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Research Communications

Dietary fiber stimulates the extra-renal route of nitrogen excretion in partially nephrectomized rats

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*The purpose of this study was to determine the effect of an indigestible carbohydrate/dietary fiber (the oligosaccharide/fiber blend, or O/F blend) on extra-renal nitrogen excretion in nephrectomized rats. The O/F blend provided a diversified source of soluble and insoluble fibers: 41.2% fructooligosaccharides, 26.4% insoluble oat fiber, 17.7% soy polysaccharides, 10.3% gum arabic, and 4.4% carboxymethylcellulose. Forty partially nephrectomized rats were randomized to one of four dietary treatments that varied in protein and O/F blend content. Dietary treatments were administered for 17 days (an adaptation phase of 10 days, followed by an experimental phase of 7 days) and included the following treatment groups: (1) 8% casein, 0% O/F blend, (2) 8% casein, 8% O/F blend, (3) 14% casein, 0% O/F blend, and (4) 14% casein, 8% O/F blend. Compared with nonnephrectomized normal rats (*n = *10), the nephrectomy procedure induced a marked renal insufficiency, with significant increases in plasma urea and creatinine concentrations (90% and 44%, respectively). In this model of renal insufficiency, feeding the fermentable fibers had the same effect as in previous studies in normal rats: The O/F blend increased cecal weight and cecal blood flow, leading to accelerated diffusion of blood urea into the cecal lumen (by threefold), urealysis to ammonia and protein synthesis by the microflora, and increased fecal excretion of nitrogen. The efficiency of O/F blend in stimulating the extra-renal route of nitrogen excretion was greatly enhanced by the simultaneous use of a low protein rate: Fecal nitrogen excretion accounted for 23% of total nitrogen excretion in rats fed a 14% casein diet, compared with 45% in those receiving the 8% casein diet. The increase of fecal nitrogen excretion was accompanied by an equal and significant decrease in urinary nitrogen excretion and a decrease in blood urea nitrogen. In conclusion, addition of an O/F blend to a low protein diet exerts a potent urea lowering effect in renally insufficient rats, suggesting that these dietary conditions could help delay the progression of renal failure or prevent its consequences.* (J. Nutr. Biochem. 9:613–620, 1998)

Keywords: dietary fiber; dietary protein; renal failure; plasma urea; nitrogen excretion; rats

Introduction

Considerable attention has been given during the past few years to the impact of nutrition on kidney disease.[1–3] Interventions that restrict protein intake lower the plasma urea concentration, alleviate adverse clinical manifestations,[4–6] and may slow the progression of chronic renal failure.[7–10] Another dietary approach may involve the use of a fiber enriched diet, which increases the nitrogen excretion via the fecal route.[11–13] Such an effect has been reported in several species including healthy humans and patients with cirrhosis or diabetes.[13–17]

In rats, a substantial increase in the supply of fermentable

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Received May 19, 1998; accepted July 28, 1998.

655 Avenue of the Americas, New York, NY 10010
0955-2863/98/$19.00
PII S0955-2863(98)00062-X

carbohydrate to the large bowel can lead to cecal hypertrophy. This hypertrophy includes an enlargement of the cecal absorptive mucosa and increased blood flow, which favor the diffusion of blood urea into the cecal lumen. The presence of a highly ureolytic microflora maintains a urea concentration gradient favorable to a net uptake of blood urea by the large intestine.[18] Ammonia generated by urease-positive bacteria is used for bacterial protein synthesis, thus trapping nitrogen for eventual elimination in the feces.

In a previous rat experiment,[19] we observed that the consumption of an oligosaccharide/fiber blend (the O/F blend) that contained fructooligosaccharides (FOS), oat and soy fiber, gum arabic, and a small amount of carboxymethylcellulose (CMC) to a low protein diet resulted in an expansion of fecal nitrogen excretion such that fecal and urinary nitrogen rates were nearly equal (50% of total nitrogen excretion by each route). Although the fermentable fibers (gum arabic and soy polysaccharide) and FOS increase fecal nitrogen, the nonfermentable fibers (oat fiber and CMC) tend to bolster fecal wet weight and accelerate intestinal transit, thus limiting exposure of the colonic mucosa to putrefactive end products of nitrogen metabolism.

The purpose of this study was to determine the effect of feeding an O/F blend on fecal nitrogen excretion in the presence of two different levels of protein (8% and 14% casein) in partially nephrectomized rats.

Materials and methods

Animals and diets

We used 40 male Sprague-Dawley rats (IFFA-CREDO, l'Arbresle, France) that weighed approximately 200 g and had undergone surgical ablation of approximately 70% of the renal mass, as previously described.[20] Under light pentobarbital anesthesia, the right kidney was gently dissected from surrounding tissue and removed. After isolation of the left kidney, the two poles were excised with scissors. The nephrectomized rats were randomized to one of four dietary treatment groups (*Table 1*): (1) 8% casein, 0% O/F blend, (2) 8% casein, 8% O/F blend, (3) 14% casein, 0% O/F blend, and (4) 14% casein, 8% O/F blend. The O/F blend, which consisted of 41.2% FOS, 26.4% oat fiber, 17.7% soy polysaccharide, 10.3% gum arabic, and 4.4% CMC, was substituted for wheat starch in the diets. In addition to the nephrectomized rats, 10 nonnephrectomized controls (referred to as "normal rats") were fed the 14% casein, 0% O/F blend to determine the effects of the nephrectomy procedure.

Rats were allowed free access to water and diets and the dark period lasted from 10:00 PM to 8:00 AM. During the adaptation period (10 days), rats were housed two per cage in a temperature controlled room (22°C). Following the adaptation phase, rats were individually housed for 7 days in metabolic cages fitted with urine/feces separators suitable for feces and urine collection (experimental period). Daily food consumption and body weight were recorded every 3 days during the adaptation period, then daily during the last 5 days of the experimental period. During these days, urine (acidified by HCl, final concentration of 5 mmol/L) and feces were collected for determination of nitrogen excretion. Animals were maintained and handled according to the recommendations of the Institutional Ethic Committee of the University of Clermont-Ferrand.

Table 1 Composition of semi-purified diets expressed as g/100 g of diet (dry basis)

Ingredients	Low protein		Normal protein	
	FF	O/F	FF	O/F
Casein	8	8	14	14
DL-Methionine	0.3	0.3	0.3	0.3
Wheat starch	78.7	70.7	72.7	64.7
Oligosaccharide/fiber blend[1]	0	8	0	8
Corn oil	5	5	5	5
Mineral mixture[2]	7	7	7	7
Vitamin mixture[2]	1	1	1	

[1]Oligosaccharide/fiber blend (O/F): 41.2% fructooligosaccharide, 26.4% oat fiber, 17.7% soy polysaccharide, 10.3% gum arabic, and 4.4% carboxymethylcellulose. This product was supplied by Ross Products Division, Abbott Laboratories, Columbus, OH USA).
[2]Vitamins and minerals supplied in mg/kg (except as noted) of diet: thiamin, 20; riboflavin, 15; pyridoxine, 10; nicotinamide, 100; calcium panthotenate, 70; folic acid, 5; biotin, 0.3; cyanocobalamin, 0.05; retinyl palmitate, 1.5; DL-α-tocopheryl acetate, 125; cholecalciferol, 0.15; menadione, 1.5; ascorbic acid, 50; myo-inositol, 100; choline, 1.36 g; $CaHPO_4$, 15 g; K_2HPO_4, 2.5 g; KCl, 5 g; NaCl, 5 g; $MgCl_2$, 2.5 g; Fe_2O_3, 2.5; $MnSO_4.H_2O$, 125; $CuSO_4.5H_2O$, 0.2; $ZnSO_4.7H_2$), 100; KI, 0.4. Purchased from UAR (Villemoisson/Orge, France).
FF–fiber-free diets.

Sampling procedure

Rats were sampled just after the dark period (between 8:00 and 9:00 AM). The procedure of blood sampling from anesthetized rats (40 mg sodium pentobarbital/kg body weight) for determination of arteriovenous differences across the cecum has been previously described.[21] For blood flow measurement, bromo-sulfophtalein in saline solution (4.7 mmol/L) was infused at a rate of 50 μL/min into the small afferent vein, on the internal curvature of the cecum. Dilution of the marker in the vein draining the whole cecum allows determination of the cecal blood flow. After blood sampling, the cecum and its contents were removed and weighed (total cecal weight). Duplicate samples of cecal contents were transferred to 2 mL microfuge tubes, which were immediately stored at –20°C. The cecal wall was flushed clean with ice-cold saline, blotted on filter paper, and weighed (cecal wall weight). Cecal water was determined by difference between wet weight and dry weight of aliquots of cecal contents that were dried to constant weight. Supernatants of the digestive contents were obtained by centrifuging the microfuge tubes at 20,000× g for 10 minutes at 4°C.

Analytical procedures

Short-chain fatty acids (SCFA) were measured by gas-liquid chromatography on aliquots of supernatants from cecal content.[22] Ammonia concentration was determined enzymatically on neutralized perchloric acid extracts of plasma or digestive contents.[23] Urea was determined on perchloric extracts of plasma using the diacetylmonoxime procedure.[24] Creatinine was measured by colorimetric method in plasma at 500 nm.[25] Amino acids were determined on a Chromakon 500 autoanalyzer (Kontron, Zürich, Switzerland), using lithium buffers and postcolumn ninhydrin detection. The nitrogen of food, cecal content, feces, and urine was determined by Kjeldahl method: Homogenized samples (0.5–1 g of food, cecal content, or feces; 1 mL of urine) were treated with 6 mL of sulfuric acid (36 mol/L) in the presence of a catalyst (K_2SO_4, 1.5 g; Se, 7.5 mg). Finally, the ammonia was extracted and trapped in a solution of boric acid, then determined by direct titration with sulfuric acid.

Table 2 Effect of nephrectomy procedure in rats fed the fiber-free diet with 14% casein[1]

	Total renal mass (g)	Plasma urea concentration (mmol/L	Plasma creatinine concentration (μmol/L)	Nitrogen fecal excretion (mg/day)	Nitrogen urinary excretion (mg/day)
Normal rats	2.30 ± 0.08	3.12 ± 0.22	38.7 ± 1.6	30.7 ± 1.2	190 ± 7
Nephrectomized rats	1.24 ± 0.04[2]	5.92 ± 0.40[2]	55.6 ± 2.1[2]	32.0 ± 1.6	245 ± 14[2]

[1]Each value is the mean ±SEM, $n = 10$. Measurements were made 10 days post-partial nephrectomy. Statistical evaluation of data was carried out by Student's *t*-test.
[2]Significant difference ($P < 0.05$) between group of normal rats and group of nephrectomized rats.

Statistical analysis

Values are given as the means ±SEM and, where appropriate, significance of differences between mean values were determined by analysis of variance (ANOVA; Super ANOVA, ABACUS, Berkeley, CA USA). When necessary, data were normalized by log or reciprocal transformations before ANOVA. P-values of less than 0.05 were considered significant.

Results

The effects of the nephrectomy procedure are presented in *Table 2*. In normal rats, the total renal mass (both kidneys) was 2.30 g. In nephrectomized rats, the remnant renal mass (one partial kidney) was 1.34 g. It is apparent that total renal mass, which at the time of surgery had been decreased by 70% (i.e., only 30% remaining), had recovered by compensatory hypertrophy of the single remaining partial kidney to approximately 58% of the total renal mass in the normal rats. In these nephrectomized rats, the plasma urea and creatinine concentrations were 90% and 44% greater, respectively, than those in the nonnephrectomized normal rats receiving the same diet. At the time during which the rats were studied (10 days after the nephrectomy), the rate of fecal nitrogen excretion did not differ between normal and nephrectomized animals, although the nitrogen urinary excretion was 29% higher in the nephrectomized rats than in the normal rats.

Table 3 summarizes daily food intake, weight gain, and parameters of cecal fermentations. No significant differences in food intake were noted throughout the study. In contrast, there was a significant effect of dietary protein level on body weight gain. The animals fed the 14% protein diet were 25 to 30% heavier on average than their counterparts fed the 8% protein diet. Within protein level, feeding the O/F blend led to a significant enlargement of the cecum, which included an enlargement of the cecal wall and an increase in the contents of the cecum. In parallel with the development of cecal wall, cecal blood flow increased by over 50%. The cecal pH was close to neutral in rats fed the fiber-free diets, whereas it was significantly depressed to pH values in the low 6 range in rats fed the O/F blend.

As shown in *Figure 1*, the total cecal SCFA pool produced from endogenous substrates in rats fed fiber-free diets was approximately 50% greater in rats fed 14% casein than in those fed 8% casein. When the O/F blend was added to the diets containing either protein level, the SCFA concentration in cecum increased by another 50% and the total cecal pool increased approximately threefold. Moreover, feeding the O/F blend altered the molar ratio of

Table 3 Effect of diets on daily food intake, daily weight gain, and parameters of cecal fermentations[1]

			Cecum					
Diets	Daily food intake (g/day)	Daily weight gain (g/day)	Total weight (g)	Wall weight (g)	Blood flow (mL/min)	pH	SCFA concentration (mmol/L)	SCFA molar ratio (Ac/Pr/Bu)
Casein 8%								
FF	22.2 ± 0.9	5.32 ± 0.45	1.83 ± 0.17	0.56 ± 0.03	0.96 ± 0.06	7.08 ± 0.03	89 ± 5	74/16/10
O/F blend	22.8 ± 1.2	5.10 ± 0.21	3.61 ± 0.26[2]	0.81 ± 0.04[2]	1.47 ± 0.07[2]	6.24 ± 0.07[2]	137 ± 6[2]	64/20/16
Casein 14%								
FF	22.6 ± 0.9	6.71 ± 0.79[3]	2.40 ± 0.36	0.58 ± 0.03	1.11 ± 0.08	7.04 ± 0.02	104 ± 7	75/17/8
O/F blend	23.5 ± 1.0	6.82 ± 0.81[3]	4.48 ± 0.42[2,3]	1.07 ± 0.08[2,3]	1.68 ± 0.09[2,3]	6.01 ± 0.08[2,3]	155 ± 8[2,3]	62/24/14
Significance of effects by Super ANOVA								
Casein	NS	$P < 0.005$	$P < 0.03$	$P < 0.01$	$P < 0.01$	$P < 0.02$	$P < 0.01$	
O/F blend	NS	NS	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	
Casein x O/F blend	NS	NS	N	$P < 0.02$	NS	NS	NS	

[1]Each value is the mean ±SEM, $n = 10$. Statistical evaluation of data was carried out by Super ANOVA. NS–nonsignificant. Ac–acetate. Pr–propionate. Bu–butyrate.
[2]Significant difference ($P < 0.05$) between groups of rats fed fiber-free diets (FF) and those fed the oligosaccharide/fiber blend (O/F blend).
[3]Significant difference ($P < 0.05$) between groups of rats fed 8% or 14% casein diets.

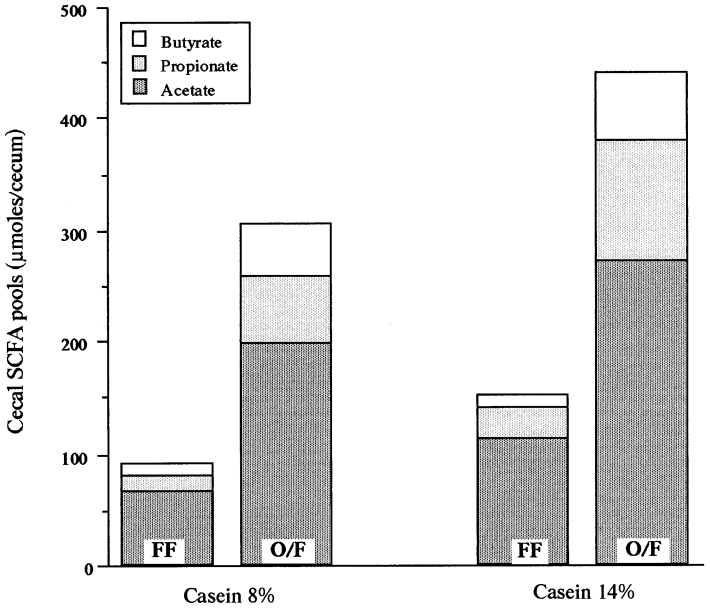

Figure 1 Effect of diets on cecal short-chain fatty acids (SCFA) pools in nephrectomized rats fed fiber-free (FF) or oligosaccharide/fiber blend (O/F) diets. Cecal SCFA pools (μmoles/cecum) = SCFA concentration (mmol/L) × cecal water (mL). Each value is the mean of 10 rats.

acetate/propionate/butyrate with a significant increase of propionate and butyrate at the expense of acetate (*Table 3*).

Figure 2 illustrates the effect of diets on plasma urea. In the non-O/F groups, reducing protein from 14% to 8% of diet caused an average decrease of over 50% in plasma urea concentrations. At either protein level, addition of the O/F blend further reduced plasma concentration of urea by an average of just over 30%.

As shown in *Figure 3A*, within fiber level, cecal ammonia concentrations were over 50% higher in rats fed the 14% casein diet than in those fed the 8% casein level. Within protein level, the addition of the O/F blend in the diet depressed cecal ammonia concentration by over 50%. In parallel, nitrogen accumulation in the cecal contents was

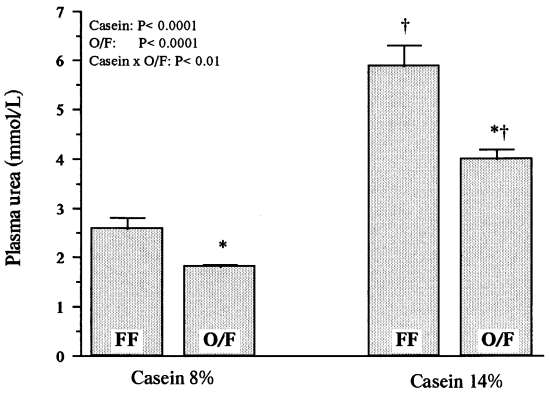

Figure 2 Effect of diets on plasma urea in nephrectomized rats fed fiber-free (FF) or oligosaccharide/fiber blend (O/F) diets. Each value is the mean ±SEM, $n = 10$. Statistical evaluation of data was carried out by Super ANOVA. *Significant difference ($P < 0.05$) between groups of rats fed FF diets and those fed O/F blend diets. †Significant difference ($P < 0.05$) between groups of rats fed the 8% casein level and those fed the 14% casein level.

significantly greater (at least twofold higher) in rats fed high fiber diets than in rats fed fiber-free diets (*Figure 3B*). There was no significant effect of protein intake on cecal total nitrogen in the non-fiber group. In the rats fed O/F, cecal total nitrogen was significantly elevated with the 14% casein treatment.

In the cecum, essential or semi-essential amino acid pools (*Figure 4A*) and nonessential amino acid pools (*Figure 4B*) were influenced by both dietary protein and dietary fiber intake. In rats fed the fiber-free diets, elevation of dietary protein level led to an increase of all cecal amino acid pools. At the lower protein level, the addition of fibers led to an increase of all cecal amino acids except proline. In contrast, with the 14% casein diet, the addition of O/F decreased the cecal pools of glycine, serine, and proline, as well as all of the essential and semi-essential amino acids.

The fluxes of urea and ammonia across the cecum were clearly influenced by dietary conditions (*Figure 5*). There was a net flux of urea from blood compartment to the cecal lumen. This flux depended on both plasma urea concentration and cecal development. There was a significant direct relationship between protein and fiber level and urea flux into the cecal lumen. In parallel, both the addition of fiber and an increase in protein level resulted in a significant increase in the absorption of ammonia from the cecum to the blood compartment. The net balance (urea nitrogen–ammonia nitrogen), which reflects the final utilization of urea, was positive in all cases, but was significantly greater with the O/F diets compared with fiber-free diets at either protein level. The cecal nitrogen balance represents the retention of urea nitrogen in the cecum. This retention, when expressed as a proportion of urea nitrogen absorbed, is 37% in rats fed the 14% casein diets and 60% in rats fed the 8% casein level.

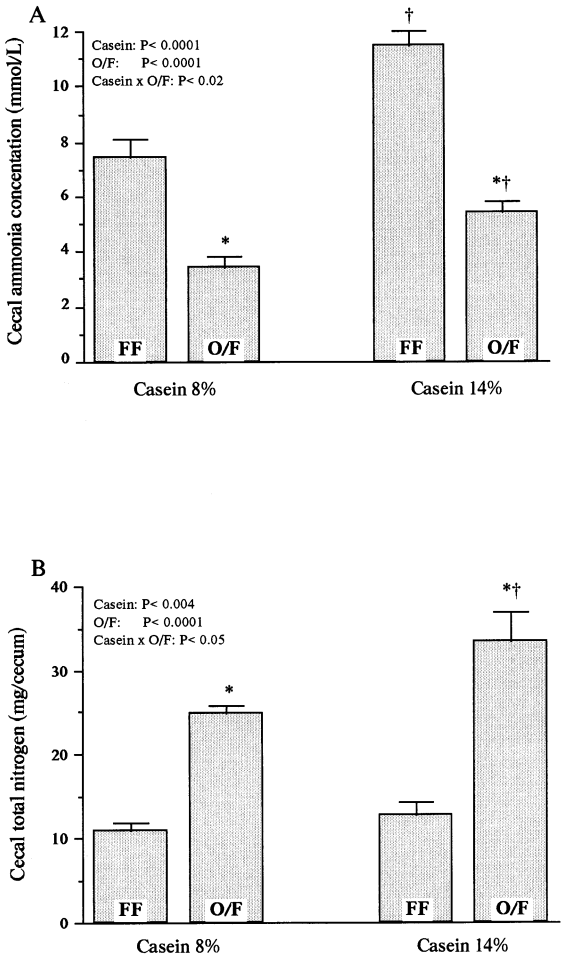

Figure 3 Effect of diets on cecal ammonia (*Figure 3A*) and cecal total nitrogen (*Figure 3B*) in nephrectomized rats fed fiber-free (FF) or oligosaccharide/fiber blend (O/F) diets. Cecal ammonia pool (μmoles/cecum) = cecal ammonia concentration (mmol/L) × cecal water (mL). Each value is the mean ±SEM, $n = 10$. Statistical evaluation of data was carried out by Super ANOVA. *Significant difference ($P < 0.05$) between groups of rats fed FF diets and groups of rats fed O/F blend diets. †Significant difference ($P < 0.05$) between groups of rats fed the 8% casein level and those fed the 14% casein level.

As shown in *Table 3*, daily food intakes did not differ between groups, indicating that daily nitrogen intakes within protein level were not different (270 mg/day in the 8% casein group and 490 mg/day in the 14% casein group). As expected, nitrogen excretion was greater in rats fed the 14% casein diets than in rats fed the 8% casein diets (*Figure 6A*). Within both the 8% and 14% casein diets, the O/F diet produced a significant increase in the percentage of total nitrogen excreted in the feces and a significant decrease in urinary nitrogen excretion compared with the fiber-free diet. As a percentage of total nitrogen excretion, fecal nitrogen excretion was higher in rats fed the 8% casein diet than in rats fed the 14% casein diet (*Figure 6B*). Overall, the net nitrogen balance was more positive in rats fed the high protein level (215 mg/day) than in those fed the low protein level (160 mg/day) and was not significantly influenced by addition of O/F blend.

Discussion

The present study was designed to evaluate the effect of an O/F blend on the extra-renal elimination of nitrogen in partially nephrectomized rats. Digestive disposal of urea has been reported in normal animals and humans.[12,26] The intestinal route of excretion may be emphasized when renal function is compromised, because an increase in plasma urea would favor uptake by the cecum and favor the development of a urealytic microflora.[27] The results of the present experiment indicate that an O/F blend can significantly reduce plasma urea in rats, particularly if the animals are also fed a low protein diet.

A shift in nitrogen excretion from urine to feces depends largely on the effectiveness of fibers in enhancing cecal bacterial proliferation[12,28] and increasing fecal bacterial mass. Bacteria comprise approximately 55% of dry stool weight in humans on a western diet,[29] and because bacteria are 7 to 8% nitrogen (dry weight),[30] an increase in their cecal proliferation will increase fecal mass and nitrogen excretion through this route. As shown in previous studies,[12,19] the use of carbohydrates with different degrees of fermentability produce complementary effects. The highly or moderately fermentable fibers such as FOS, gum arabic, and soy polysaccharide contribute to an increase in bacterial growth, which results in a rise of fecal nitrogen. In contrast, poorly fermentable dietary fibers such as oat fiber and CMC increase fecal bulking and accelerate intestinal transit time.

In the presence of diets containing the O/F blend, the usual sources of nitrogen (digestive enzymes and sloughed mucosal cells) may be insufficient to sustain maximal bacterial growth. In such conditions, blood urea constitutes the largest and the most readily available source of nitrogen for bacterial protein synthesis in the cecum.[26,31] Urea can be captured directly from the cecal blood supply or can diffuse into the small intestine and enter the cecum in the ileal effluent. In addition, dietary protein level can influence nitrogen accumulation in the cecum directly due to a lack of complete digestion in the small intestine and indirectly due to increases in plasma urea resulting from its metabolism.

When the O/F diet with the low protein level was fed, the cecal microflora synthesized almost all amino acids, resulting in large increases in cecal pools of these amino acids. When fed the O/F diet with the high protein level, there was an apparent shift from production of essential amino acids toward utilization of essential amino acids (*Figure 4A*). Insofar as rats are coprophagic, net bacterial amino acid synthesis might improve amino acid status in animals fed a low protein diet. With regard to human relevance, the question arises whether the large intestine had the capacity to absorb significant amino acids. In rats, although cecal amino acid pools shifted very significantly, there was no significant influence of fermentable fibers on arterial amino acid concentrations or on nitrogen balance (results not shown). However, it has been reported that in humans lysine is absorbed from the large intestine.[32]

Even though the O/F blend lowered the ammonia concentration in the cecal contents (*Figure 3A*), the O/F blend significantly increased cecal absorption of ammonia (*Figure 5*). This result can be explained by a large increase in cecal

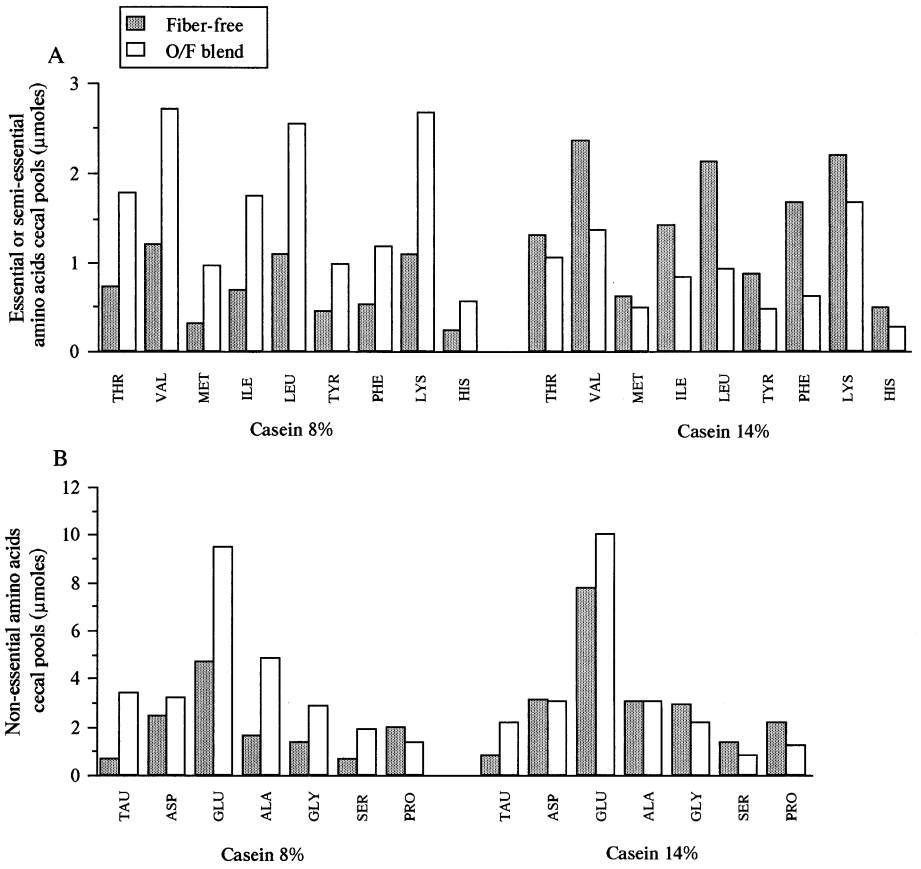

Figure 4 Effect of diets on cecal essential or semi-essential amino acid pools (*Figure 4A*) and nonessential amino acid pools (*Figure 4B*) in nephrectomized rats fed fiber-free (FF) or oligosaccharide/fiber blend (O/F) diets. Cecal amino acid pools (μmoles/cecum) = amino acid concentrations (mmol/L) × cecal water (mL). Each value is the mean of triplicate determination of supernatant pools of 10 rats.

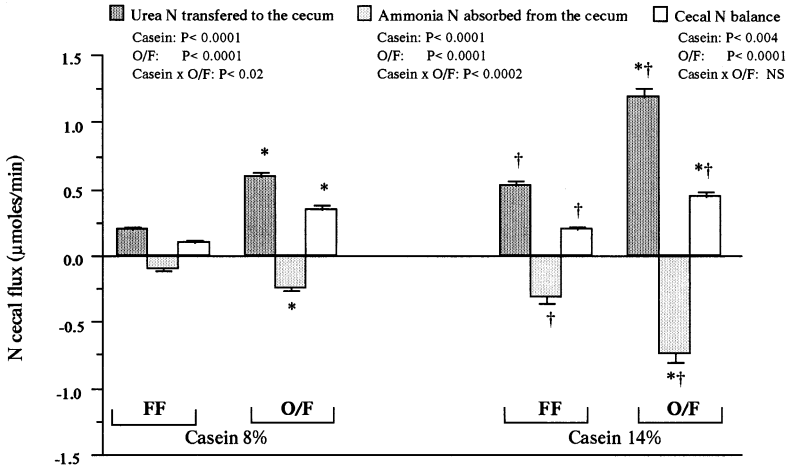

Figure 5 Effect of diets on cecal nitrogen (N) flux in nephrectomized rats fed fiber-free (FF) or oligosaccharide/fiber blend (O/F) diets. Fluxes (μmoles/min) = arteriovenous differences across the cecum (mmol/L) × cecal blood flow (mL/min). Each value is the mean ±SEM, $n = 10$. Statistical evaluation of data was carried out by analysis of variance with multiple comparisons between treatments by Student-Newman-Keuls' test. *Significant difference ($P < 0.05$) between groups of rats fed FF diets and groups of rats fed O/F blend diets. †Significant difference ($P < 0.05$) between groups of rats fed the 8% casein level and those fed the 14% casein level.

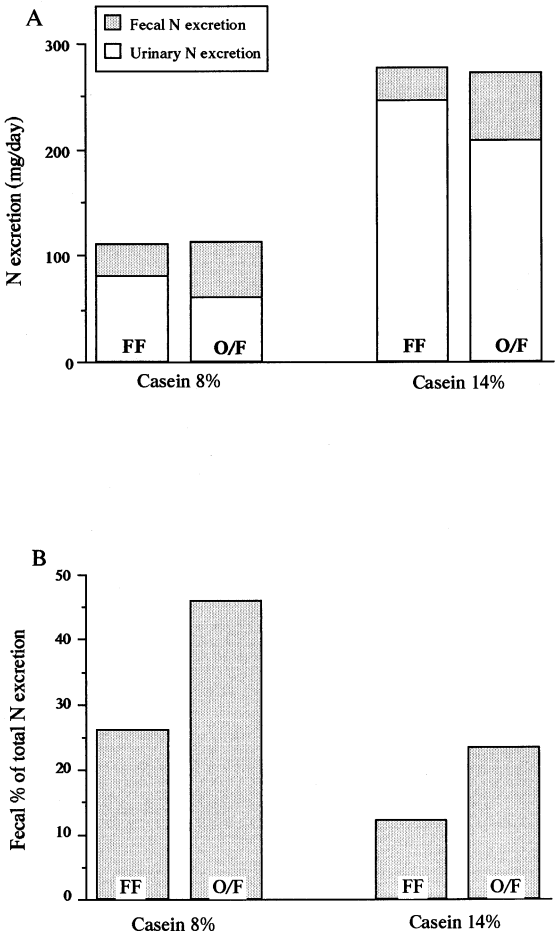

Figure 6 Effect of diets on urinary and fecal nitrogen (N) excretions (*Figure 6A*) and fecal percentage of total nitrogen excretion (*Figure 6B*) in nephrectomized rats fed fiber-free (FF) or oligosaccharide/fiber blend (O/F) diets. Each value is the mean of 10 rats.

contents, an enlarged surface of exchange between the luminal fluid and blood, and by a favorable effect of SCFA absorption. Ammonia and SCFA are generally considered to be transported across biological membranes as uncharged molecules[33]; with the colonocyte, at a neutral pH, the protons required for NH_4+ formation arise from SCFA dissociation. Ammonia, once absorbed from the large intestine into portal blood can contribute to glutamine synthesis in the liver.[34]

When these nephrectomized rats were fed a diet that was lower in protein (e.g., 8% casein instead of 14% casein), total nitrogen excretion was decreased from approximately 270 to 280 mg/day in the animals fed the higher level of protein to approximately 110 mg/day in the animals fed the lower amount of protein. Blood urea levels were decreased from 5.9 mmol/L to 2.6 mmol/L, a decrease of approximately 56%.

When the nephrectomized animals also were fed the O/F blend, there was an adaptive hypertrophy of the cecum and its blood supply, which allowed for efficient removal of urea from the blood and transfer to the cecal lumen. In the cecal lumen, urea was hydrolyzed to ammonia, some of which was used for bacterial protein synthesis and excreted in the feces and some of which was reabsorbed. These changes resulted in an increase in the amount of nitrogen that was excreted in the feces and a equal decrease in the amount of nitrogen that was excreted in the urine. Although there was no change in the amount of nitrogen excreted, the retained nitrogen is used more efficiently, resulting in further decreases in blood urea levels from 2.6 mmol/L to 1.8 mmol/L, a decrease of over 30%.

In conclusion, the net effect of protein restriction and of feeding the O/F blend was to decrease urinary nitrogen excretion from approximately 250 mg/day (14% casein fiber-free diet) to approximately 60 mg/day (8% casein, O/F blend diet), a 75% decrease in urinary nitrogen output. Furthermore, plasma urea was decreased from approximately 5.9 mmol/L (14% casein fiber-free diet) to approximately 1.8 mmol/L (8% casein, O/F blend diet), a decrease of almost 70%.

This approach to treatment of early renal failure, which involves the intake of fermentable and nonfermentable fiber in addition to decreasing protein intake, may further reduce the role of kidney in the excretion of nitrogen and reduce blood urea concentration. These changes may help to delay the progression of renal failure and prevent the consequences of uremia.

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