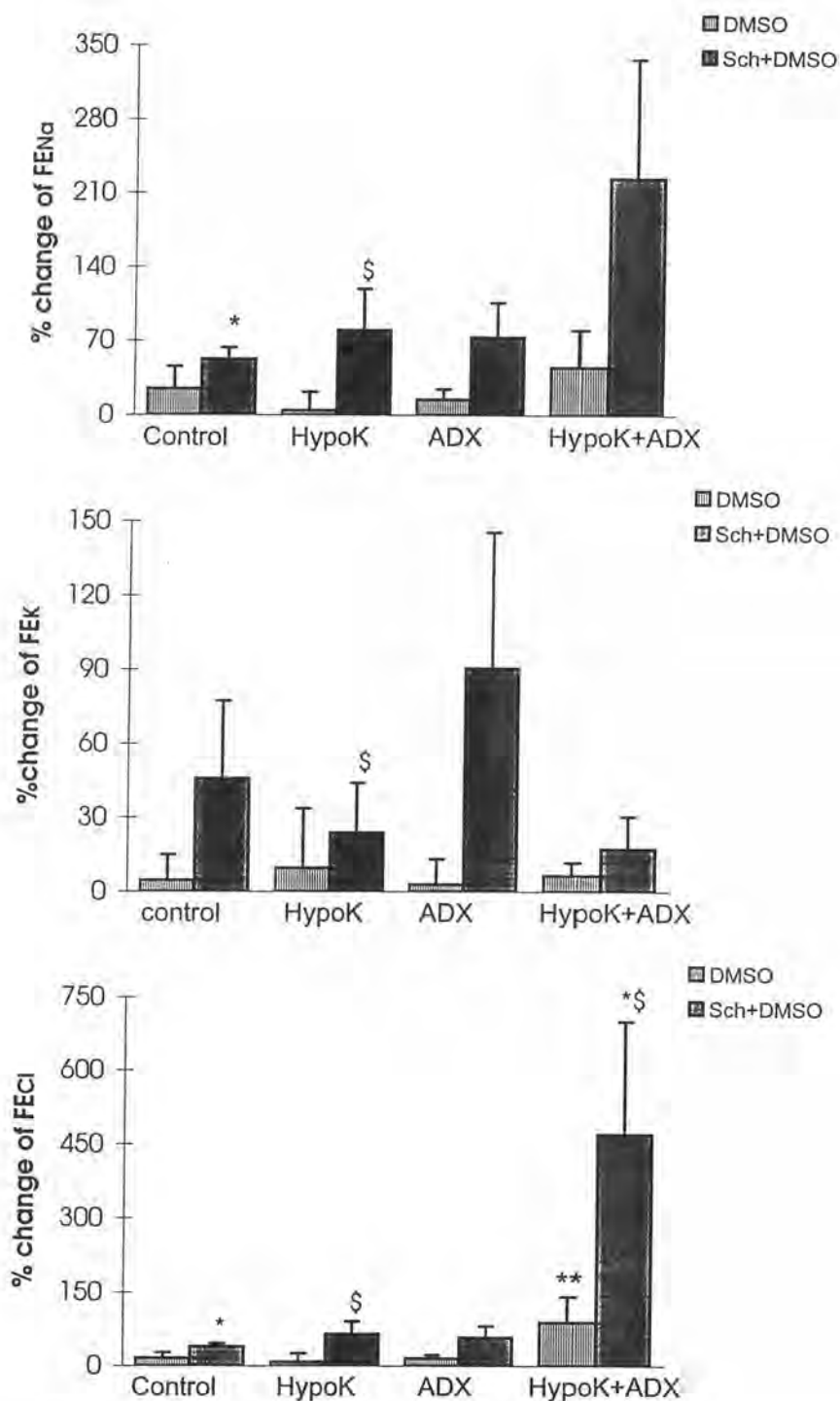


Figure 5 Percentage of changes of the fractional sodium excretion (FENa), fractional potassium excretion (FEK), fractional chloride excretion (FECI) within 40 min. after intrarenal arterial injection of Sch28080 in the control group, hypokalemic group (Hypo K), adrenalectomized group (ADX) and hypokalemic adrenalectomized group (Hypo K + ADX).

Significant difference values using pair t-test * $P < 0.05$, ** $P < 0.01$, compared with the control period; \$ $P < 0.05$, compared with the period given dimethyl sulfoxide (DMSO).

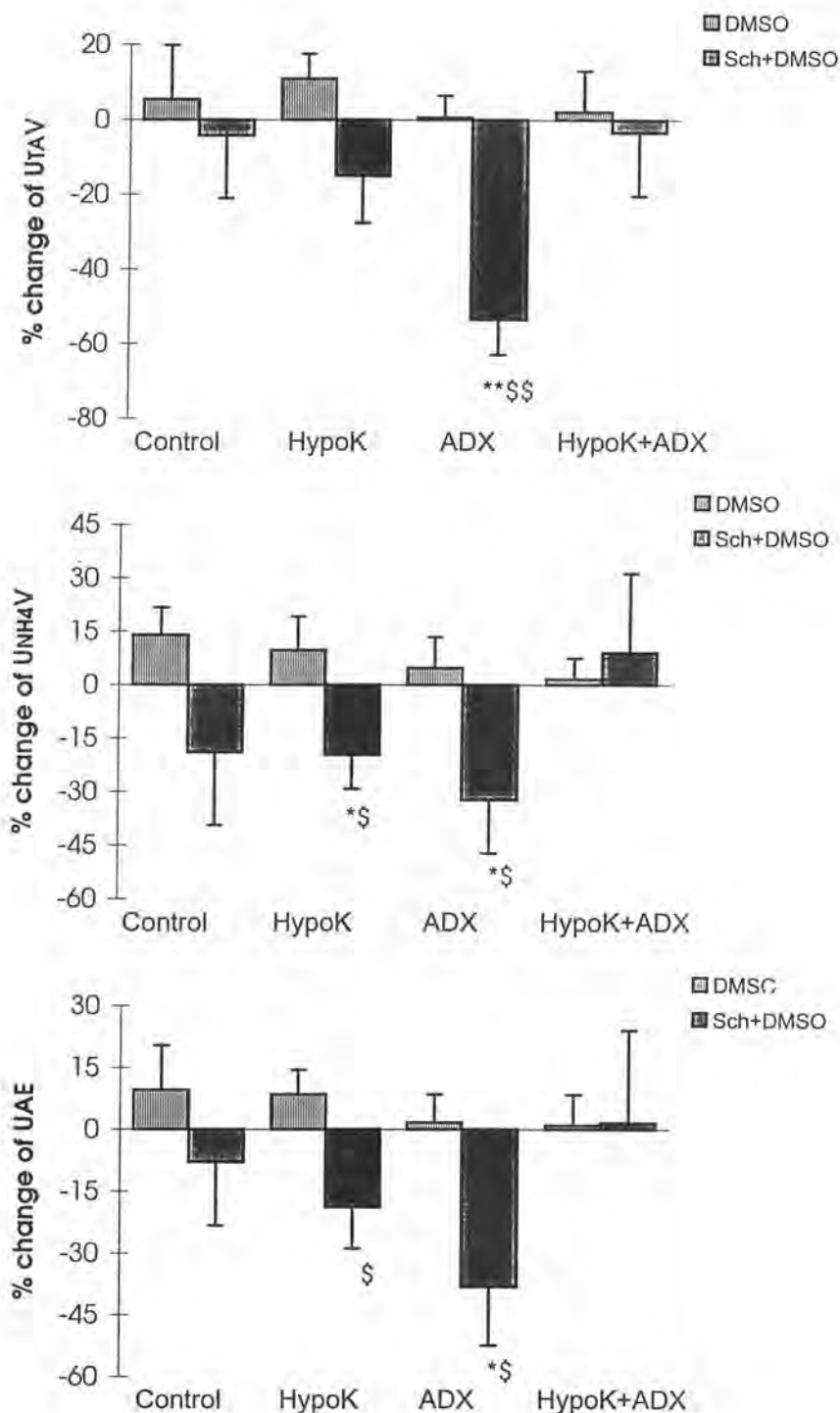


Figure 6 Percentage of changes of the urinary titratable acid excretion (UTAV),urinary ammonium excretion (UNH₄V) and urinary acid excretion (UAE) within 40 min. after intrarenal arterial injection of Sch28080 in the control group, hypokalemic group(Hypo K), adrenalectomized group (ADX) and hypokalemic adrenalectomized group (Hypo K + ADX). Significant difference values using pair t-test *P<0.05,**P<0.01, compared with the control period;\$ P<0.05,\$\$ P< 0.01compared with the period given dimethyl sulfoxide(DMSO).