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Renal Glutaminase and Carbonic Anhydrase Activities in Potassium-Deficient Rats.* (23562)

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The kidney enzymes carbonic anhydrase and glutaminase are believed to play an important role in renal electrolyte excretion (1,2). An increase of renal glutaminase activity has been observed in rats after administration of NH_4Cl(3-6) and a reduction after administration of $NaHCO_3$ or $KHCO_3$(3,4,6). The carbonic anhydrase activity has been found to be reduced after NH_4Cl administration(3). On the other hand, both glutaminase activity(3,5,7) and carbonic anhydrase activity(3,7) appear to be elevated in potassium-deficient rats. The results of recently reported studies on dogs(8) indicated the possibility that levels of kidney glutaminase and carbonic anhydrase activities are influenced by the dietary anion and cation content and by adrenal cortical activity. Consequently, the present studies were conducted with (a) intact rats fed diets containing varied amounts of K, Na or Cl, with and without simultaneous administration of desoxycorticosterone acetate (DCA), and (b) adrenalectomized rats fed a control or a low-potassium diet, with and without simultaneous administration of DCA.

Methods. Young adult male rats of the Wistar strain, of a uniform age and weighing between 250 and 300 g, were placed on a control diet for a period of 7 days before the experimental periods of 14 days were begun. The control diet was the same as the one employed in previous studies(3,7). The experimental diets represented the control diet altered only with respect to the content of K, Na or Cl. The adrenalectomized rats fed the control and the low-potassium diets were allowed 0.25 M NaCl *ad libitum*. The intact and adrenalectomized rats given DCA received 2 mg DCA (Percorten, Ciba Pharmaceutical Products)/rat/day by subcutaneous injection. At the close of the dietary period, the animals selected for the kidney enzyme studies were killed by decapitation and exsanguinated. The kidneys were quickly removed and subjected to the enzymatic analyses according to the procedures previously described(7). The remaining animals were placed under sodium pentobarbital anesthesia for the collection of blood and skeletal muscle (gastrocnemius from both hind legs). The chemical analyses of plasma and muscle were carried out by methods previously reported (3).

Results. The results of the chemical analyses of plasma and skeletal muscle and of the analyses of kidney glutaminase and carbonic anhydrase activities of intact and adrenalectomozed rats are presented in Table I.

Kidney Glutaminase. With intact rats, the kidney glutaminase activity was found increased in animals fed the low-potassium diet, and, following administration of DCA to animals maintained on (a) low-potassium, (b) low-potassium and low-chloride, and (c) low-potassium, low-chloride and low-sodium diets (lines 3, 4, 6 and 8). On the other hand, reduced glutaminase activity was found when the animals were fed the following diets: (a)

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TABLE I. Average Electrolyte Content of Plasma and Muscle and Kidney Glutaminase and Carbonic Anhydrase Activity.*

	Plasma				Skeletal muscle					Kidney	
Diet†	HCO_3	Cl	Na	K	H_2O, g	Cl	Na	K	N, mg	Glutaminase, U	Carbonic anhydrase, U
	mEq					mEq					
1. Control	27.8	106.6	156.3	4.5	324.3	5.1	9.5	45.7	31.9 ± 1.6	3040 ± 217	383 ± 49
2. " + DCA	37.7	98.6	154.6	3.2	326.7	5.1	15.3	37.9	32.4 ± 1.8	3244 ± 336	315 ± 50
3. Low K	29.5	104.8	156.9	3.2	321.7	5.0	13.5	37.5	32.3 ± .9	4984 ± 390	609 ± 17
4. " + DCA	42.5	91.7	159.6	2.5	332.4	4.9	17.6	32.0	31.0 ± .9	7836 ± 132	633 ± 21
5. Low K and low Cl	47.7	83.4	153.4	2.9	322.5	4.4	18.3	34.4	33.3 ± .5	2590 ± 230	620 ± 61
6. *Idem* + DCA	54.4	77.9	154.7	1.9	326.2	4.3	22.8	29.6	33.8 ± 1.5	5792 ± 287	644 ± 32
7. Low K, low Cl and low Na	31.1	102.0	151.9	3.7	319.8	4.7	10.1	45.3	34.3 ± .1	2416 ± 120	578 ± 57
8. *Idem* + DCA	33.1	102.6	150.9	3.0	322.0	4.8	13.9	38.3	33.7 ± .1	5179 ± 445	503 ± 46
9. Low Na and low Cl	30.9	103.2	150.5	5.1	324.0	5.0	8.6	48.6	32.8 ± .8	2257 ± 187	457 ± 18
10. *Idem* + DCA	32.0	105.8	151.1	5.0	331.3	5.2	9.0	47.5	33.0 ± .4	3243 ± 391	406 ± 21
11. Adrenal X and control	27.2	113.8	156.5	5.4	339.1	6.7	10.8	47.2	33.1 ± 1.2	2805 ± 255	379 ± 33
12. *Idem* + DCA	41.5	99.9	160.2	2.6	320.4	5.2	18.7	34.2	33.9 ± .2	2150 ± 211	256 ± 26
13. Adrenal X and low K	27.1	111.7	152.2	4.9	336.8	6.3	12.1	45.8	33.7 ± .4	3763 ± 291	190 ± 57
14. *Idem* + DCA	43.0	98.4	161.5	2.5	325.1	5.7	19.6	34.0	34.2 ± .6	3828 ± 322	224 ± 42

* Plasma values are expressed/kg plasma water; muscle values/100 g fat-free solids; kidney nitrogen as mg/g fresh kidney; and kidney glutaminase and carbonic anhydrase activities as units/g kidney N.

† Dietary period of 2 wk. Plasma and muscle values are based on 3 pairs of rats, while kidney data are based on 5 or 6 individual rats.

low-potassium and low-chloride, (b) low-potassium, low-chloride and low-sodium, and (c) low-sodium and low-chloride (lines 5, 7 and 9). A perusal of the data will reveal a lack of correlation between the glutaminase activity and the plasma bicarbonate concentration, or between the glutaminase activity and the concentrations of skeletal muscle potassium or sodium. In general, administration of DCA tended to raise level of glutaminase activity, particularly when the diet was deficient in potassium.

Adrenalectomized rats maintained on the control diet and allowed 0.25 M sodium chloride solution *ad libitum* exhibited a normal level of glutaminase activity (line 11). Glutaminase activity was reduced in adrenalectomized rats fed the control diet and administered DCA, and was increased significantly when the adrenalectomized rats were maintained on the low-potassium diet, with or without simultaneous DCA administration (lines 13 and 14). It is evident that in the absence of the adrenal gland kidney glutaminase activity can be increased, but the increase is smaller than observed in intact rats under comparable experimental conditions (compare lines 13 and 14 with 3 and 4).

Kidney carbonic anhydrase. With intact rats, carbonic anhydrase activity was found increased in animals fed a potassium-deficient diet, with or without simultaneous administration of DCA (lines 3 through 8). It will be noted that while the enzyme activity was increased in rats fed the low-potassium, low-chloride and low-sodium diet, with or without simultaneous DCA administration (lines 7 and 8), the carbonic anhydrase activity was not significantly increased in comparable animals maintained on a diet deficient only in sodium and chloride (lines 9 and 10). However, there appears to be a species difference regarding the influence of DCA on kidney carbonic anhydrase activity when given to animals on low-potassium or low-potassium and low-chloride diets. A reduced activity was observed in dogs(8) and a very slight increased activity in rats. There is no evident explanation for this difference. An inspection of the data will reveal that the carbonic anhydrase activity cannot be correlated with the plasma bicarbonate concentration (for example, compare lines 2 and 3) nor with the muscle sodium or potassium contents (compare lines 2 and 7). On the other hand, carbonic anhydrase activity was found reduced in adrenalectomized rats fed a low-potassium diet (line 13) and in adrenalectomized animals maintained on the control or the low-potassium diets and administered DCA (lines 12 and 14). It therefore appears that the same experimental conditions which result in decreased carbonic anhydrase activity in adrenalectomized rats lead to a significantly increased activity in the intact rats (compare lines 13 and 14 with 3 and 4).

Discussion. The results of the present experiments revealed that the kidney glutaminase activity and the carbonic anhydrase activity can be altered independently, by factors which are not clearly identifiable. Neither the glutaminase activity nor the carbonic anhydrase activity could be definitely correlated with the plasma bicarbonate concentration or with the composition of skeletal muscle in respect to potassium and sodium. Similar conclusions were arrived at by other workers(2,9) studying changes in kidney glutaminase activity. The present results indicate some relationship between dietary potassium and carbonic anhydrase activity, since with intact rats significant elevations of this enzyme were encountered only under circumstances of dietary potassium deficiency.

It has been previously reported(10,11) that the renal glutaminase activity is unchanged in adrenalectomized rats. Wilson and Seldin (11) found further that the adaptation of the glutaminase enzyme system following NH_4Cl loads was unimpaired in adrenalectomized rats. They therefore concluded that adrenal hormones are not required either for the maintenance or optimum activation of the glutaminase enzyme system in the rat. The results of the present experiments also indicated that kidney glutaminase activity can increase in the absence of the adrenal gland. However, such increases were of less magnitude than those observed in intact rats under comparable experimental conditions. In contrast, the carbonic anhydrase activity in adrenalectomized rats became reduced in experimental situations which in intact rats led to increased enzyme activity. Perhaps inadequate renal carbonic anhydrase activity may be a factor in the impaired ammonia production noted in adrenal-insufficient rats(12).

Summary. Kidney glutaminase and carbonic anhydrase activities were determined in intact and adrenalectomized rats maintained on normal and potassium-deficient diets, with and without simultaneous administration of DCA. The changes of enzyme activity could not be related to plasma or muscle electrolytes. The activities of the 2 enzymes were found unaltered in adrenalectomized rats. Experimental conditions resulting in increased glutaminase activity in adrenalectomized rats had the same effect to a greater degree in intact rats. Kidney carbonic anhydrase activity failed to increase in adrenalectomized rats under circumstances which in intact rats led to increased activity.

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