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Formation of Serotonin by Rat Kidneys *in Vivo* (42216)

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Abstract. Renal formation of serotonin by decarboxylation of its amino acid precursor L-5-hydroxytryptophan (L-5-HTP) has been demonstrated with renal tissue homogenates and isolated perfused rat kidneys. Our objective in the present study was to determine whether the conversion of L-5-HTP to serotonin was associated with functional changes by kidneys *in vivo*. Renal clearance studies were conducted in anesthetized, volume-expanded male Sprague–Dawley rats receiving either saline ($n = 9$) or L-5-HTP (15 and 75 μg/min iv, $n = 9$). No change in mean arterial pressure was measured during infusions of L-5-HTP at either dose, whereas glomerular filtration rate (GFR), as measured by the clearance of inulin, and effective renal plasma flow (C_{PAH}) decreased by 34 ± 5% (mean ± SE, $P < 0.001$) and 26 ± 7% ($P > 0.07$), respectively. Urine flow and sodium excretion decreased by 41 ± 9% ($P < 0.01$). Serotonin and 5-HTP were determined in urine and plasma using HPLC. High levels of 5-HTP were present in plasma, but not urine. Urinary serotonin increased in the rats receiving L-5-HTP without concomitant increases in plasma serotonin. More than 20% of the infused L-5-HTP was recovered in the urine as serotonin. The decarboxylase inhibitor carbidopa (20 μg/min) markedly reduced urinary serotonin excretion in the rats which received L-5-HTP and reversed the changes in GFR, C_{PAH}, urine flow, and sodium excretion. Infusions of the amino acid precursor of L-5-HTP, L-tryptophan ($n = 7$), did not alter kidney function or increase plasma or urinary 5-HTP or serotonin levels. These results are consistent with the intrarenal formation of serotonin by renal decarboxylase with attendant alterations in renal hemodynamics and salt and water excretion.

Serotonin is formed from its amino-acid precursor, L-5-hydroxytryptophan (L-5-HTP), following decarboxylation by aromatic L-amino acid decarboxylase. Aromatic L-amino acid decarboxylase activity is particularly high in the kidney, and conversion of L-5-HTP to serotonin occurs readily in renal tissue homogenates (1, 2). In a recent study, performed in isolated rat kidneys perfused with Krebs–Henseleit solution, we demonstrated the endogenous formation of serotonin from L-5-HTP in whole kidneys with subsequent excretion into the urine (3). Serotonin is a vasoactive amine and its injection into animals has been reported to decrease renal blood flow, glomerular filtration rate, and the urinary excretion of water and electrolytes (4, 5). Therefore, we hypothesized that endogenous as well as exogenous serotonin might be associated with changes in renal hemodynamics and excretory function and that endogenous serotonin has a potential role as an intrarenal hormone. The present study using L-5-HTP in rat kidneys *in vivo* was designed to provide data relevant to this hypothesis. Additionally, Cooper and Melcer (6) have reported that the kidney contains significant quantities of tryptophan-5-hydroxylase which can convert the essential amino acid L-tryptophan to 5-HTP. Thus, another purpose of the present investigation was to determine whether L-tryptophan might also be converted to serotonin by kidneys *in vivo*, in association with changes in renal function.

Materials and Methods. Experiments were performed on 25 adult male Sprague–Dawley rats (436 ± 10 g body wt) which were allowed food and water *ad libitum* before study. Anesthesia was induced by injection of sodium pentobarbital (65 mg/kg body wt ip). The rats were maintained at a constant body temperature of 36–37°C using a thermostatically regulated lamp. The trachea was cannulated and the rat was allowed to respire spontaneously. Three polyethylene catheters were inserted into the right jugular vein for infusion of drugs, inulin and paraaminohippurate (PAH), and injections of supplemental doses of anesthetic. The left femoral artery was catheterized to measure arterial blood pressure and obtain blood samples. Arterial blood pressure was monitored with a Statham model P-23 Db

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strain gauge transducer and a Grass polygraph recorder. The left femoral vein was cannulated for drug infusions. The urinary bladder was exposed by an abdominal incision and catheterized with PE-90 tubing. The wound was sutured with the free end of the catheter exteriorized for collection of urine samples.

During surgery the rats received an iv infusion of 0.9% NaCl at 400 μl/min to a total volume of 3 ml/100 g body wt. Thereafter, 0.9% NaCl containing inulin (55 mg/100 g body wt/hr) and PAH (8 mg/100 g body wt/hr) was infused at 150 μl/min. Two additional infusions of 0.9% NaCl at 20 μl/min were made into the jugular and femoral veins. Clearance studies were carried out after an equilibration period of approximately 80 min. Urine was collected for consecutive 20-min periods before (periods 1 and 2) and during low- (periods 3 and 4) and high- (periods 5 and 6) dose infusions of L-5-HTP, L-tryptophan, or 0.9% NaCl (solvent). Subsequently, an infusion of carbidopa (periods 7 and 8) was added to inhibit aromatic L-amino acid decarboxylase in each group. Femoral arterial blood samples were taken at the midpoint of each observation period for measurement of inulin, PAH, and indole concentrations. After the two initial control observation periods, intravenous infusions of L-5-HTP ($n = 9$) or L-tryptophan ($n = 7$) at 15 μg/min were started. After 10 min for equilibration, two consecutive 20-min urine collections were obtained. The dose of L-5-HTP or L-tryptophan was then increased to 75 μg/min and, after 10-min equilibration, two more 20-min urine collections were obtained. An infusion of carbidopa at 20 μg/min was then started while the infusion of L-5-HTP or L-tryptophan (75 μg/min) was continued and, after an additional 10-min equilibration period, two final 20-min urine collections were obtained. In nine control experiments, rats received 0.9% NaCl without L-5-HTP or L-tryptophan during the first six collection periods followed by carbidopa during the last two periods. At the end of each experiment, kidneys were excised, decapsulated, blotted dry, and weighed.

The concentration of PAH in plasma and urine was measured by the method of Bratton and Marshall (7). Plasma and urine inulin concentrations were determined by the anthrone method (8). Glomerular filtration rate (GFR) was calculated from the clearance of inulin and effective renal plasma flow from the clearance of PAH (C_{PAH}). Urine volumes were determined gravimetrically. Urinary sodium concentration was determined with an Instrumentation Laboratories flame photometer using an internal lithium standard.

Serotonin and 5-HTP were quantified using reverse-phase HPLC with electrochemical detection (9, 10). Samples of plasma (20 μl) were prepared as described by Anderson *et al.* (11). The mobile phase was 0.1 *M* sodium acetate containing 0.3 m*M* EDTA and 6% methanol adjusted to pH 4.7. The buffer was degassed under vacuum and passed through a Millipore filter before use. The system consisted of a Water's 6000A solvent delivery pump and a Bioanalytical Systems C-18-μBondapak reverse-phase column, LC-3 detector, and RYT chart recorder. The flow rate of the mobile phase was 2 ml/min and injection volumes were 20 μl. Under these conditions, quantities of 5-HTP and serotonin less than 30 and 60 pg, respectively, could be detected.

Statistical analyses comparing indole levels between the L-5-HTP- and saline-infused control groups were made using Student's unpaired *t* test (Tables I and II). Comparisons of kidney function within each treatment group were made using Student's paired *t* test (Figs. 1 and 2). In addition, repeat measures analysis of variance and Student–Newman–Keul's test (12) was performed to compare changes in each variable between period 2 (predrug infusion) or period 6 (precarbidopa infusion) within each group (Table III). A similar analysis was performed for changes among the three groups at each dose level (Table IV). Differences in means with $P < 0.05$ were considered statistically significant. Data are reported as means ± SE.

Chemicals and drugs were obtained from the following sources: L-tryptophan, L-5-HTP, serotonin (5-hydroxytryptamine creatinine sulfate), and PAH (Sigma Chemical Co., St. Louis, Mo.); inulin (Eastman Kodak Co., Rochester, N.Y.); sodium pentobarbital (D-M Pharmaceuticals, Sellersville, Pa.). Carbidopa was generously supplied by Merck Sharp & Dohme Research Laboratories (Rahway, N.J.). Carbidopa was dissolved in 0.012 *N* HCl to achieve a concentration of 1 mg/ml.

Results. There were no changes in plasma or urinary levels of 5-HTP or serotonin in rats infused with saline or L-tryptophan (not

TABLE I. URINARY INDOLE EXCRETION

Period	Dose	Serotonin (ng/min)		5-HTP (ng/min)	
		Saline infusion	L-5-HTP infusion	Saline infusion	L-5-HTP-infusion
1	Control	30 ± 11	110 ± 48	24 ± 11	5 ± 2
2	Control	26 ± 8	61 ± 27	32 ± 11	5 ± 2*
3	15 μg/min	28 ± 5	6,282 ± 2,200*	33 ± 15	7 ± 3
4	15 μg/min	36 ± 10	8,671 ± 1,814**	16 ± 8	12 ± 7
5	75 μg/min	26 ± 7	35,590 ± 9,815**	27 ± 10	45 ± 26
6	75 μg/min	35 ± 14	31,210 ± 6,491**	38 ± 21	238 ± 113
7	75 μg/min + CD	39 ± 19	1,859 ± 781	29 ± 14	275 ± 61**
8	75 μg/min + CD	22 ± 8	631 ± 244	31 ± 14	980 ± 358*

Note. Means ± SE. *$P < 0.05$, **$P < 0.01$ vs saline-infused group. CD = carbidopa (20 μg/min) added to both L-5-HTP ($n = 8$) and saline-infused ($n = 6$) groups in periods 7 and 8.

shown). On the other hand, infusions of L-5-HTP at 15 and 75 μg/min caused large increases in these parameters as summarized in Tables I and II. Note the large increases in plasma levels of 5-HTP without concomitant changes in urinary L-5-HTP during its infusion. In contrast, urinary serotonin was markedly increased with only small changes in plasma serotonin. Following additions of carbidopa to inhibit aromatic L-amino acid decarboxylase, the urinary level of serotonin decreased as plasma and urinary 5-HTP increased.

Figure 1 summarizes mean urine flow and sodium excretion for each clearance period before and during infusions of saline, L-tryptophan, or L-5-HTP and subsequent additions of carbidopa to all three groups. Figure 2 provides data obtained similarly for GFR, C_{PAH}, and mean arterial pressure. Statistical analyses within each group were based on paired t tests versus control period 2 (pretreatment) as baseline. Generally, urine flow and sodium excretion were unchanged or increased slightly throughout all clearance periods during infusions of saline or L-tryptophan. With infusions of L-5-HTP at the high dose significant reductions in urine flow and sodium excretion were measured (period 6), which were reversed by additions of carbidopa to the infusate. A similar response pattern was observed for GFR and C_{PAH}; little change or slight increases were noted except for reductions during high-dose L-5-HTP, which were reversed by carbidopa. Mean arterial pressure in each group remained relatively constant throughout the studies, except for a reduction in the group which received combined L-5-HTP and carbidopa (pe-

TABLE II. PLASMA INDOLE LEVELS

Period	Dose	Serotonin (ng/ml)		5-HTP (ng/ml)	
		Saline infusion	L-5-HTP infusion	Saline infusion	L-5-HTP infusion
1	Control	31 ± 5	72 ± 42	<14 ± 4	<6 ± 2
2	Control	34 ± 8	50 ± 26	<16 ± 5	<5 ± 2
3	15 μg/min	35 ± 5	28 ± 10	<11 ± 3	901 ± 243**
4	15 μg/min	23 ± 4	23 ± 9	<11 ± 4	1,412 ± 223***
5	75 μg/min	29 ± 3	27 ± 14	<7 ± 1	4,646 ± 884**
6	75 μg/min	27 ± 3	34 ± 16	<14 ± 4	6,850 ± 900***
7	75 μg/min + CD	26 ± 4	44 ± 18	<12 ± 3	7,468 ± 852***
8	75 μg/min + CD	30 ± 4	85 ± 50	<11 ± 3	9,796 ± 2,013**

Note. Means ± SE. **$P < 0.01$, ***$P < 0.001$ vs saline-infused group. CD = carbidopa (20 μg/min) added to both L-5-HTP ($n = 8$) and saline-infused ($n = 6$) groups in periods 7 and 8.

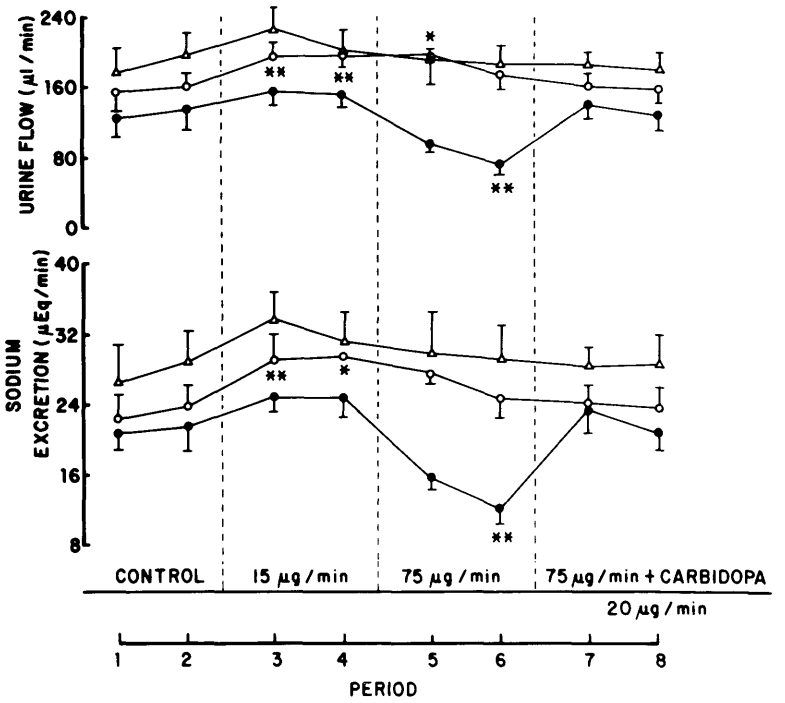

FIG. 1. Urine flow and sodium excretion during consecutive 20-min clearance periods in anesthetized, volume-expanded rats during saline (○) (n = 9) and low- and high-dose infusions of L-tryptophan (△) (n = 7) and L-5-HTP (●) (n = 9). Carbidopa was administered during continued high-dose infusions of amino acids or saline. Values are means ± SE, $^*P < 0.05$, $^{**}P < 0.01$ vs predrug infusion values (period 2) within each treatment group.

riods 7 and 8). In the latter case, the reduced perfusion pressure was not associated with a lower GFR or C_{PAH} or diminished urine flow or sodium excretion.

To account for the repeated nature of our measurements and different baseline levels in each group, it was necessary to repeat our statistical analyses using repeat measures analysis of variance, and Student–Newman–Keul's test, the results of which are shown in Tables III and IV. No significant differences in changes from baseline were observed for urine flow, sodium excretion, GFR, C_{PAH}, or mean arterial pressure during infusions of saline or L-tryptophan (Table III). In contrast, with L-5-HTP progressively greater and more significant changes of reduced urine flow and sodium excretion were measured as the infusion rate increased from 15 to 75 µg/min. Within each group (Table III) the changes from baseline for GFR and C_{PAH} were also significantly greater during infusion of L-5-HTP at 75 µg/min than at 15 µg/min, but the changes in mean arterial pressure did not differ at either infusion rate. In the case of between-group comparisons, the analyses were made on the basis of average (2 periods) changes which occurred at each dose level. Significantly, greater reductions in sodium and water excretion from baseline were observed with the 75 µg/min infusion of L-5-HTP (periods 5 + 6) (Table IV). There was a trend for GFR and C_{PAH} to decrease relative to control with the 75 µg/min infusion of L-5-HTP; but, this did not achieve statistical significance, because of the variability in responses between groups. However, with carbidopa infusion (periods 7 + 8), the changes in urine flow, sodium excretion, and C_{PAH} significantly increased in the group infused with L-5-HTP as compared to the groups infused with L-tryptophan or saline (Table IV). GFR showed a tendency to increase and mean arterial pressure a tendency to decrease after carbidopa plus 5-HTP. The changes in urine flow, sodium excretion, GFR, C_{PAH}, and mean arterial pressure from base-

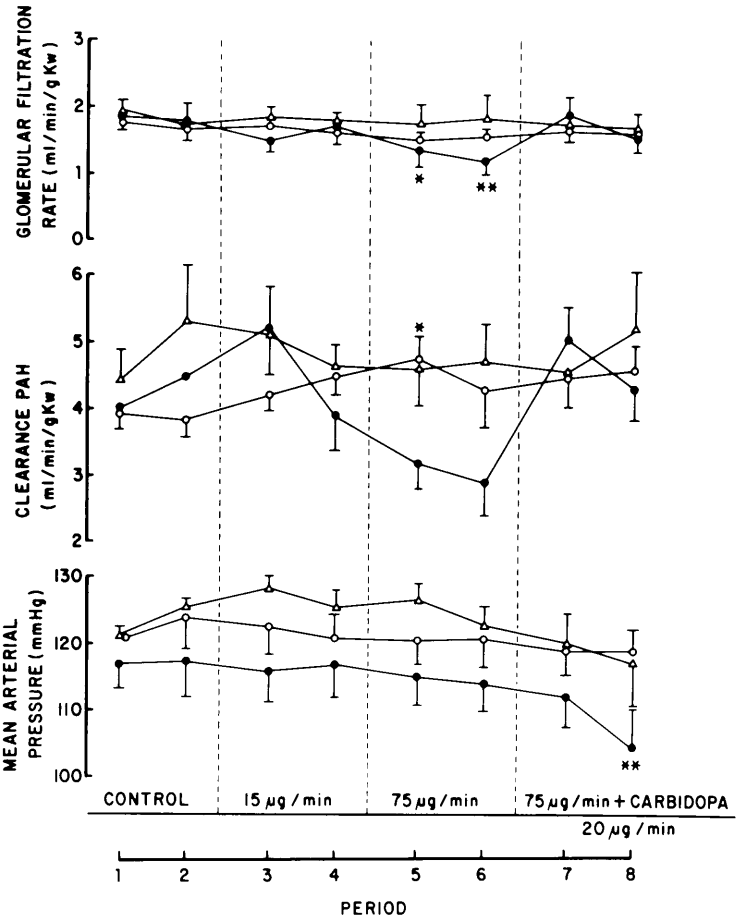

FIG. 2. GFR, C_{PAH} and mean arterial pressure during consecutive 20-min clearance periods in anesthetized, volume-expanded rats during saline (○) (n = 9) and low- and high-dose infusions of L-tryptophan (△) (n = 7) and *L*-5-HTP (●) (n = 9). Carbidopa was administered during continued high-dose infusions of amino acids or saline. Values are means ± SE, $*P < 0.05$, $**P < 0.01$ vs predrug infusion values (period 2) within each treatment group.

line (period 2) were not significantly different among groups during carbidopa infusion (Table IV).

Discussion. Our data demonstrate that L-5-HTP is readily converted to serotonin by rat kidneys *in vivo*. Further, serotonin is efficiently excreted into the urine, since urinary levels of serotonin increase without concomitant increases in plasma levels. In contrast, L-5-HTP, without decarboxylation, appears to be reabsorbed efficiently by the kidney, since little appeared in the urine during its infusion, whereas plasma levels increased. Our data indicate that at least 20% (on a molar basis) of the L-5-HTP infused each minute was excreted rapidly as serotonin. The urinary serotonin was probably produced by the kidney, since plasma levels entering the kidney were not high and remained unaltered over the course of the experiment. This conclusion is supported by our previous experience with isolated perfused kidneys which demonstrated appreciable conversion of L-5-HTP and excretion as serotonin within a single pass (5). In contrast to L-5-HTP, our present data indicate that renal conversion of L-tryptophan to 5-HTP and serotonin is not very efficient since L-5-HTP or serotonin did not increase in blood or urine during infusions of L-tryptophan. Although the enzyme required to convert L-tryptophan to L-5-HTP, tryptophan-5-hydroxylase, has been reported to be present in renal homogenates, for some

TABLE III. WITHIN-GROUP COMPARISONS: CHANGES IN KIDNEY FUNCTION FROM PERIOD 2 (PREDRUG INFUSION)

	Baseline Period 2	15 μg/min		75 μg/min	
		Period 3	Period 4	Period 5	Period 6
Control					
Urine flow, μl/min	159.1 ± 17.9	+35.4 ± 10.2	+39.4 ± 11.7	+32.6 ± 12.0	+12.1 ± 16.2
Sodium excretion, μeq/min	23.5 ± 2.7	+5.6 ± 1.4	+5.8 ± 1.9	+4.0 ± 2.4	+1.2 ± 1.8
GFR, ml/min/g KW	1.66 ± 0.16	+0.07 ± 0.14	+0.02 ± 0.13	−0.17 ± 0.16	−0.12 ± 0.09
C_{PAH}, ml/min/g KW	3.82 ± 0.23	+0.38 ± 0.26	+0.66 ± 0.31	+0.94 ± 0.32	+0.45 ± 0.55
Mean arterial pressure, mm Hg	123.8 ± 4.8	−1.4 ± 1.5	−3.0 ± 2.4	−3.3 ± 2.0	−3.3 ± 2.6
L-5-HTP					
Urine flow, μl/min	135.7 ± 24.3	+20.4 ± 11.3	+16.4 ± 13.8	−39.3 ± 18.6*,**	−64.5 ± 16.4*,**,***
Sodium excretion, μeq/min	21.5 ± 2.8	+3.4 ± 2.0	+3.4 ± 1.7	−5.8 ± 2.6*,**	−9.4 ± 2.0*,**,***
GFR, ml/min/gKW	1.80 ± 0.26	−0.07 ± 0.20	−0.09 ± 0.15	−0.46 ± 0.18	−0.60 ± 0.10*,**
C_{PAH}, ml/min/gKW	4.48 ± 1.04	+0.67 ± 0.65	−0.59 ± 0.75*	−1.30 ± 0.76*,**	−1.57 ± 0.73*,**
Mean arterial pressure, mm Hg	117.1 ± 5.1	−1.4 ± 3.1	−0.5 ± 3.0	−2.2 ± 3.4	−2.9 ± 3.3
L-Tryptophan					
Urine flow, μl/min	197.5 ± 24.7	+28.2 ± 18.7	+4.0 ± 16.9	−6.1 ± 17.6	−12.9 ± 12.6
Sodium excretion μeq/min	28.8 ± 3.5	+4.8 ± 2.2	+2.1 ± 2.5	+1.0 ± 3.2	+0.1 ± 2.7
GFR, ml/min/g KW	1.74 ± 0.25	+0.10 ± 0.14	−0.01 ± 0.23	−0.01 ± 0.35	−0.26 ± 0.25
C_{PAH}, ml/min/g KW	5.30 ± 0.88	−0.08 ± 0.53	−0.69 ± 0.54	−0.71 ± 0.74	−0.59 ± 0.73
Mean arterial pressure, mm Hg	125.2 ± 1.3	−2.8 ± 1.6	−0.1 ± 2.3	+1.4 ± 2.5	−2.5 ± 3.0

Note. Means ± SE. *$P < 0.05$ vs period 3; **$P < 0.05$ vs period 4; ***$P < 0.05$ vs period 5 by repeat measures ANOVA.

reason this was ineffective *in vivo*. Perhaps L-tryptophan transported by the kidney is not available to this renal hydroxylase. A recent report has suggested the presence of serotonergic nerve endings in the rat renal medulla (13). Thus, unlike the decarboxylase enzyme which is thought to be of tubular origin (14), the hydroxylase may reside in neuronal cells. The failure of L-tryptophan to be converted to 5-HTP or serotonin may also relate to its limited availability to enter these cells. This may be a consequence of the fact that L-tryptophan is highly protein bound (>90%), which would limit its filtration at the glomerulus and perhaps its secretion by renal tubular cells, as well.

When L-5-HTP was provided in high doses, GFR and C_{PAH} decreased in association with reductions in urine flow and sodium excretion. These effects of L-5-HTP appear dependent upon its renal conversion to serotonin, since they correlated with high levels of urinary serotonin, and were reversed by carbidopa which inhibited the production of serotonin by the kidney. These results are consistent with our previous findings in the isolated rat kidney that L-5-HTP produced increases in renal vascular resistance, which were reversed by carbidopa (5). They may relate also to the findings that renal cortical necrosis can be produced by L-5-HTP (15) and serotonin (16, 17), which could be prevented in the former case by decarboxylase inhibition. In addition, Erspamer and Bertaccini (18) have reported reductions in urine flow after administration of DL-5-HTP to conscious rats. Our own study is highly suggestive of renal functional effects of serotonin formed within the kidney itself, as plasma serotonin did not rise and blood pressure was constant during L-5-HTP infusions. Although these effects may be due to serotonin directly, our results do not rule out the participation of other modulators of renal function secondary to increased serotonin. In contrast,

TABLE IV. BETWEEN-GROUP COMPARISONS: CHANGES IN KIDNEY FUNCTION

	Changes from predrug infusion period 2			Changes from period 6
	15 μg/min Periods 3 + 4	75 μg/min Periods 5 + 6	75 μg/min + CD Periods 7 + 8	75 μg/min + CD Periods 7 + 8
Δ Urine flow, μl/min				
Control	37.38 ± 9.26	22.34 ± 13.26	−2.44 ± 15.14	−14.53 ± 7.27
L-5-HTP	18.42 ± 12.04	−51.90 ± 17.36*	−5.07 ± 13.54	59.38 ± 11.47*,**
Tryptophan	16.08 ± 16.11	−9.52 ± 13.76	−39.14 ± 13.50	−20.93 ± 9.13
Δ Sodium excretion, μeq/min				
Control	5.71 ± 1.45	2.61 ± 1.93	0.02 ± 2.05	−1.21 ± 0.96
L-5-HTP	3.39 ± 1.78	−7.57 ± 2.25*,**	0.54 ± 2.66	9.88 ± 2.39*,**
Tryptophan	3.46 ± 2.22	0.56 ± 2.82	−3.12 ± 2.68	−3.56 ± 1.87
Δ GFR, ml/min/g KW				
Control	0.04 ± 0.12	−0.15 ± 0.11	−0.03 ± 0.10	0.09 ± 0.09
L-5-HTP	−0.08 ± 0.16	−0.53 ± 0.13	−0.10 ± 0.22	0.50 ± 0.19
Tryptophan	0.05 ± 0.15	−0.25 ± 0.28	−0.23 ± 0.23	−0.05 ± 0.26
Δ C_{PAH}, ml/min g KW				
Control	0.52 ± 0.27	0.69 ± 0.42	0.70 ± 0.48	0.25 ± 0.45
L-5-HTP	0.04 ± 0.70	−1.44 ± 0.73	0.17 ± 1.01	1.74 ± 0.55*,**
Tryptophan	−0.38 ± 0.47	−0.65 ± 0.73	−0.49 ± 0.54	0.10 ± 0.38
Δ Mean arterial pressure, mm Hg				
Control	−2.2 ± 1.9	−3.3 ± 2.1	−4.4 ± 2.7	−1.16 ± 2.04
L-5-HTP	−0.9 ± 3.0	−2.6 ± 3.3	−8.6 ± 3.1	−5.67 ± 1.70
Tryptophan	1.3 ± 1.9	−0.6 ± 2.6	−6.7 ± 5.4	−4.23 ± 2.81

Note. Means ± SE; CD = Carbidopa 20 μg/min.
* $P < 0.05$ vs control.
** $P < 0.05$ vs tryptophan.

L-tryptophan, which did not increase urinary serotonin, had little effect on renal function in the rat kidney. Similarly, carbidopa with or without L-tryptophan had little effect on renal function in our studies. Although L-tryptophan has been reported to decrease water and electrolyte excretion when administered in doses >200 mg/kg, this may relate to its conversion to serotonin in the gastrointestinal tract since oral administration is more effective than parenteral administration in accomplishing this effect (19).

An additional result of our studies was the demonstration that the combination of L-5-HTP and carbidopa diminished blood pressure of our rats. We do not know the reason for this, but are considering the possibility that the hypotensive effect may depend upon an increased ratio of central (brain) to peripheral serotonin, since carbidopa (in the presence of high plasma quantities of L-5-HTP) would favor central production by inhibiting aromatic L-amino acid decarboxylase activity in the periphery (20). We are currently testing this hypothesis in a series of chronic rat experiments.

Although we have demonstrated alterations in renal function, following the intrarenal formation of serotonin using pharmacologic doses of L-5-HTP, we are not certain whether this constitutes an intrarenal control mechanism under physiologic circumstances. 5-HTP is normally present in plasma, but in low concentrations. Plasma levels appear dependent upon peripheral aromatic L-amino acid decarboxylase activity, since in the presence of decarboxylase inhibition, the 5-HTP concentration may increase fourfold or more. Conceivably, changes in dietary intake of amino acids, protein metabolism, or certain other conditions might cause alterations in plasma concentrations of 5-HTP, or renal aromatic L-amino acid decarboxylase activity to affect renal serotonin formation. In this context it will be important in the future to determine

whether alterations in usual plasma concentrations of 5-HTP give rise to changes in renal performance in association with alterations in the urinary excretion of serotonin.

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