Sodium, potassium and chloride utilization by rats given various inorganic anions

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The purpose of the present studies was to examine the effect of ingestion of sodium and potassium salts of various fixed anions on blood pressure, and to assess interactions among electrolytes. In the first study, Sprague–Dawley rats fed on purified diets supplemented with Na salts of chloride, sulphate, bisulphate, carbonate and bicarbonate for 7 weeks developed higher blood pressures than rats fed on the basal diet. In a second study, rats fed on Na or K salts of HSO_4, HCO_3 or Cl had higher blood pressures than rats fed on the basal diet. Blood pressure measurements were not correlated with plasma volume, plasma renin activity, or plasma atrial natriuretic peptide concentrations at 7 weeks. Plasma renin activity was depressed in rats fed on supplemental Na and even more in rats fed on supplemental K salts rather than the basal diet. Generally, rats fed on supplemental Na excreted Na in urine and absorbed Na in the gut more efficiently than rats fed on the basal diet or diets supplemented with K, but the anions fed also altered Na absorption and excretion. In a third study, rats fed on diets supplemented with any Cl salt, but especially KCl, absorbed K more efficiently than those fed on the basal diet. In studies 1 and 2, the efficiency of urinary excretion of K was greatest when HCO_3 and CO_3 salts were fed and least when HSO_4 salts were fed. Despite large variations in the efficiency of absorption and excretion of Na and K, tissue levels of the electrolytes remained constant.

Sodium: Potassium: Chloride: Blood pressure: Rat

Ingestion of not only sodium chloride, but also excess potassium chloride, lysine monohydrochloride and choline chloride, has been found to increase blood pressure and depress plasma renin activity (Kotchen *et al.* 1983; Whitescarver *et al.* 1984; Kaup *et al.* 1991). The aim of the present study was to determine whether other fixed anions, such as sulphate and bisulphate, duplicated the effect of chloride on blood pressure, because Greger *et al.* (1987), Kaup & Greger (1990), Kaup *et al.* (1991), Whiting & Draper (1981) and Whiting & Cole (1986) observed that these fixed anions (e.g. Cl, SO_4 and HSO_4) affected kidney function.

The mechanisms by which ingestion of excess Cl induces elevated blood pressure are not known. The ingestion of excess Na is believed to induce changes in blood pressure through one or more of the following mechanisms: expansion of plasma volume, changes in kidney function and changes in plasma renin activity (Tarazi, 1976; Kurtz *et al.* 1987).

It is also possible that some of the effects of dietary anions could be mediated by changes in excretion and retention of Na and K. Several investigations have reported that the ingestion of excess NaCl increased urinary excretion of K (Castenmiller *et al.* 1985; Charlton & Armstrong, 1989). Furthermore, other groups have demonstrated that negative balances with regard to K (Lemann *et al.* 1965; Ching *et al.* 1989) and tissue depletion of

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K (Scandling & Ornt, 1987) occurred in humans and animals in whom metabolic acidosis was induced by feeding excess ammonium chloride.

Accordingly, in the present studies the effect of variations in dietary anions on blood pressure was assessed and factors monitored that could help explain the mechanisms, i.e. plasma volumes, plasma renin activities, plasma atrial natriuretic polypeptide (ANP) concentrations and excretion and retention patterns of Na and K.

MATERIALS AND METHODS

Animals and diets

Two studies were conducted to examine the effect of various inorganic anions. In study 1, rats (eight per treatment) were fed one of six semi-purified diets for 56 d: a basal diet or the basal diet supplemented with Na (0·4 mmol/g) as NaCl, Na_2SO_4, $NaHSO_4$, Na_2CO_3 or $NaHCO_3$. In study 2, rats (eight per treatment) were fed on one of seven semi-purified diets for 56 d: a basal diet, the basal diet supplemented with Na (0·4 mmol/g) as NaCl, $NaHSO_4$, or $NaHCO_3$, or the basal diet supplemented with K (0·4 mmol/g) as KCl, $KHSO_4$ or $KHCO_3$.

In order to assess the effect of variations in electrolyte intake more completely, urinary and faecal samples from a previous study (study A) were also analysed. In study A, rats (eight per treatment) were fed on one of five semi-purified diets for 119 d: a basal diet or the basal diet supplemented with Cl (0·4 mmol/g) as NaCl, KCl, lysine monohydrochloride and lysine monohydrochloride with 0·2 mmol calcium/g as calcium carbonate.

Weanling, male Sprague–Dawley rats (Harlan Sprague–Dawley, Madison, WI) were housed individually in stainless-steel, wire-bottomed cages. The facilities met the requirements of the Institutional Animal Care and Use Committee.

The diets contained (g/kg): 200 lactalbumin (Teklad Test Diets, Madison, WI), 50 cellulose (Teklad Test Diets), 50 maize oil, 10 AIN-76 vitamin mixture (Teklad Test Diets), 2·3 choline dihydrogen citrate, 500 sucrose, 50–150 maize starch and 35 AIN-76 mineral mix (American Institute of Nutrition, 1977). The salts were added to the respective diets with maize starch being varied to balance the diets. The analysed electrolyte contents of diets are listed in Table 1.

Deionized water was offered *ad lib*. Feed consumption was recorded daily. Rats were weighed once weekly.

Sample collection and analyses

Systolic blood pressure measurements were made during weeks 7–8 in both studies 1 and 2 by an indirect rat-tail cuff blood-pressure system (Harvard Apparatus, South Natick, MA). Rats were placed in a restrainer and the blood pressure was monitored. It was determined that the systolic blood pressure readings stabilized after rats had been placed in the restrainer two or three times. Then, blood pressure was measured at least twice on each rat on at least two different days. Thus, the averages of at least four measurements in stabilized rats are reported.

Urine was collected on days 53–54 and 117–118, days 50–51, and days 52–53 of studies A, 1 and 2 respectively. Urine was acidified, diluted and frozen. Faeces were collected on days 53–59 and 113–117 of study A. Faeces were dried to a constant weight, cleaned of foreign adhering matter and ground to a fine powder.

Rats were fasted overnight, anaesthetized and killed by exsanguination at the conclusion of each study. Plasma volume was determined in study 1 using an Evans blue dye binding method as modified and described previously (Kaup *et al.* 1991) In study 2, blood was collected via cardiac puncture in EDTA-treated tubes with aprotinin (500 trypsin inhibitor

Table 1. *Chloride, sodium and potassium content (mg/g) of diets**

Diets	Chloride	Sodium	Potassium
Study A			
Basal	1·8	1·4	3·4
Basal supplemented with:			
Sodium chloride	15·5	11·2	3·4
Potassium chloride	15·3	1·3	19·1
Lysine monohydrochloride	15·6	1·2	3·4
Lysine monohydrochloride +calcium	15·4	1·1	3·4
Study 1			
Basal	2·1	1·4	3·2
Basal supplemented with:			
Sodium chloride	17·4	10·4	3·4
Sodium sulphate	1·9	10·1	3·4
Sodium bisulphate	2·0	10·3	3·6
Sodium carbonate	2·0	9·8	2·8
Sodium bicarbonate	2·0	10·0	3·0
Study 2			
Basal	1·7	1·4	3·4
Basal supplemented with:			
Sodium chloride	15·8	11·6	3·6
Potassium chloride	14·8	1·5	20·4
Sodium bisulphate	1·5	11·6	3·6
Potassium bisulphate	1·6	1·0	18·0
Sodium bicarbonate	1·5	11·1	3·0
Potassium bicarbonate	1·7	1·6	17·0

* For details of dietary treatments, see p. 524.

units (Sigma Chemical Co., St. Louis, MO)/tube), trypsin inhibitor (1000 sodium-benzoyl-L-arginine ethyl ester (BAEE) units/tube) and phenylmethanesulphonyl fluoride (1×10^{-5} M). Plasma was stored at −60° and subsequently used for determination of plasma renin activity and ANP. Kidneys and tibias were excised, cleaned and weighed. All tissue samples were placed in acid-washed containers and frozen until analyses were done. Plasma levels of ANP (pmol/l) were measured using a commercial radioimmunoassay (Peninsula Laboratories, Belmont, CA). Plasma renin activity was measured by using a commercial radioimmunoassay for angiotensin I (Du Pont Company, Billerica, MA). Plasma renin activity was expressed as ng generated angiotensin I/ml per h.

Diets, urine, faeces and tissues were analysed for Na and K by atomic absorption spectroscopy (Greger & Snedeker, 1980). Diets, urine and faeces were analysed for Cl by a colorimetric procedure (Jeffery & Hutchinson, 1981). Milk standard (SRM 1549) and urine standard (SRM 2670) obtained from the National Institute of Standards and Technology (NIST) (Gaithersburg, MD) were analysed with experimental samples. Milk standards were determined to contain (%) 111 (*n* 52), 96 (*n* 36) and 102 (*n* 37) of the certified NIST value for Na, K and Cl. Urine standards were determined to contain (%) 91 (*n* 31), 94 (*n* 33) and 109 (*n* 9) of the certified NIST value for Na, K and Cl.

Percentage urinary excretion of minerals was calculated by the formula: (urinary loss/intake) × 100. Percentage apparent absorption of minerals was calculated by the formula: ((intake − faecal loss)/intake) × 100.

Table 2. *Study 1‡. Systolic blood pressures and plasma volumes of rats fed on sodium salts of various inorganic anions§*

(Values are means of eight observations)

Dietary treatments	Systolic blood pressure‖ (mmHg)	Plasma volume‖ (ml/kg body-wt)
Basal	149**	2·96
Basal supplemented with:		
Sodium chloride	160	2·90
Sodium sulphate	169†	2·78†
Sodium bisulphate	159	3·08
Sodium carbonate	162	2·89
Sodium bicarbonate	156	2·84
Pooled SEM	3	0·09

Value for basal diet was significantly different from those for all other treatments: ** $P < 0·01$.

Values for basal diet supplemented with Na_2SO_4 were significantly different from those for basal diet supplemented with sodium bisulphate: † $P < 0·05$.

‡ For details of procedures, see p. 524.

§ For details of dietary treatments, see p. 524.

‖ Significant comparisons by orthogonal contrasts.

Statistical analysis

The effects of dietary treatments were evaluated within the framework of general linear models for analysis of variance (SAS Institute Inc., 1985). In studies 1 and 2, balanced orthogonal contrasts were devised and used to differentiate among means for variables that had been significantly ($P < 0·05$) affected by the treatments. In study A, tests for least significant differences were used to differentiate among means.

RESULTS

In both studies 1 and 2, rats fed the supplemental salts (Na or K) for 7 weeks had elevated blood pressures (Tables 2 and 3). In study 1, rats fed on supplemental HSO_4 had lower blood pressures than rats fed on supplemental SO_4.

The mechanisms are not clear. In study 1, the dietary treatments did not generally have a sustained effect on plasma volume. However, rats fed on $NaHSO_4$ had proportionally larger plasma volumes than rats fed on Na_2SO_4. Increases in blood pressures were not correlated with plasma volume measurements.

In study 2, rats fed on Na or K salts had significantly lower plasma renin activity than rats fed on the basal diet, and rats fed on supplemental K had lower renin activity than rats fed on supplemental Na. Ingestion of supplemental HSO_4 rather than HCO_3 also significantly affected plasma renin activity.

Plasma ANP did not appear to be affected differently by the ingestion of Na or K salts, but plasma ANP activity was greater when rats consumed HSO_4 rather than HCO_3. Neither plasma renin activity nor ANP concentrations were correlated to blood pressure measurements.

The differences in blood pressure of rats were not related to the weights of the rats. At the end of 56 d in study 1, rats fed on the basal diet, or diets supplemented with NaCl, Na_2SO_4, $NaHSO_4$, Na_2CO_3 or $NaHCO_3$ weighed 325, 310, 306, 246, 304 and 309 g respectively. Those rats fed on $NaHSO_4$ weighed significantly less than the other rats. At the end of 58 d in study 2, rats fed on the basal diet or diets supplemented with NaCl, KCl,

Table 3. *Study 2§. Systolic blood pressures, plasma renin activities and plasma atrial natriuretic polypeptide (ANP) concentrations of rats fed on sodium or potassium salts of various inorganic anions‖*

(Values are means of eight observations)

Dietary treatments	Systolic blood pressure¶ (mmHg)	Plasma renin activity¶ (ng generated angiotensin I/ml per h)	Plasma ANP¶ (pmol/l)
Basal	148**	9·78**	249**
Basal supplemented with:			
Sodium chloride	156	7·59††	210
Potassium chloride	157	5·42	306
Sodium bisulphate	163	9·48††	310
Potassium bisulphate	157	5·73	260
Sodium bicarbonate	157	8·09††	216‡
Potassium bicarbonate	162	5·64	192‡
Pooled SEM	3	0·69	23

Values for basal diet were significantly different from those for all other treatments: ** $P < 0.01$.

Values for basal diets supplemented with Na were significantly different from those for basal diets supplemented with K: †† $P < 0.01$.

Values for HCO_3 treatments were significantly different from those for HSO_4 treatments: ‡ $P < 0.05$.

§ For details of procedures, see pp. 524–525.

‖ For details of dietary treatments, see p. 524.

¶ Significant comparisons by orthogonal contrasts.

Table 4. *Study A*. Urinary excretion (%) of chloride, sodium and potassium by rats fed on various chloride salts†*

(Values are means of eight observations)

	Cl		Na		K	
Dietary treatments	Week 7	Week 16	Week 7	Week 16	Week 7	Week 16
Basal	47^{b}	66^{c}	37^{c}	59^{bc}	54^{c}	65
Basal supplemented with:						
Sodium chloride	101^{a}	102^{ab}	72^{a}	65^{ab}	60^{bc}	71
Potassium chloride	90^{a}	108^{a}	38^{c}	52^{bc}	74^{a}	72
Lysine monohydrochloride	100^{a}	102^{ab}	48^{bc}	48^{c}	60^{bc}	67
Lysine monohydrochloride +calcium	103^{a}	91^{b}	57^{b}	70^{a}	63^{b}	60
Pooled SEM	5·4	4·3	4·1	3·3	2·9	2·8

a,b,c. Means in columns with unlike superscript letters were significantly different ($P < 0.05$).

* For details of procedures, see pp. 524–525.

† For details of dietary treatments, see p. 524.

$NaHSO_4$, $KHSO_4$, $NaHCO_3$ or $KHCO_3$ weighed 319, 309, 299, 240, 270, 307 and 292 g respectively. Those rats fed on $NaHSO_4$ weighed less than all other rats; those rats fed on $KHSO_4$ weighed less than rats fed on the basal diet or diets supplemented with NaCl, KCl or $NaHCO_3$.

Excess dietary Cl was efficiently excreted in urine (Table 4). Changes in dietary sources of Cl had little impact on its excretion. However, in study A after 16 weeks, rats fed on lysine monohydrochloride with calcium excreted Cl less efficiently than rats fed on KCl.

Table 5. *Study A*. Apparent absorption (%) of chloride, sodium and potassium by rats fed on various chloride salts*†

(Values are means of eight observations)

Dietary treatments	Apparent absorption Cl Week 16	Apparent absorption Na		Apparent absorption K	
		Week 7	Week 16	Week 7	Week 16
Basal	94·9^{b}	94·9^{bc}	91·1^{b}	91·3^{c}	85·8^{c}
Basal supplemented with:					
Sodium chloride	97·4^{a}	97·5^{a}	96·8^{a}	93·2^{b}	91·2^{b}
Potassium chloride	97·5^{a}	93·6^{d}	90·9^{b}	96·5^{a}	95·9^{a}
Lysine monohydrochloride	97·5^{a}	96·0^{b}	94·8^{a}	94·3^{b}	91·0^{b}
Lysine monohydrochloride +calcium	96·7^{a}	94·7^{cd}	91·9^{b}	93·3^{b}	90·2^{b}
Pooled SEM	0·4	0·4	0·8	0·6	1·0

a, b, c, Means in columns with unlike superscript letters were significantly different ($P < 0·05$).

* For details of procedures, see pp. 524–525.

† For details of dietary treatments, see p. 524.

The apparent absorption of Cl by rats was extremely efficient, ranging from 94·9 to 97·5% (Table 5). Apparent absorption of Cl in rats fed on diets supplemented with Cl was about 2–3% higher than among rats fed on the basal diet.

Excretion of Na and K was somewhat more sensitive to changes in the type of Cl salts or other anions fed. In study A, rats fed on supplemental NaCl or lysine monohydrochloride with Ca excreted Na in urine more efficiently than rats fed on the basal diet or supplemental KCl at 7 weeks. Rats fed on supplemental Na or lysine monohydrochloride in study A also absorbed Na from the gut more efficiently than rats fed on KCl or lysine monohydrochloride with calcium for 7 or 16 weeks. Apparent absorption of Na was more efficient among rats fed on NaCl rather than lysine monohydrochloride at 7 weeks.

The efficiency of urinary excretion of K was greater among rats fed on KCl than among other rats after 7 weeks, but the differences were not statistically significant after 16 weeks. Percentage apparent absorption of K was also consistently greater among rats fed on KCl than among rats fed on other diets, but rats fed any of the supplemental chloride salts absorbed K more efficiently than rats fed on the basal diet.

Because Na and K excretion appeared to be affected by the anions fed in study A, Na and K excretion and retention in tissues were examined more thoroughly in studies 1 and 2. In study 1 rats fed on excess Na, regardless of the accompanying anions, excreted Na more efficiently than rats fed on the basal diet (Table 6). However, the efficiency of urinary Na excretion was greater when CO_3 rather than HSO_4 was fed. The findings from study 2 confirmed the observations of study 1. Efficiency of Na excretion tended to be greater when Na rather than K salts were fed. Despite these variations in the efficiency of Na excretion and apparent absorption, Na concentrations in kidneys did not change when excess Na or K were ingested. The higher concentration of Na in tibias of rats fed on Na_2HSO_4 partly reflects their smaller size in study 2.

The efficiency of urinary excretion of K was greatest in study 1 when $NaCO_3$ or $NaHCO_3$ was fed and lowest when $NaHSO_4$ was fed (Table 7). Similarly in study 2, the efficiency of urinary excretion of K was greatest when $NaHCO_3$ or $KHCO_3$ was fed and lowest when $KHSO_4$ was fed. Despite the large differences in urinary excretion of K, tissue K concentrations did not vary.

Table 6. *Studies 1 and 2*‖. *Urinary excretion and tissue concentrations of sodium among rats fed on sodium or potassium salts of various inorganic anions*¶
(Values are means of eight observations)

Dietary treatments	Urinary Na‖‖ (% intake)	Tibia Na‖‖ (mg/g tibia)	Kidney Na (mg/g kidney)
Study 1			
Basal	52**	4·69	1·53
Basal supplemented with:			
Sodium chloride	86	4·71	1·52
Sodium sulphate	87††	4·80	1·56
Sodium bisulphate	77††	4·89	1·54
Sodium carbonate	95	4·87	1·57
Sodium bicarbonate	88	4·84	1·60
Pooled SEM	2·5	0·06	0·02
Study 2			
Basal	52*	4·49	1·51
Basal supplemented with:			
Sodium chloride	77‡‡	4·51‡	1·54
Potassium chloride	54	4·46	1·54
Sodium bisulphate	48‡‡	4·72‡	1·53
Potassium bisulphate	78	4·47	1·49
Sodium bicarbonate	76‡‡	4·45‡§	1·58
Potassium bicarbonate	44	4·46§	1·56
Pooled SEM	2·6	0·06	0·03

Values for basal diet were significantly different from those for all other treatments: $*P < 0·05$, $**P < 0·01$.
Values for basal diet supplemented with Na_2SO_4 or $NaHSO_4$ were significantly different from those for basal diet supplemented with Na_2CO_3 or $NaHCO_3$: $††P < 0·01$.
Values for high-Na treatments were significantly different from those for high-K treatments: $‡P < 0·05$, $‡‡P < 0·01$.
Values for HCO_3 treatments were significantly different from those for HSO_4 treatments: $§P < 0·05$.
‖ For details of procedures, see pp. 524–525.
¶ For details of treatments, see p. 524.
‖‖ Significant comparisons by orthogonal contrasts.

DISCUSSION

Most investigators studying the effects of dietary salt on blood pressure have attributed the effect to Na (Luft & Weinberger, 1982). The findings from study 1 were consistent with the hypothesis that Na is a factor in the aetiology of hypertension. The rats fed on excess Na as NaCl, Na_2SO_4, $NaHSO_4$, Na_2CO_3 or $NaHCO_3$ had elevated blood pressure after 7 weeks.

However, our previous work (Kaup *et al.* 1991) and the work of Kotchen *et al.* (1983) and Whitescarver *et al.* (1984) demonstrated that rats fed on excess chloride as NaCl, KCl or lysine monohydrochloride had elevated blood pressure. Similarly in study 2, we demonstrated that rats fed on KCl had higher blood pressures than rats fed on the basal diet.

In study 2 we also found that rats fed on excess electrolytes with HSO_4, Cl or HCO_3 had elevated blood pressures. These findings suggest that examining the effect on blood pressure of individual dietary anions or cations may be counterproductive, and that perhaps the total amount of inorganic anions and cations consumed may be more important, at least with this model.

A number of investigators attempting to explain the effects of electrolytes on blood pressure have examined the effect of infusion or ingestion of two or three salts on plasma renin activity. Kotchen *et al.* (1980) and Kirchner *et al.* (1978) reported that the infusion of NaCl, lysine monohydrochloride or hydrochloric acid but not sulphuric acid or

Table 7. *Studies 1 and 2*‖. *Urinary excretion and tissue concentrations of potassium among rats fed on sodium or potassium salts of various inorganic anions*¶

(Values are means of eight observations)

Dietary treatments	Urinary K‖‖ (% intake)	Tibia K (mg/g tibia)	Kidney K (mg/g kidney)
Study 1			
Basal	71	1·22	2·11
Basal supplemented with:			
Sodium chloride	67*	1·17	2·08
Sodium sulphate	73†††‡‡	1·16	2·20
Sodium bisulphate	62††	1·20	2·15
Sodium carbonate	86	1·15	2·20
Sodium bicarbonate	82	1·21	2·19
Pooled SEM	2·8	0·03	0·07
Study 2			
Basal	64	1·25	2·48
Basal supplemented with:			
Sodium chloride	66	1·23	2·38
Potassium chloride	73	1·18	2·45
Sodium bisulphate	55	1·25	2·46
Potassium bisulphate	35	1·25	2·26
Sodium bicarbonate	72§§	1·29	2·26
Potassium bicarbonate	77§§	1·28	2·32
Pooled SEM	2·9	0·03	0·06

Values for basal diet supplemented with NaCl were significantly different from those of other high-Na treatments: $*P < 0·05$.

Values for basal diet supplemented with Na_2SO_4 or $NaHSO_4$ were significantly different from those for basal diet supplemented with Na_2CO_3 or $NaHCO_3$: $††P < 0·01$.

Values for basal diet supplemented with Na_2SO_4 were significantly different from those for basal diet supplemented with $NaHSO_4$: $‡‡P < 0·01$.

Values for basal diets supplemented with $NaHCO_3$ or $KHCO_3$ were significantly different from those for basal diet supplemented with $NaHSO_4$ or $KHSO_4$: $§§P < 0·01$.

‖ For details of procedures, see pp. 524–525.

¶ For details for dietary treatments, see p. 524.

‖‖ Significant comparisons by orthogonal contrasts.

$NaHCO_3$, decreased plasma renin activity. Stephens *et al.* (1978) observed that infusion of sodium lactate, potassium lactate or potassium sulphate depressed renin secretion. Kurtz *et al.* (1987) reported that ingestion of NaCl or sodium citrate suppressed plasma renin activity in male subjects. Our findings from study 2 are consistent with the previous findings. Plasma renin activity of rats on Na or K salts was lower than that of rats fed on the basal diet. Our findings suggest that K had greater effects on plasma renin than Na.

The sensitivity of Sprague–Dawley rats to dietary changes in these studies may reflect their tendency to develop nephropathy with age. Among male Sprague–Dawley rats, histological changes are noted in glomerular basement membranes at 3 months and 81% have chronic progressive nephropathy by 2 years of age (Goldstein *et al.* 1988). In the present study, a semi-purified diet with generous amounts of protein (200 g lactalbumin/kg) and high amounts of sugar (500 g sucrose/kg) was fed from weaning; this could increase the sensitivity of the rats to the electrolyte load.

One means by which renal impairment could ultimately affect blood pressure is through alterations in the size of fluid compartments. However, plasma volumes of rats after 7 weeks of dietary treatments in study 1 did not differ despite differences in blood pressure. Similarly, Whitescarver *et al.* (1986) found no difference in plasma volume between Dahl salt-sensitive rats fed on high or low levels of NaCl. Perhaps transient changes in fluid

compartments occurred in our rats before 5 weeks, but compensation occurred. However, Simchon *et al.* (1989) observed that increased plasma volumes among Dahl salt-sensitive rats fed on additional NaCl were sustained for at least 4 weeks.

Our observation in study 2 that plasma ANP varied among treatments but not in a consistent pattern suggests that adjustments may have occurred. ANP, which is secreted by atrial myocytes, initially induces hyperfiltration in the kidneys and suppresses renin release (Brenner *et al.* 1990). This ultimately leads to natriuresis. In all three studies, urinary Na excretion tended to be more efficient when NaCl rather than basal diet was fed, but there were no correlations between plasma ANP levels and excretion of Na, K or Cl in study 2. In future work, plasma volume, renin activity and ANP concentrations need to be monitored before changes in blood pressure are observed.

Another potential way that changes in dietary intake of electrolytes could ultimately affect blood pressure is through tissue electrolyte composition. However, kidney and bone concentrations of Na and K were insensitive to the dietary alterations in studies 1 and 2.

Several groups have observed that tissue K levels were depleted when metabolic acidosis was induced by feeding ammonium chloride (Lemann *et al.* 1965; Scandling & Ornt, 1987; Ching *et al.* 1989). However, ingestion of NaCl or Na_2SO_4 did not induce excess excretion of acid in these studies (Greger *et al.* 1991). Moreover, rats fed on CO_3 or HCO_3 in both studies tended to excrete K more efficiently than the other rats. The ingestion of these anions was associated with reduced urinary acid excretion.

It was observed that the ingestion of supplemental Na or K salts of inorganic anions induced elevated blood pressure in rats not bred or surgically altered to be susceptible to hypertension. Further work is needed to characterize the mechanisms by which alterations in electrolyte intake influence blood pressure in this model and to assess its relevance to human hypertension. The amount of Na fed in these studies was not extreme. The concentration of Na (on a dry-weight basis) in the diets supplemented with Na salts was about 130% of the Na concentration in average adult diet composites prepared by the Food and Drug Administration in the Total Diet Studies (Pennington *et al.* 1984).

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