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Influence of triiodothyronine and dexamethasone on renal amino acid handling in rats loaded with various amino acid mixtures

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Summary. In adult female rats, the influence of dexamethasone or triiodothyronine on renal amino acid handling was investigated in amino acid loaded animals. Amino acids were administered intravenously as two mixtures, each containing four amino acids to overload amino acid reabsorption capacity. Bolus injections of both mixtures were followed by temporary increase in fractional excretion of the administered amino acids as well of the amino acids which were not covered in the mixtures. The administration of the two mixtures was followed by different interactions between various amino acid carriers.

After dexamethasone pretreatment (60 μg/100 g b.wt. for 3 days, once daily) a stimulation of the renal amino acid handling could be shown. Triiodothyronine (20 μg/100 g b.wt. for 3 days, once daily) did not increase tubular reabsorption capacity for amino acids. It even increased fractional amino acid excretion in amino acid loaded rats as a sign of enhanced amino acid metabolism in the kidney and/or increased amino acid uptake into the tubular cells from the luminal site.

Keywords: Amino acid transport – Kidney – Triiodothyronine – Dexamethasone – Amino acid load – Rats

Introduction

It could be shown previously that renal amino acid handling is controlled by various hormones. For example, testosterone was shown to stimulate amino acid uptake in mouse renal cortical slices (Koenig et al., 1982), parathyroid hormone increases amino acid excretion inhibiting amino acid reabsorption (Scriver and Bergeron, 1974), and dexamethasone stimulates taurine transport in flounder renal tubules (King et al., 1982). In own experiments (Fleck, 1992a), repeated administration of triiodothyronine (T3) or dexamethasone caused significant changes of endogenous amino acid plasma concentrations

in young (10 days old) and adult rats (2 months old). In the kidney, the reabsorbed fraction of endogenous amino acid was enhanced after both T3 and dexamethasone treatment in young rats, whereas in adult rats the two hormones were without influence on the tubular reabsorption of amino acids. In young animals, the fractional excretion of endogenous amino acids was reduced in 15 of 22 amino acids after dexamethasone and in 12 of 23 amino acids after T3 treatment, indicating stimulatory effects of both hormones on tubular amino acid carrier systems in immature animals. In adult rats the stimulatory effects of hormone treatment could not be found under physiological conditions. On the other hand, in rats of both age groups it is possible to stimulate the renal excretion of p-aminohippurate after similar treatment with the two hormones (Bräunlich, 1984; Bräunlich et al., 1986). This means that the tubular secretion of organic anions, located at the basolateral membrane of the renal tubuli (Ullrich, 1994), can also be stimulated in adult animals. Therefore the question arose, whether or not the transport carriers located at the luminal membrane, e.g. amino acid transporters, can be stimulated in mature animals, too. To clarify this question, suitable experimental conditions were necessary, because under physiological conditions 98–99.9% of the amino acids are reabsorbed from the ultrafiltrate (Silbernagl, 1992). After loading the animals with high amounts of amino acids it should be possible to prove stimulating hormone effects, because amino acid reabsorption is employed to capacity under these conditions (Silbernagl, 1988). Nevertheless, using amino acid loading, both renal and metabolic effects must be taken into consideration in *in vivo* experiments and the possible stimulation of renal amino acid reabsorption is doubtlessly a phenomenon basing on different mechanisms.

Material and methods

Animals

Investigations were performed on female Wistar rats (Han:Wist) of our institute's own out-bred stock. At the beginning of the experiments the animals were 55 days old and the average body weight was 160 ± 7 g. The rats were kept under standardized conditions including standard Altromin diet and free access to tap water.

Experimental design

The rats were anaesthetized with ketamine (Ursotamin® Serumwerk Bernburg, F.R.G., 7.5 mg/100 g b.wt.) and xylazine (Ursonarkon® Serumwerk Bernburg, F.R.G., 1.2 mg/100 g b.wt.). Both substances were administered intramuscularly. A catheter was placed in a tail vein. The animals were then infused isotonic saline containing 4 g/l fluorescein isothiocyanate (FITC)-inulin (Bioflor, Uppsala, Sweden) at a priming rate of 3 ml/100 g b.wt. per 1 hour for 15 minutes and then at 2 ml/100 g b.wt. per 1 hour for the remainder of the experiment. Thereafter a polyethylene catheter was inserted into the urinary bladder. To minimize urine collecting periods for the determination of GFR and fractional amino acid excretion (FE), urine was collected in 20-minute periods over 3 hours. In previous experiments it could be shown that under these experimental conditions both hematocrit (Fleck et al., 1992) and blood pressure (Fleck and Bräunlich, 1986) remain

nearly constant during the clearance study. In the middle of each period and at the end of the experiment blood was collected from the retrobulbar plexus.

Glomerular filtration rate (GFR) was determined by inulin clearance. Inulin concentration was measured spectrofluorometrically using FITC-inulin (Sohtell et al., 1983) in blood and urine samples. Fluorescence was measured at 480 nm excitation and 520 nm emission wave lenght in a HITACHI F-2000 spectrofluorometer.

Amino acid load

Rats were loaded with two different types of amino acid mixtures. Amino acids were chosen for the following reasons:

- characterization of hormone effects on different types of amino acid carriers
- determination of competition phenomena between various carriers
- estimation of the effect of differently composed amino acid mixtures on the transport of one amino acid (glutamine)
- administration of an extremely high amino acid dose (β-alanine) with respect to normal plasma concentration.

Amino acid doses were determined in previous experiments. It was the goal of the experimental schedule to enhance amino acid plasma concentration more than tenfold, whereas toxic effects of amino acids should be prevented. β-alanine is an exception from this rule: its physiological plasma concentration is very low. Therefore it was possible to increase β-alanine plasma level more than one-hundredfold without any toxic sign. Amino acids were dissolved in distilled water. The injection solutions of both mixtures had an osmolarity of about 1,100 mosmol and a pH of 5.2. From the mixtures 2 ml per 100 g b.wt. were administered as a bolus injection intravenously at the beginning of the clearance experiment. Control animals received the same volume of normal saline. For the composition of the two mixtures see Table 1.

Table 1

Mixture 1				
amino acid	concentration (mg/ml)	MW (g/mol)	pKa	reaction (pH)
arginine	25	174.2	2.0; 9.0; 12.5	basic (10.76)
glutamine	45	146.1	2.2; 9.1	neutral
alanine	45	89.1	2.3; 9.9	neutral (6.1)
taurine	10	125.1	1.5; 8.7	neutral
Mixture 2				
amino acid	concentration (mg/ml)	MW (g/mol)	pKa	reaction (pH)
β-alanine	45	89.1	3.6; 10.2	neutral (6.0–7.3)
glutamine	45	146.1	2.2; 9.1	neutral
valine	25	117.2	2.3; 9.7	neutral (6.0)
leucine	10	131.2	2.3; 9.8	neutral (6.0)

Hormone pretreatment

Triiodothyronine (T_3; SIGMA, St. Louis, U.S.A.) was administered in doses of 20 μg/100 g b.m. once daily for 3 days. In this dose range, hormone receptor sites are completely saturated (Azimova et al., 1986).

Dexamethasone (Dexa; Fortecortin® Mono, (E. Merck, Darmstadt, F.R.G.): 60 μg/100 g b.m. were given for 3 days, once daily. Following this dose, glucocorticoid receptor sites are completely saturated by dexamethasone (Rafestin-Oblin et al., 1986). Both types of treatment were performed via the intraperitoneal route. Substances were dissolved in normal saline (1 ml/100 g b.m.). Controls received the solvent only.

Amino acid determination

The determination of amino acids by column chromatography with fluorescence detection is based on that developed by Roth and Hampai (1973) and has been described in detail elsewhere (Silbernagl, 1983). Briefly, proteins were removed from urine and plasma samples by addition of trichloroacetic acid. After centrifugation, the supernatant was neutralized by adding 0.4 N NaOH. Then the samples were diluted with citrate buffer and analyzed by HPLC on an amino acid analyzer (Knauer, Berlin, F.R.G.) with o-phthalaldehyde as a fluorescent amino ligand (Roth, 1971). Calibration runs were performed with freshly prepared amino acid solutions composed of analytical grade amino acids (Serva, Heidelberg, F.R.G.)

Mode of presentation and statistics

Clearances (CL) of amino acids (AA) were calculated as usual:

$$CL_{AA} = (\text{urine conc.}_{AA} * \text{urine volume}) : \text{plasma conc.}_{AA}$$

To calculate the amounts of amino acids reabsorbed in the renal tubules, the difference between filtered amount (plasma $\text{conc.}_{AA} * \text{clearance}_{inulin}$) and amount excreted into urine ($\text{urine conc.}_{AA} * \text{urine volume}$) was determined. The fractional excretion (FE) of amino acids is given in % of $\text{clearance}_{inulin}$:

$$FE_{AA} = (\text{clearance}_{AA} : \text{clearance}_{inulin}) * 100$$

The results are summarized as arithmetic means ± S.E.M. with n = 6 in each group. The level of significance for differences between observations was assessed with Student's t-test and were considered statistically significant when $p \leq 0.05$ or ≤ 0.0001.

Results

In Table 2, the plasma concentrations and various parameters characterizing renal amino acid handling are given for those amino acids administered as bolus injection at the beginning of the clearance experiment. Values are shown for control rats, which were not loaded with amino acids and not pretreated with hormones. With the exception of β-alanine and taurine, transported by a separate carrier system (Chesney et al., 1988), the fractional excretion of the other amino acids is below 1%. In these control experiments, the mean urine flow was 0.042 ml/min * 100 g b.wt. and the GFR reached 0.62 ml/min * 100 g b.wt.

The administration of amino acid mixtures as single bolus injections caused distinct changes in renal function and renal transport of the amino acids measured. The glomerular filtration rate increased both after amino acid

Table 2. Normal plasma concentrations and various parameters characterizing the renal transport of amino acids (AA) administered in following experiments as bolus injection in mixture 1 and 2. Arithmetic means ± S.E.M.; n = 12

Amino acid	Plasma concentration [μM]	AA-clearance [μl/min * 100 g]	Fractional excretion [%]	Amount		
				filtered	excreted	reabsorbed
				[μmol/30 min * 100 g b.m.]		
β-Ala	11 ± 8	31 ± 18	5.75 ± 4.22	0.20 ± 0.13	0.01 ± 0.01	0.19 ± 0.13
Tau	115 ± 28	25 ± 14	4.37 ± 2.74	2.20 ± 0.99	0.09 ± 0.05	2.12 ± 0.97
Arg	136 ± 26	3 ± 1	0.54 ± 0.33	2.61 ± 0.98	0.01 ± 0.01	2.60 ± 0.98
Leu	173 ± 28	2 ± 2	0.45 ± 0.28	3.14 ± 1.10	0.01 ± 0.01	3.13 ± 1.10
Val	250 ± 56	2 ± 2	0.41 ± 0.29	4.49 ± 1.75	0.02 ± 0.01	4.48 ± 1.75
Ala	301 ± 68	4 ± 2	0.73 ± 0.44	5.42 ± 2.28	0.03 ± 0.01	5.38 ± 2.28
Gln	344 ± 33	5 ± 3	0.89 ± 0.53	6.15 ± 3.76	0.04 ± 0.02	6.10 ± 3.76

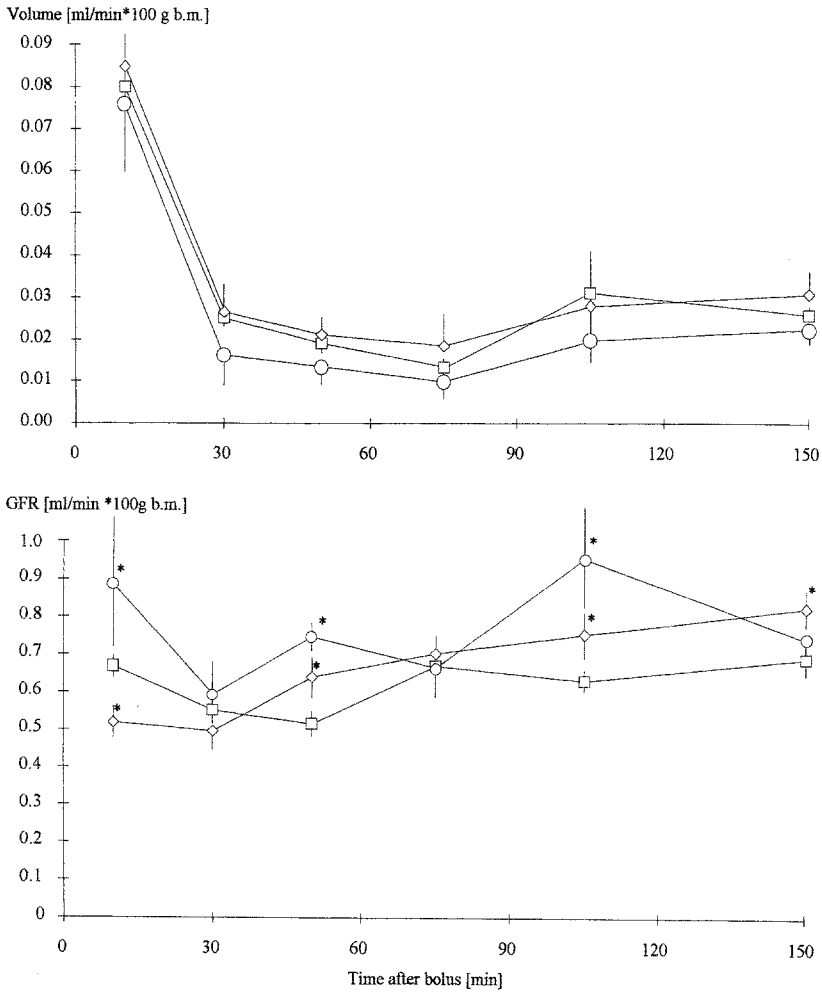

Fig. 1. Time course of urine flow and GFR after volume load (2 ml/100 g b.m.) as a bolus of either saline or amino acid mixture at the beginning of the clearance study. During the experiments continuous infusion of normal saline was performed in all groups (cp. method). □ NaCl bolus; ○ mixture 1 (Arg, Gln, Ala, Tau); ◇ mixture 2 (β-Ala, Gln, Val, Leu). Arithmetic means ± S.E.M., n = 6. * significantly different from saline group ($p \leq 0.05$)

mixtures 1 and 2, more pronounced following administration of mixture 1 (Fig. 1). Interestingly, the urine flow is not affected by the two mixtures. The polyuric effect of the volume load was visible in saline and amino acid treated rats only in the first clearance period (Fig. 1).

As expected, plasma concentrations of amino acids, administered in mixtures 1 and 2, increased significantly more than tenfold three minutes after bolus injection (Fig. 2; see also Table 3) and reached control values after about 2 hours. The plasma disappearances of alanine, arginine, β-alanine, and

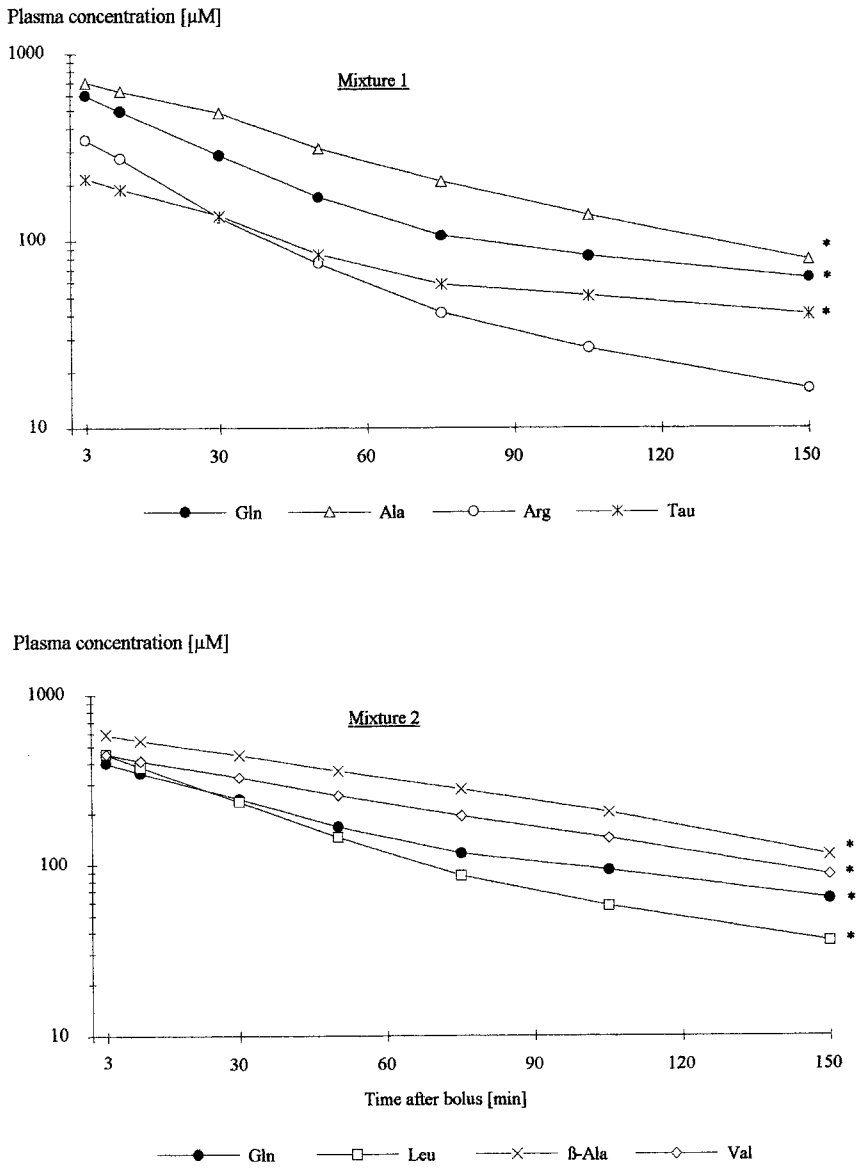

Fig. 2. Plasma disappearance of amino acids administered in mixture 1 or 2, respectively. Semilogarithmic presentation of the arithmetic means of rats treated with saline (n = 6). Values of controls without amino acid bolus see Table 1. * significantly different from controls without amino acid bolus ($p \leq 0.05$)

Table 3. Amino acid plasma concentrations and fractional excretion (FE) of amino acids in rats 3 and 30 minutes after bolus injection, respectively, of mixture 1 or 2 in comparison with saline treatesd animals

Amino acid	Plasma concentration [μM]			Fractional excretion [%]		
	NaCl	mixture 1	mixture 2	NaCl	mixture 1	mixture 2
β-Ala	11 ± 1	5 ± 0	****5,803** ± 250	5.7 ± 0.5	*68.5 ± 9.6	***46.8** ± 10.1
Asp	47 ± 2	87 ± 5	42 ± 11	1.9 ± 0.2	*98.8 ± 27.2	*97.4 ± 14.5
Met	61 ± 2	54 ± 3	59 ± 2	1.0 ± 0.1	*8.5 ± 0.7	*6.9 ± 0.2
His	66 ± 4	31 ± 8	65 ± 11	0.9 ± 0.1	*70.9 ± 23.2	*27.3 ± 3.1
Asn	70 ± 2	*147 ± 3	88 ± 6	1.0 ± 0.1	*18.0 ± 3.6	*48.2 ± 3.2
Phe	77 ± 4	125 ± 71	53 ± 4	3.7 ± 0.7	5.0 ± 1.3	7.1 ± 0.7
Tyr	80 ± 5	103 ± 25	83 ± 6	1.3 ± 0.2	*11.4 ± 3.9	*11.4 ± 2.4
Trp	112 ± 3	94 ± 6	96 ± 5	0.5 ± 0.1	*2.6 ± 0.4	*2.6 ± 0.6
Tau	115 ± 4	****2,152** ± 47	*481 ± 26	4.4 ± 0.3	***10.6** ± 1.3	*145.8 ± 14.1
Ile	135 ± 3	148 ± 4	152 ± 40	0.4 ± 0	*7.5 ± 0.7	*6.6 ± 0.9
Arg	136 ± 3	****3,473** ± 98	*247 ± 33	0.5 ± 0	***11.1** ± 1.2	*2.5 ± 0.4
Glu	146 ± 5	*469 ± 31	352 ± 47	1.8 ± 0.3	*112.4 ± 15.3	*103.4 ± 16.2
Leu	173 ± 22	279 ± 6	****4,470** ± 113	0.5 ± 0.1	*4.3 ± 0.4	***9.0** ± 0.6
Gly	183 ± 3	*500 ± 43	280 ± 33	1.7 ± 0.1	*33.5 ± 2.9	*56.7 ± 6.7
Ser	185 ± 5	*548 ± 47	321 ± 30	1.0 ± 0.1	*31.4 ± 3.6	*35.8 ± 5.6
Lys	250 ± 8	*405 ± 18	*588 ± 26	0.4 ± 0	*44.3 ± 9.7	*37.9 ± 5.6
Val	250 ± 7	262 ± 4	******4,424 ± 186	0.4 ± 0	*7.8 ± 1.2	***35.3** ± 1.4
Ala	301 ± 9	****7,013** ± 443	*479 ± 18	0.7 ± 0.1	***11.1** ± 0.9	*21.5 ± 3.5
Gln	344 ± 42	****5,990** ± 176	****3,941** ± 240	0.9 ± 0.1	***12.7** ± 1.7	***52.7** ± 4.8
Thr	424 ± 16	*846 ± 63	509 ± 30	0.6 ± 0.1	*54.7 ± 7.9	*91.6 ± 49.3

Bold values = amino acids were administered in the respective mixture.
Arithmetic means ± S.E.M.; n = 6–12. * significantly different from saline bolus ($p \leq 0.0001$); ** increase in plasma concentration more than 10fold compared to saline bolus.

valine followed a first order kinetics whereas those of glutamine, taurine, and leucine seemed to be biphasic.

The fractional excretion of the administered amino acids increased in parallel to enhanced plasma amino acid concentrations (Fig. 3). After injection of mixture 1, this increase is highly significant only 30 minutes after amino acid loading. But following administration of mixture 2, the fractional amino acid excretion is significantly enhanced for about one hour and maximal effects are approximately 4 to 5 times higher compared to mixture 1. The fractional excretion of β-alanine, administered in an extremely high dose related to the physiological plasma concentration, remained enhanced over the whole clearance study (Fig. 3).

As shown in Table 3, the administration of amino acid mixtures 1 and 2 also changed the plasma concentrations and the fractional excretion of those amino acids which were not contained in the mixtures. Because of the well-known physiological variance of amino acid plasma concentrations, an unusally high level of probability was taken into consideration. Nevertheless, in 10 cases the plasma concentrations of endogenous amino acids were significantly enhanced 3 minutes after bolus injection of mixtures 1 and 2. With few exceptions, the fractional excretions of all amino acids investigated were significantly increased in the first clearance period after amino acid loading.

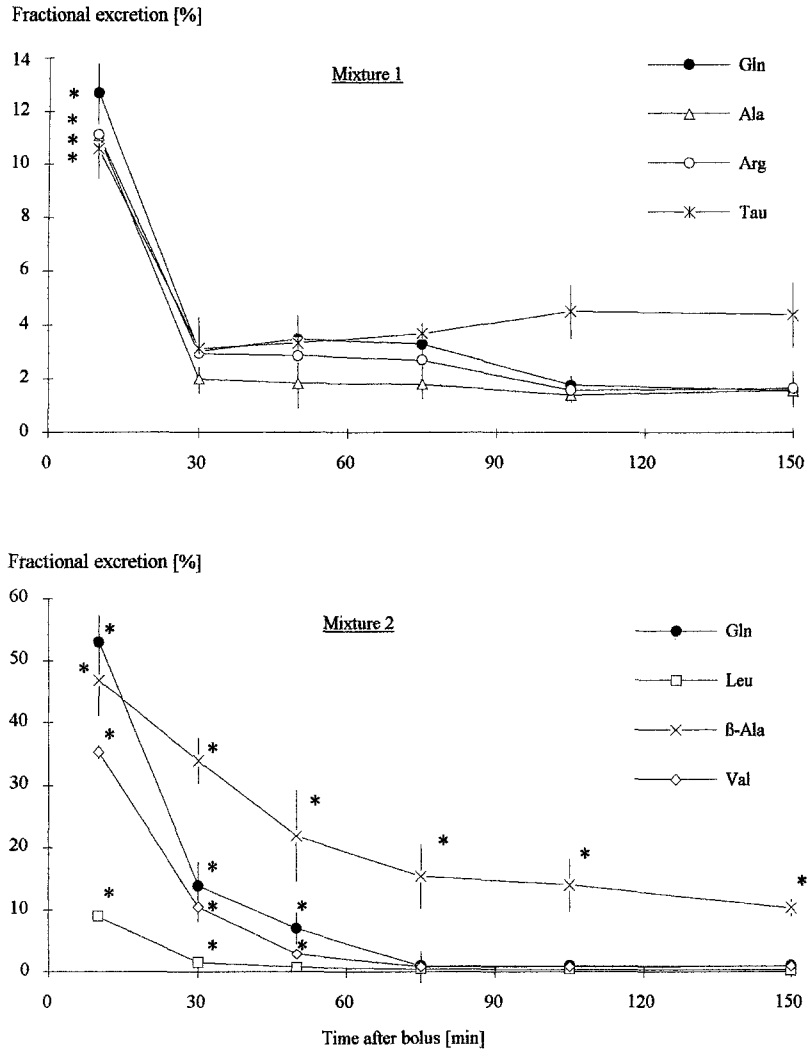

Fig. 3. Fractional excretion of amino acids administered in mixture 1 or 2, respectively. Arithmetic means ± S.E.M., n = 6. * significantly different from nonloaded rats ($p \leq 0.05$)

For further characterization of the unexpected effects of the amino acid bolus on plasma concentrations of those amino acids which were not administered within the mixtures, in Fig. 4 the time course of the plasma levels of these amino acids is given. It can be stated that the concentrations of a couple of amino acids is unchanged after both mixture 1 and 2. But after mixture 1 the levels of threonine, serine, glycine, valine, lysine, and leucine and after mixture 2 those of alanine, threonine, glutamine, lysine, taurine, serine, glycine, arginine, and aspartate raised distinctly. Most of the enhanced plasma concentrations did not return to base line up to the end of the clearance experiment.

Under the experimental conditions described above, the renal amino acid reabsorption capacity seemed to be employed to capacity. Therefore, in

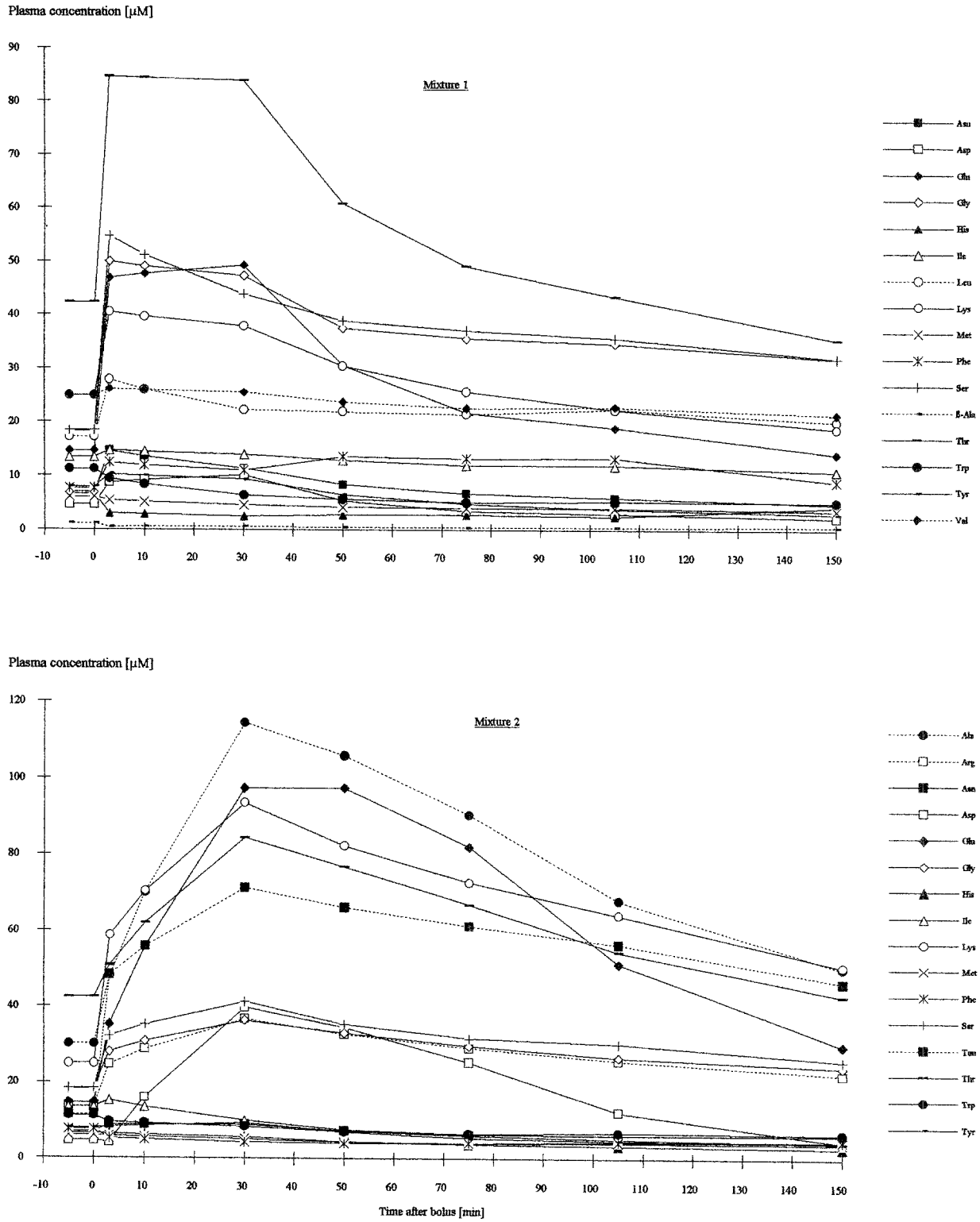

Fig. 4. Plasma concentrations of amino acids which were not administered in mixture 1 (upper graph) or mixture 2 (lower graph) in saline pretreated rats. Arithmetic means, n = 6

the second part of experiments, the influence of triiodothyronine and dexamethasone should be investigated under load conditions. The effect of treatment with both hormones on urine flow and GFR is shown in Fig. 5. T3 pretreatment reduced urine production and GFR in amino acid loaded rats (mean of mixtures 1 and 2). The dexamethasone effect on both parameters is not different from the group pretreated with 0.9% NaCl. The correlation of the reabsorbed amounts of amino acids to their plasma concentrations after administration of mixture 1 shows, with one exception (glutamate), that the

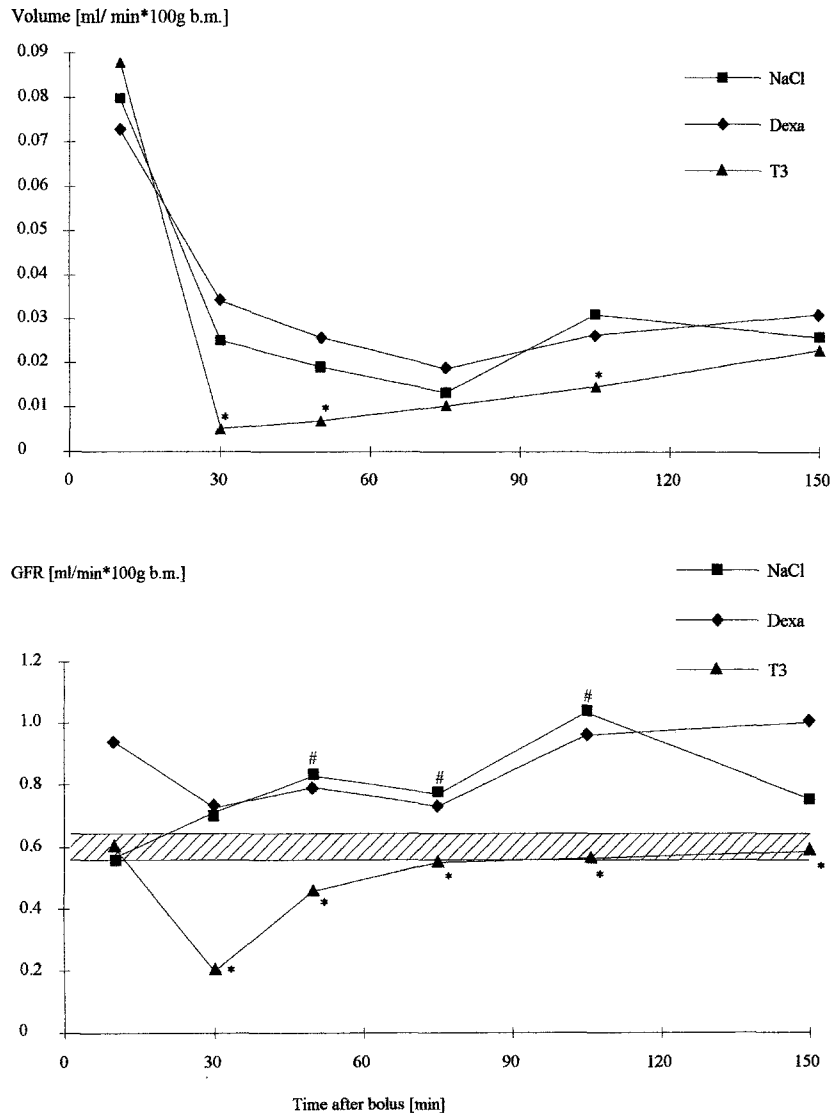

Fig. 5. Effects of hormone treatment (◆ dexamethasone, ▲ T_3, ■ NaCl) on urine flow and GFR in rats laoded with a bolus of saline or amino acids as mixture 1 or 2. Arithmetic means of mixtures 1 and 2, n = 10–12, * significant influence of hormones ($p \leq 0.05$); # significant influence of amino acid load compared to NaCl treated rats ($p \leq 0.05$); Homogenous band – mean GFR of rats without amino acid load

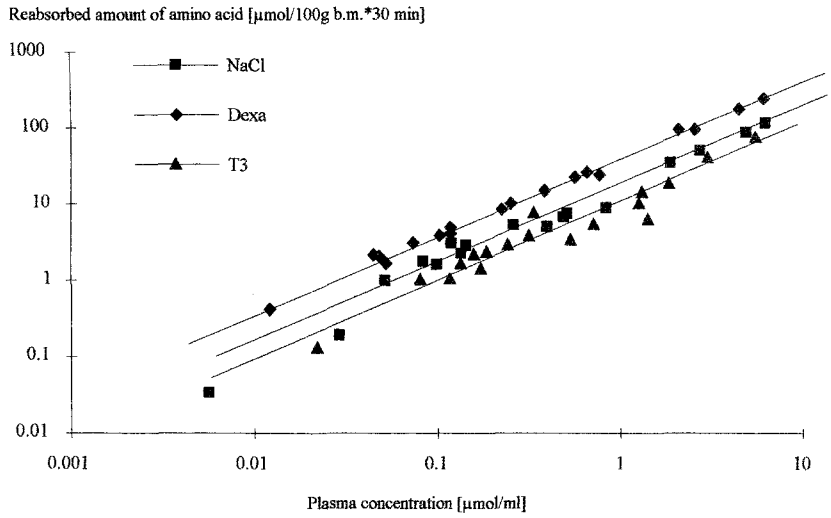

Fig. 6. Effects of hormone pretreatment (◆ dexamethasone, ▲ T_3, ■ NaCl) on reabsorbed amounts of amino acids in dependence on respective amino acid plasma concentration. Values are given for the first clearance period after administration of mixture 1. Each symbol represents means of one amino acid, n = 6

amino acid reabsorption capacity is distinctly enhanced after dexamethasone pretreatment (Fig. 6). On the other hand, after T3 treatment amino acid reabsorption is less effective compared to non-hormone treated animals. This reduction in reabsorption capacity becomes more impressive after administration of mixture 2 (not shown).

Discussion

The physiological values of amino acid plasma concentrations and the normal parameters describing renal amino acid handling, measured in this study, are in good accordance with own previous findings (Fleck, 1992a,b) and data from the literature (Lingard et al., 1974). Differences between these three sources, caused by differences in food intake, animal strain, sex, and in methodological difficulties, can be neglected for further interpretation of the results.

Immediately after administration of a volume load (2 ml/100 g b.wt.), urine flow is significantly enhanced. This polyuria should be kept in mind, because it shortens the contact time of the ultrafiltrate within the tubuli followed by a possibly reduced amino acid reabsorption. However, this effect is quite similar in amino acid and saline loaded rats and, therefore, it is without consequence for the following comparisons between the different groups. The administered bolus volume is nearly completely excreted within the first clearance period and hyperhydratation is avoided. Furthermore, glomerular filtration is slightly enhanced after amino acid load. This well-known phenomenon is described to be caused e.g. by glucagon, the secretion of which after amino acid administration is distinctly enhanced (Brenner et al., 1982; Alvestrand and Bergström, 1984).

As expected, after amino acid load, plasma concentrations and fractional excretion of the administered amino acids increased distinctly even if an unusually high level of confidence ($p \leq 0.0001$) is considered. But the latter parameter reaches baseline values already after 30 minutes. This finding reflects the effective regulation of amino acid homoeostasis within the organism. Only in the case of β-alanine (mixture 2) the plasma concentration remains significantly enhanced at the end of the clearance study. This is due to the enormous dosage of this amino acid calculated in relation to the physiologically low endogenous β-alanine concentration.

However, the amino acid load interferes also with the transport of endogenous amino acids which were not contained in the respective amino acid mixture. The reason for this phenomenon could be a direct competition at the amino acid carrier sites (Christensen, 1990) or it could be caused by displacement of endogenous amino acids by the amino acids administered within the mixtures. Transamination steps are of minor importance because changes in plasma amino acid concentrations were observed already 3 to 5 minutes after amino acid load. The most probable reason for the general increase in endogenous amino acid plasma concentrations seems to be the interferences at the transport carrier systems, because the fractional excretion of many endogenous amino acids was significantly enhanced after amino acid loading. In some cases this indicates a direct competition at the carrier molecules, if the respective amino acids are transported by the same carrier (Collarini and Oxender, 1987), but also interactions concerning intracellular energy supply could be possible reasons for these effects. Alltogether, the amino acids which were not contained within the two mixtures can be divided into three groups:

- unchanged plasma concentration after amino acid load
- extremely increased plasma concentrations after amino acid bolus injection
- moderate rise in plasma concentration after amino acid loading

First of all this differentiation is caused by different extents of interrelationship between endogenous and administered amino acids. At the end of the clearance experiments amino acids administered were completely excreted and plasma concentrations of endogenous amino acids reached baseline values, too.

The pretreatment of the animals with T3 or dexamethasone, two catabolic hormones, caused different effects on renal amino acid handling. After T3, kidney weight is significantly increased (1151 ± 35 vs. 834 ± 38 mg/100 g b.m.) whereas after dexamethasone it is unchanged. Urine flow is reduced after T3 in amino acid loaded rats and not changed after dexamethasone. The glomerular filtration rate is also significantly diminished after T3; after dexamethasone it is distinctly enhanced in amino acid loaded animals. In principle these findings confirm results obtained previously in nonloaded rats. In these experiments slight to moderate changes in urine flow and GFR could be found after hormone pretreatment, too (Bräunlich, 1984; Bräunlich et al., 1986).

For the renal transport of p-aminohippurate (PAH) it could be shown that both T3 and dexamethasone are able to stimulate this transport at the

basolateral site of the renal tubular cell (Bräunlich, 1988). This phenomenon should be proved in our study for transport steps located at the luminal membrane, e.g. for amino acid reabsorption. As mentioned in the introduction, a stimulation of amino acid transport can be expected only after employment of the transport capacity. Therefore, in this study hormone effects were investigated after amino acid loading as described above. Taking together all results, it must be stressed that only dexamethasone has slight effects on renal amino acid handling *in vivo*. The fractional excretion of amino acids, the most important parameter describing the transport capacity, is not significantly reduced after dexamethasone. This means, despite distinct overloading of amino acid reabsorption, followed by a significant increase in fractional excretion of the administered and the endogenous amino acids, there is, with the exception of valine, nearly no reduction of the fractional excretion of amino acids after dexamethasone pretreatment. Only the distinctly enhanced absolutely reabsorbed amino acid amounts correlated to their plasma concentrations indicate a moderate stimulation of amino acid transport capacity after dexamethasone. One reason for this unexpected result could be the dexamethasone effect on amino acid metabolism (Baxter, 1976). Possibly the catabolic hormone actions, resulting in distinct changes in amino acid plasma concentrations (not shown in detail), could mask renal effects of dexamethasone. Because of enhanced metabolism within the renal tubular cells the so-called house-keeping of the tubular cells requires higher amounts of amino acids followed by a nonspecifical increase in cellular uptake of amino acids (Silbernagl, 1988). Therefore, the uptake of amino acids from the blood vessels at the basolateral site could be enhanced after dexamethasone, too. This uptake is followed by an enhanced intracellular amino acid concentration and, therefore, by a reduced concentration gradient between tubular fluid and tubular cell. This could be the reason for a diminished driving force for amino acid reabsorption and could mask stimulatory hormone effects at the luminal site. This hypothesis is supported by the results obtained after T3 pretreatment. In this experimental approach the fractional excretion of amino acids was increased and the amounts of reabsorbed amino acid were reduced. These phenomena reflect the overlapping between possible effects of T3 directly at the amino acid carrier sites and its catabolic action within the tubular cell. In further experiments it remains to characterize *in vitro* effects of both hormones directly at the luminal membrane to distinguish between unspecific catabolic hormone effects and specific influences of the two hormones on transport processes.

References

Alvestrand A, Bergström J (1984) Glomerular hyperfiltration after protein ingestion, during glucagon infusion, and insulin-dependent diabetes is induced by a liver hormone: deficient production of this hormone in hepatic failure causes hepatorenal syndrome. Lancet i: 195–197

Azimova S, Normatov K, Umarova G, Kalontarov A, Makhmudova A, Kashimova Z, Abdukarimov A (1986) Nature of thyroid hormone receptors. Intracellular functions of thyroid-binding prealbumin. Biochemistry 50: 1651–1659

Baxter JD (1976) Glucocorticoid hormone action. Pharmacol Ther [B]: 605–659
Bräunlich H (1984) Postnatal development of kidney function in rats receiving thyroid hormones. Exp Clin Endokrinol 83: 243–250
Bräunlich H (1988) Hormonal control of postnatal development of renal tubular transport of weak organic acids. Pediatr Nephrol 2: 151–155
Bräunlich H, Köhler A, Schmidt I (1986) Acceleration of p-aminohippurate excretion in immature rats by dexamethasone treatment. Med Biol 64: 267–270
Brenner BM, Meyer TW, Hostetter TH (1982) Dietary intake and the progressive nature of kidney disease: the role of hemodynamically mediated glomerular injury in the pathogenesis of progressive glomerulus sclerosis in aging, renal ablation and intrinsic renal disease. N Engl J Med 307: 652–659
Chesney RW, Zelikovic I, Dabbagh S, Friedman A, Lippincot S (1988) Development of β-amino acid transport in the kidney. J Exp Zool 248: 25–32
Christensen HN (1990) Role of amino acid transport and countertransport in nutrition and metabolism. Physiol Rev 70: 43–71
Collarini EJ, Oxender DL (1987) Mechanisms of transport of amino acids across membranes. Ann Rev Nutr 7: 75–90
Fleck C (1992a) Renal transport of endogenous amino acids. I. Comparison between immature and adult rats. Renal Physiol Biochem 15: 257–265
Fleck C (1992b) Renal transport of endogenous amino acids. II. Influence of treatment with triiodthyronine or dexamethasone in immature and adult rats. Renal Physiol Biochem 15: 266–276
Fleck C, Bräunlich H (1986) Relation between renal and hepatic excretion of drugs: I Phenol red in comparison with p-aminohippurate and indocyanine green. Exp Pathol 29: 179–192
Fleck C, Börner A, Kretzschmar M, Machnik G, Sprott H, Zimmermann T, Keil E, Bräunlich H (1992) Liver function after bilateral nephrectomy. Liver 12: 319–325
King PA, Beyenbach KW, Goldstein L (1982) Taurine transport by isolated flounder renal tubules. J Exp Zool 223: 103–114
Koenig H, Goldstone A, Lu CY (1982) Testosterone induced a rapid stimulation of endocytosis, amino acid and hexose transport in mouse kidney cortex. Biochem Biophys Res Commun 106: 346–353
Lingard JM, Turner B, Williams DB, Young JA (1974) Endogenous amino acid clearance by the rat kidney. Aust J Exp Biol Med Sci 52: 687–695
Rafestin-Oblin ME, Lombes M, Lustenberger P, Blanchardic P, Michaud A, Claire M (1986) Affinity of corticosteroids for mineralcorticoid and gluccocorticoid receptors of the rabbit kidney: Effect of steroid substitution. J Steroid Biochem 25: 527–534
Roth M (1971) Fluorescence reaction for amino acids. Anal Chem 43: 880–882
Roth M, Hampai A (1973) Column chromatography of amino acids with fluorescence detection. J Chromatogr 83: 353–356
Scriver CR, Bergeron M (1974) Amino acid transport in kidney. The use of mutation to dissect membrane and transepithelial transport. In: Nyhan WL (ed) Heritable disorders of amino acid metabolism, Willey, New York, pp 515–592
Silbernagl S (1988) The renal handling of amino acids and oligopeptides. Physiol Rev 68: 911–1007
Silbernagl S (1992) Amino acids and oligopeptides. In: Seldin DW, Giebisch G (eds) The kidney, vol 2. Raven Press, New York, pp 2889–2920
Sohtell M, Kalmark B, Ulfendahl H (1983) FITC-inulin as a kidney tubule marker in the rat. Acta Physiol Scand 119: 313–316
Ullrich KJ (1994) Specificity of transporters for organic anions and organic cations in the kidney. Biochim Biophys Acta 1197: 45–62

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