# Effects of exchange of dietary medium chain triglycerides for long-chain triglycerides on serum biochemical variables and subjectively assessed well-being of dogs with exocrine pancreatic insufficiency

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**Objective**—To test the hypothesis that exchange of medium-chain triglycerides (MCTs) for long-chain triglycerides (LCTs) in the diet of dogs with well-managed exocrine pancreatic insufficiency (EPI) changes serum biochemical variables and to subjectively assess the well-being of dogs with EPI in response to experimental diets.

**Animals**—21 dogs with EPI and 6 healthy control dogs.

**Procedure**—The effects of 3 diets containing 0%, 16%, or 35% of the total fat content as MCTs were examined in a randomized controlled double-blind crossover trial. The 3 diets were fed for 12 weeks each. Dietary effects were evaluated by both subjective and objective variables.

**Results**—Analysis of subjective data revealed no significant difference in appetite, attitude, drinking behavior, volume of feces, defecation frequency, color of feces, consistency of feces, flatulence, or borborygmus among dogs fed the 3 experimental diets. A high MCT content in the diet was associated with significantly higher serum vitamin E, cholesterol, triglyceride, retinyl stearate, retinyl palmitate, and total vitamin A concentrations in dogs with EPI and significantly higher serum vitamin E concentrations in control dogs, compared with low MCT content. High MCT content in the diet was also associated with significantly lower concentrations of serum linoleic acid ($C_{18:2[n-6]}$) in dogs with EPI and in control dogs, compared with low MCT content.

**Conclusions and Clinical Relevance**—A high MCT content in the diet leads to increases in serum concentrations of cholesterol and certain fat-soluble vitamins. However, no effect was found on the subjective well-being of the dogs as evaluated by their owners. (*Am J Vet Res* 2004;65:1293–1302)

**Exocrine pancreatic insufficiency (EPI)** is attributable to insufficient synthesis and secretion of digestive enzymes by pancreatic acinar cells.[1] In dogs with clinical signs of EPI, the diagnosis can be readily made on the basis of serum **canine trypsin-like immunoreactivity (cTLI)** concentrations, as measured by a radioimmunoassay.[2] Although weight loss and diarrhea can be controlled in most dogs by enzyme supplementation, fat digestion does not return to normal and some clinical signs of fat maldigestion and malabsorption remain. Moreover, secondary conditions caused by insufficient absorption of essential fatty acids or vitamins, particularly fat-soluble vitamins and cobalamin, can occur.[3,4]

Absorption of lipids and lipophilic nutrients is impaired in dogs with EPI and patients with EPI of other species. For example, in dogs with EPI that is experimentally induced through ligation of the pancreatic duct, daily fecal fat output increased from 1.7 ± 0.27 g/10 kg to 15.2 ± 1.2 g/10 kg.[4] Also, fat malabsorption not only leads to steatorrhea but also malabsorption of the fat-soluble vitamins A and E.[a,b] Furthermore, vitamin K deficiency-induced coagulopathy associated with EPI has been reported for a cat.[5] Additionally, vitamin D and cholesterol malabsorption has been reported for humans with chronic pancreatitis.[6,7] Even with supplementation of pancreatic enzymes, fat digestion remains impaired because of sensitivity of pancreatic lipase contained in the enzyme supplement to gastric acid.[1] Dietary recommendations for dogs with EPI have been controversial, and there have been few studies[8,9] to date that evaluate the effect of diet on dogs with EPI.

On the basis of studies on digestion and absorption of **medium chain triglycerides (MCTs)**, it has been suggested that replacing **long-chain triglycerides (LCTs)** with MCTs in the diet of dogs with EPI may improve fat absorption and absorption of fat-soluble vitamins and essential fatty acids.[10-13] The MCTs can be absorbed directly into the portal blood, either in the form of intact triglycerides or as products of hydrolysis as monoglycerides and free fatty acids. In addition, MCTs, like LCTs, can be absorbed via chylomicron formation and through the lymphatic system. The goals of the study reported here were to test the hypothesis that exchange of MCTs for LCTs in the diet of well-managed dogs with EPI alters serum biochemical variables and to subjectively assess the well-being of these dogs with EPI while consuming the experimental diets.

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## Materials and Methods

**Study design**—The clinical study was designed and performed as a controlled double-blind trial with a crossover design that included 24 dogs with EPI (EPI group dogs) and 6 healthy dogs (control group dogs) of a variety of combinations of breed, sex, and age (**Appendix 1**). The enrolled dogs were randomized into 6 feeding order groups by use of a replicated Latin-square design based on the date of enrollment into the trial. Each feeding order group received 3 different experimental diets in a different order. During the study, each dog received each of the 3 experimental diets for 3 months. The first month of each feeding period was considered the washout period, and the data were not used for analysis. During the study, all dogs remained in the household of their owners, who had committed to feeding nothing but the experimental diets (as well as a pancreatic enzyme supplement to the dogs with EPI) to their dogs as far as possible. An exception was made for 8 dogs in the EPI group, which received some additional foods. However, the owners had to agree to feed their dogs only the specified additional food in small amounts and in a consistent manner. Because of the crossover design in which dogs served as their own control, this was not considered a problem. Of the 8 EPI group dogs, 1 dog was fed 1 milkbone[c] daily, 2 dogs were fed half a carrot each day, 1 dog was fed raw eggs once a week, 2 dogs were given 1 of 2 types of vitamin capsules[d,e] each day, 1 dog received 1 teaspoon of fat-free chicken broth each day, and 1 dog was given a raw bone each week. Nutritional analysis was not available for these additional foods. All owners signed an informed consent form before participating in the study. The experimental protocol was reviewed and approved by the Clinical Research Review Committee at Texas A&M University.

**Animals**—To be eligible for enrollment into this study, affected dogs had to have clinical signs compatible with EPI (semiformed or loose stools and weight loss or lack of weight gain) before being treated with pancreatic enzymes. In addition, the EPI group dogs had to have a serum cTLI concentration of $< 2$ μg/L. In all dogs, concurrent conditions were ruled out by a medical evaluation that consisted of a physical examination, CBC determination, serum biochemical analysis, urinalysis, and microscopic fecal examination for the diagnosis of parasite infestation, including 3 zinc sulfate fecal flotations to rule out *Giardia* infestation. Before enrollment into the study, all results from the medical evaluation had to be unremarkable and the fecal examination had to be negative for any evidence of either helminth or protozoal infestation. Laboratory results from the medical evaluation are referred to as baseline variables. Finally, EPI group dogs had to have an adequate response to treatment with the prescribed enzyme supplement[f] for at least 1 month before enrollment into the study. If the dog was not already treated with the prescribed enzyme supplement but with another form of enzyme supplementation, the dog was started on the prescribed enzyme supplement for 1 month before entering the experimental design of the study. For the purpose of this study, adequate response to treatment was defined as an overall improvement of stool quality and a period of weight gain, followed by a period with an appropriate stable body weight, which was not necessarily the ideal body weight but an improvement over the body weight prior to treatment. Also, 6 clinically normal dogs with a serum cTLI concentration of $> 5.0$ μg/L were enrolled as a negative control group. The same medical evaluation as described for the dogs with EPI was performed in the control group dogs.

**Diets and feeding management**—The 3 experimental diets were prepared commercially.[g] Diets were prepared in 3 batches (**Appendix 2**). All 3 diets were based on a regular maintenance diet with differing concentrations of MCTs. The ingredients by weight were as follows: moisture, 10.36% to 10.61%; ash, 5.44% to 5.55%; protein, 25.53% to 25.77%; total fat, 10.06% to 11.23%; crude fiber, 1.26% to 1.74%; vitamin A, 23,148.5 to 32,187.5 IU/kg; vitamin D, 2.73 to 3.75 IU/g; and vitamin E, 3.81 to 6.37 mg/100 g. The total calories of the diets were 452 to 456 kcal/100 g of diet with 25.79% to 26.12% of calories from protein, 27.55% to 28.55% of calories from fat, and 45.33% to 46.65% of calories from carbohydrates. Experimental diet A contained 0% of the total fat as MCTs, experimental diet B contained 16% of the total fat as MCTs, and experimental diet C contained 35% of the total fat as MCTs. The MCT preparation consisted predominantly of lauric acid ($C_{12:0}$) and traces (1.5% to 3.3%) of caproic ($C_{6:0}$), caprylic ($C_{8:0}$), and capric acid ($C_{10:0}$). The diets were analyzed by the commercial manufacturer.[g] All diets were packaged in bags labeled A, B, and C so that neither the investigators nor the owners of the dogs were aware of which diet was contained in which bag.

**Questionnaires**—During each of the 3-month feeding periods, the owners closely monitored their dogs and filled out a brief daily questionnaire. The following variables were evaluated by the owner as follows: attitude (0 = more quiet or lethargic than normal, 1= normal, and 2 = overly active or playful), appetite (0 = very poor, 1= poor, 2 = normal, 3 = very good, and 4 = excessive), drinking (0 = less than normal, 1= normal, and 2 = more than normal), defecation frequency (in numbers, ≥ 5 = 5 defecations), volume of feces (0 = normal, 1 = copious, and 2 = very copious), consistency of feces (0 = hard, 1 = normal, 2 = pulpy, and 3 = loose and watery), color of feces (0 = darker than normal, 1 = normal, 2 = gray, and 3 = yellowish), coprophagia (0 = no and 1 = yes), borborygmus (0 = no, 1 = some, and 2 = frequent), and flatulence (0 = no, 1 = some, and 2 = frequent). Owners were asked to maintain the daily questionnaire by answering the same questions each day. Before owners were made aware of treatments (ie, unblinded), they were asked to judge the overall performance of the 3 diets in a final questionnaire. The questions asked were as follows: "Which diet would you consider best for your dog?" and "Which diet would you consider worst for your dog?" At the beginning of the study and the end of each feeding period, the dogs were weighed and the body condition score[h] was determined.

**Sample collection**—At the time of enrollment and after each feeding period, the following laboratory data were collected: cTLI concentration, serum cobalamin and folate concentrations, serum biochemical analysis (including serum triglycerides and cholesterol concentrations), a serum profile of vitamin A compounds (retinol, retinyl palmitate, retinyl oleate, and retinyl stearate concentrations), 25-hydroxy cholecalciferol (vitamin D) concentration, α-tocopherol (vitamin E) concentration, and a serum profile of fatty acid concentrations.

Blood samples were obtained by the local veterinarians and shipped to the Gastrointestinal Laboratory, Department of Small Animal Medicine and Surgery, College of Veterinary Medicine at Texas A&M University, for further processing and to ensure that the same laboratory performed the analysis of blood samples for the entire study group. Blood smears were prepared, and blood samples in EDTA were cooled in the refrigerator. Serum tubes were wrapped in aluminum foil before filling and covered with aluminum foil after filling. The serum was immediately frozen at –20°C. All samples were shipped on frozen ice packs and by overnight express.

After arrival of the blood smears, blood samples in EDTA, and a portion of the serum samples, they were submitted to the Texas Veterinary Medical Diagnostics Laboratory in College Station, Tex, where the following tests

were performed: 1) CBC determination and serum biochemical analysis that included determination of total protein, albumin, globulin, calcium, phosphorus, glucose, BUN, creatinine, cholesterol, triglycerides, electrolytes, and total bilirubin concentrations and alkaline phosphatase, **aspartate amino transferase (AST)**, **alanine amino transferase (ALT)**, gamma glutamyl transferase, creatine kinase, and amylase activities on an automated system[i]; 2) determination of lipase activity, which was measured with a lipase assay kit[j]; and 3) determination of vitamin E (α-tocopherol) concentration, which was measured by use of **high-performance liquid chromatography (HPLC)**.

Briefly, vitamin E was extracted by absolute ethanol with 0.01% butylhydroxytoluen and hexane, mixed on a glass rotary extractor, and then centrifuged. The vitamin E was then separated on a column[k] by use of 2 mobile phases (mobile phase A, 98.5% chloroform with 1.5% absolute ethanol; mobile phase B, 100% HPLC grade hexane). The run was started with 50% mobile phase A and 50% mobile phase B with a flow rate of 0.60 mL/min and was changed at 10 minutes to 30% mobile phase A and 70% mobile phase B with a flow rate of 0.70 mL/min. At 15 minutes, the gradient was changed to 10% mobile phase A and 90% mobile phase B and maintained for 5 minutes. At 20 minutes, the run was continued with 50% mobile phase A and 50% mobile phase B with a flow rate of 0.60 mL/min and maintained at this condition for the remainder of the run. Each run was completed at 60 minutes. Peaks were observed and identified by use of a UV light detector[l] at 280 nm. The sample runs were compared with a standard curve established with a 1:10, 1:12.5, 1:16.6, 1:25, and 1:50 dilution of the vitamin E standard DL-α-tocopherol[m] by use of a commercial software package.[n]

Vitamin D concentration was determined at the Endocrinology Laboratory at Michigan State University by use of a $^{125}$I-25-hydroxyvitamin D radioimmunoassay kit.[o] Cobalamin, folate, and cTLI concentrations were measured at the Gastrointestinal Laboratory. Vitamin $B_{12}$ and folic acid kits were used on an automated immunoluminescent analyzer,[p] and a radioimmunoassay kit[q] was used to determine serum cobalamin, folate, and cTLI concentrations, respectively.

Profiles of vitamin A (retinol, retinyl stearate, retinyl palmitate, and retinyl oleate concentrations) and fatty acid concentrations were determined by the Comparative Nutrition Laboratory at Texas A&M University by use of HPLC[r] and gas chromatography, respectively. The extraction was performed in a dark room with a minimal light source to avoid degradation of vitamin A. Retinal acetate[s] was added to the serum as an internal standard, and vitamin A compounds were extracted and injected by use of chloroform as diluent. Vitamin A compounds were then separated on a reversed-phase column.[t] Two mobile phases (mobile phase, 42.5% acetonitrile, 42.5% ethanol, and 15% water with 0.1 mL/L diethylamine; mobile phase B, 50% acetonitrile and 50% ethanol with 0.1 mL/L diethylamine) were used at a flow rate of 2 mL/min. The run was started with 100% mobile phase A and changed to 100% mobile phase B at 2 minutes by use of a linear gradient.[u] The run continued at 100% mobile phase B for 17 minutes. At 17.1 minutes, it was changed to 100% mobile phase A for the remainder of the run. The run was completed at 21 minutes. Peaks were observed and identified by use of a UV light detector at 242 nm. Peak identification was based on retention times that were compared with authentic retinol[v] and retinol ester standards.[w]

For determination of fatty acid concentrations, the lipids were extracted from serum according to the method described by Folch et al,[14] separated by gas chromatography, and detected by flame ionization. Briefly, the samples were methylated and then fractionated on a gas chromatograph[x] with a 30-m column.[y] Samples were run at a constant head pressure of 8.9 psi at 170°C with a linear velocity of 23.2 cm/s. This run used a temperature program that began at 175°C and remained at that temperature for 6 minutes, then the run was ramped at 2°C/min to 236°C and held at that condition for 20 minutes. Samples were run at a split flow of 1:50 with helium as carrier gas. Peaks were observed by use of a software package.[z] Peak identification was based on retention times of the sample runs, compared with authentic fatty acid standards.[aa]

**Statistical analysis**—Baseline variables of EPI group dogs and control group dogs obtained at the time of the medical evaluation before enrollment into the study were compared by use of an unpaired 2-tailed Student *t* test. Data obtained during the course of the study were evaluated by use of an ANOVA according to a crossover design with a software package. The level of significance was set at a value of $P < 0.05$. In the ANOVA model, EPI group, control group, diet (0%, 16%, and 35%), and their interaction were modeled with fixed effects. Differences among dogs and among periods were modeled with random effects. Time effects were considered to be unique within both the EPI and control groups. This allowed a fair comparison of diets if, for example, control group dogs stayed healthy through 9 months, although signs of EPI got worse in the affected dogs. Data are reported as least-square mean ± SEM. Use of least-square means compensates for missing values and unbalanced data by estimating the mean values that would have been obtained if all diets and groups had been represented equally. Then, a Tukey multiple comparison procedure was used to determine whether pair-wise differences among the 6 group-diet combinations were significant.

For the questionnaires, the possibility of a time effect for each diet was examined by allowing 2 responses for each dog consuming each diet as follows: the mean of days 29 to 56 (second month of diet) and the mean of days 57 to 90 (third month of diet). These were evaluated with a repeated-measures ANOVA model within the same crossover design. Data that were not entered into questionnaires with numbers were regarded as missing. When multiple values were listed for 1 response (eg, "2, 3" or "1+"), the first number listed was retained for the calculations. Laboratory values with skewed distributions (WBC, neutrophil, lymphocyte, monocyte, eosinophile, and basophil counts; BUN, triglyceride, cobalamin, cTLI, retinol, retinyl oleate, retinyl stearate, retinyl palmitate, and total vitamin A concentrations; and AST and ALT activities) were $\log_{10}$ transformed before analysis.

## Results

**Data exclusion and missing data**—Except for analysis of the final questionnaires, data from 3 EPI group dogs were excluded for analysis. Data from only the first feeding period were available for 1 EPI group dog, and data from only the second and third feeding period were available for another EPI group dog.

**Adverse reactions**—Two EPI group dogs did not do well while consuming the experimental diets. Of these 2 EPI group dogs, 1 developed severe flatulence when eating the 16% MCT diet and also developed diarrhea at the beginning of that particular feeding period. After changing the dog to the 35% MCT diet, the flatulence resolved, but the dog still had a few episodes of diarrhea. The other EPI group dog did not do well while consuming the 0% and 35% MCT diets but maintained a stable weight and had no signs of EPI when fed the 16% MCT diet. All other dogs did well while consuming all 3 experimental diets.

**Daily questionnaires**—Analysis of the subjective data from the daily questionnaires revealed no significant difference among the 3 experimental diets in terms of appetite, attitude, drinking behavior, volume of feces, defecation frequency, color of feces, consistency of feces, flatulence, or borborygmus. Analysis of the monthly mean values revealed no significant differences within each group and diet between months 2 and 3 of each feeding period, between any 2 diets, or between control and EPI group dogs. The combined mean values over both months revealed no significant differences between any 2 diets and no significant difference between the EPI and control groups within each diet.

Table 1—Mean (± SE) serum biochemical variables for EPI group dogs and control group dogs before the beginning of the study (baseline data).

| Variables | Groups | | |
|---|---|---|---|
| | EPI dogs | Control dogs | *P* values |
| Total serum protein (g/dL) | 6.83 ± 0.60 | 6.30 ± 0.20 | 0.045 |
| Calcium (mg/dL) | 10.47 ± 0.57 | 9.95 ± 0.20 | 0.039 |
| Globulines (g/dL) | 3.08 ± 0.57 | 2.55 ± 0.27 | 0.039 |
| Amylase (U/L) | 516.57 ± 124.83 | 673.00 ± 130.12 | 0.013 |
| Cholesterol (mg/dL) | 257.67 ± 57.77 | 193.33 ± 23.86 | 0.014 |
| cTLI (µg/L) | 0.77 ± 0.30 | 11.20 ± 5.23 | < 0.001 |
| Cobalamin ($log_{10}$; ng/L) | 2.37 ± 0.20 | 2.70 ± 0.13 | < 0.001 |
| Folate (ng/L) | 15.64 ± 5.12 | 8.67 ± 2.90 | 0.004 |
| Retinyl palmitate ($log_{10}$; µg/dL) | 1.79 ± 0.19 | 1.97 ± 0.13 | 0.047 |
| Retinyl stearate ($log_{10}$; µg/dL) | 2.22 ± 0.17 | 2.42 ± 0.08 | 0.014 |
| Total vitamin A ($log_{10}$; µg/dL) | 2.59 ± 0.15 | 2.73 ± 0.07 | 0.034 |
| Vitamin D (nmol/L) | 106.24 ± 19.14 | 126.17 ± 11.14 | 0.023 |
| 16:0 fatty acid (%) | 13.12 ± 1.41 | 16.85 ± 6.00 | 0.018 |
| 18:1(n-7) fatty acid (%) | 3.10 ± 0.49 | 2.45 ± 0.84 | 0.023 |
| 18:2(n-6) fatty acid (%) | 21.72 ± 2.62 | 25.95 ± 0.75 | < 0.001 |
| 20:0 fatty acid (%) | 0.08 ± 0.07 | 0.18 ± 0.07 | 0.008 |

*A value of $P < 0.05$ indicates significant differences between EPI and control group dogs.
cTLI = Canine trypsin-like immunoreactivity.

**Body condition scores**—No significant differences in body condition scores were found between EPI and control groups. Also, no significant differences in body condition scores of dogs were found among the diets.

**Baseline laboratory data**—Baseline serum cholesterol, folate, total protein, serum calcium, serum globulins, and the fatty acid $C_{18:1(n-7)}$ concentrations were significantly higher in EPI group dogs, compared with control group dogs (**Table 1**). Baseline serum cobalamine, cTLI, retinyl palmitate, retinyl stearate, total vitamin A, vitamin D, $C_{16:0}$, and $C_{18:2(n-6)}$ concentrations and amylase activity were significantly lower in EPI group dogs, compared with control group dogs.

**Serum biochemical variables of control group dogs**—Serum vitamin E and palmitic acid ($C_{16:0}$) concentrations were significantly increased after feeding the diet containing 35% MCTs, compared with the diet containing 16% MCTs, but were not significantly different, compared with the 0% MCT feeding period (**Tables 2 and 3**). Serum lipase activity was significantly lower for the feeding period with the diet containing 35% MCTs, compared with the 16% MCT diet, but not significantly different from the 0% MCT diet. For

Table 2—Mean (± SEM) serum biochemical variables in healthy control group dogs and dogs with EPI that were fed various percentages of medium chain triglycerides (MCTs) in their diet for 12 weeks.

| Variables | Dog groups | Diets (% of total fat content) | | |
|---|---|---|---|---|
| | | 0% MCT | 16% MCT | 35% MCT |
| Total serum protein (g/dL) | Control | 6.37 ± 0.21 | 6.32 ± 0.21 | 5.93 ± 0.21 |
| | EPI | 6.51 ± 0.11 | 6.61 ± 0.11 | 6.64 ± 0.11* |
| Albumin (g/dL) | Control | 3.82 ± 0.13[a] | 3.77 ± 0.13 | 3.52 ± 0.13[a] |
| | EPI | 3.64 ± 0.07 | 3.63 ± 0.07 | 3.67 ± 0.07 |
| Amylase activity (U/L) | Control | 737 ± 153 | 1,150 ± 153 | 782 ± 153 |
| | EPI | 476 ± 100 | 489 ± 99* | 470 ± 98 |
| Lipase activity (U/L) | Control | 407 ± 108 | 591 ± 108[a] | 340 ± 108[a] |
| | EPI | 442 ± 59 | 459 ± 58 | 436 ± 58 |
| Cholesterol (mg/dL) | Control | 202.8 ± 25.4 | 221.3 ± 25.4 | 214.8 ± 25.4 |
| | EPI | 231.1 ± 15.2[a] | 252.1 ± 15.1[b] | 305.5 ± 14.9*[,a,b] |
| cTLI ($log_{10}$; µg/L) | Control | 1.17 ± 0.1 | 11.25 ± 0.11[a] | 0.97 ± 0.11[a] |
| | EPI | –0.10 ± 0.08* | –0.15 ± 0.08* | –0.12 ± 0.08* |
| Cobalamin ($log_{10}$; ng/L) | Control | 2.56 ± 0.06 | 2.56 ± 0.06 | 2.61 ± 0.06 |
| | EPI | 2.26 ± 0.04* | 2.23 ± 0.03* | 2.24 ± 0.03* |
| Retinyl palmitate ($log_{10}$; µg/dL) | Control | 1.58 ± 0.12 | 1.67 ± 0.12 | 1.87 ± 0.12 |
| | EPI | 1.47 ± 0.06[a] | 1.54 ± 0.06[b] | 1.83 ± 0.06[a,b] |
| Retinyl stearate ($log_{10}$; µg/dL) | Control | 2.04 ± 0.11 | 2.04 ± 0.11 | 2.21 ± 0.11 |
| | EPI | 1.91 ± 0.06[a] | 1.88 ± 0.06[b] | 2.15 ± 0.06[a,b] |
| Total vitamin A ($log_{10}$; µg/dL) | Control | 2.45 ± 0.08 | 2.44 ± 0.08 | 2.56 ± 0.08 |
| | EPI | 2.41 ± 0.06[a] | 2.39 ± 0.06[b] | 2.58 ± 0.06[a,b] |
| Vitamin E (µg/L) | Control | 12.58 ± 2.08 | 10.44 ± 2.08[a] | 14.49 ± 2.08[a] |
| | EPI | 6.51 ± 1.60[a] | 7.95 ± 1.60 | 9.35 ± 1.59[a] |

*Within a diet, significant ($P < 0.05$) difference in value for EPI group dogs, compared with control group dogs.
[a,b]Values indexed with the same letters within a row indicate values that were significantly ($P < 0.05$) different among diets within a single group (ie, control group dogs or EPI group dogs).

Table 3—Mean (± SEM) serum fatty acid concentrations in healthy control group dogs and dogs with EPI that were fed various percentages of medium chain triglycerides (MCTs) in their diet for 12 weeks.

| | | Diets (% of total fat content) | | |
|---|---|---|---|---|
| **Fatty acids** | **Dog groups** | **0% MCT** | **16% MCT** | **35% MCT** |
| 12:0 | Control | 0.020 ± 0.091[a] | 0.156 ± 0.099 | 0.472 ± 0.091[a] |
| | EPI | 0.056 ± 0.053[a,b] | 0.290 ± 0.051[a] | 0.375 ± 0.050[b] |
| 14:0 | Control | 0.293 ± 0.160[a] | 0.747 ± 0.169[b] | 1.452 ± 0.161[a,b] |
| | EPI | 0.408 ± 0.089[a,b] | 0.950 ± 0.087[a,c] | 1.535 ± 0.086[b,c] |
| 16:0 | Control | 12.31 ± 0.64[a] | 12.77 ± 0.68 | 14.49 ± 0.64[a] |
| | EPI | 11.63 ± 0.38[a,b] | 13.32 ± 0.37[a,c] | 14.38 ± 0.37[b,c] |
| 16:1(n-7) | Control | 0.517 ± 0.112[a,b] | 0.966 ± 0.119[a] | 1.014 ± 0.112[b] |
| | EPI | 0.589 ± 0.084[a] | 0.755 ± 0.084 | 0.875 ± 0.083[a] |
| 18:2(n-6) | Control | 30.06 ± 1.35[a,b] | 25.16 ± 1.45[a] | 22.41 ± 1.35[b] |
| | EPI | 29.29 ± 0.91[a,b] | 25.79 ± 0.89[a,c] | 21.32 ± 0.88[b,c] |
| 18:3(n-3) | Control | 0.447 ± 0.087 | 0.340 ± 0.095 | 0.177 ± 0.087 |
| | EPI | 0.432 ± 0.051[a] | 0.389 ± 0.050[b] | 0.181 ± 0.049[a,b] |
| 20:2 (n-6) | Control | 0.558 ± 0.107 | 0.393 ± 0.117 | 0.426 ± 0.107 |
| | EPI | 0.807 ± 0.062[a] | 0.597 ± 0.060 | 0.538 ± 0.059[a] |
| 20:3(n-6) (5, 11, 14) | Control | 0.107 ± 0.064 | 0.191 ± 0.069 | 0.306 ± 0.064 |
| | EPI | 0.121 ± 0.036[a] | 0.149 ± 0.035[b] | 0.329 ± 0.034[a,b] |
| 20:3(n-6) (8, 11, 14) | Control | 0.778 ± 0.190 | 1.015 ± 0.204 | 1.185 ± 0.190 |
| | EPI | 0.950 ± 0.106[a] | 1.105 ± 0.104 | 1.403 ± 0.102[a] |
| 22:4(n-6) | Control | 1.397 ± 0.233[a] | 1.816 ± 0.244 | 2.270 ± 0.233[a] |
| | EPI | 1.529 ± 0.128[a] | 1.652 ± 0.126[b] | 2.295 ± 0.124[a,b] |
| 22:5(n-6) | Control | 0.137 ± 0.055 | 0.185 ± 0.059 | 0.257 ± 0.055 |
| | EPI | 0.118 ± 0.032[a] | 0.163 ± 0.031[b] | 0.309 ± 0.031[a,b] |
| 22:5(n-3) | Control | 1.730 ± 0.169 | 1.778 ± 0.181 | 1.235 ± 0.169 |
| | EPI | 2.082 ± 0.094[a,b] | 1.768 ± 0.092[a,c] | 1.292 ± 0.090[b,c] |

[a,b,c]Values indexed with the same letters within a row indicate values that were significantly ($P < 0.05$) different among diets within a single group (ie, control group dogs or EPI group dogs).
The numbers in parentheses (ie, 5, 11, 14 and 8, 11, 14) specify the location of the double bonds.

serum linoleic acid ($C_{18:2}$) concentrations, the 0% MCT feeding period was significantly different from both the 16% and the 35% MCT feeding periods. The cTLI concentration was significantly higher after feeding the 16% MCT diet, compared with the 35% MCT diet, but no significant difference was found after feeding the 0% MCT diet. Serum albumin concentration was significantly lower after feeding the 35% MCT diet, compared with the 0% MCT diet, but not after feeding the 16% MCT diet.

**Serum biochemical variables of EPI group dogs**—Serum concentrations of retinyl palmitate, retinyl stearate, vitamin A, cholesterol, palmitic acid, and linoleic acid were significantly lower after feeding the 35% MCT diet, compared with either of the other treatments (Tables 2 and 3). Concentrations of serum vitamin E were significantly higher after feeding the 35% MCT diet, compared with the 0% MCT diet, but were not significantly different from the 16% MCT diet, whereas no significant differences in serum biochemical variables were observed between the 16% and 0% MCT diets.

**Comparison of serum biochemical variables between EPI and control group dogs**—Serum concentrations of cTLI and cobalamin were significantly lower in EPI group dogs than in control group dogs for all 3 MCT diets (Table 2). After feeding of the 35% diet, serum cholesterol and total serum protein were significantly higher in EPI group dogs, compared with control group of dogs. After feeding the 16% diet, serum amylase activity was significantly lower in EPI group dogs, compared with control group dogs.

**Other serum biochemical variables**—Serum triglyceride concentrations in EPI group dogs did not differ significantly with different amounts of dietary MCTs. No significant differences were found in CBC values; electrolyte, globulin, calcium, phosphorous, glucose, BUN, creatinine, total bilirubin, folate, retinol, retinyl oleate, and vitamin D concentrations; and alkaline phosphatase, creatine kinase, AST, ALT, and gamma glutamyl transferase activities between EPI group dogs and control group dogs or among the experimental diets. Significant differences in fatty acid concentrations other than those of palmitic and linoleic acid were found, but they are not mentioned here because the total content of these fatty acids was < 3% of total fat content.

## Discussion

The focus of our study was to test the benefit of dietary MCTs in dogs with well-managed EPI. This was done by choosing a crossover design with a study population of well-managed dogs with EPI. The analysis of diet-order groups to detect an initial response to treatment with MCTs would have been interesting, but we chose not to pursue this because such an approach would have caused a loss of power for detecting a treatment effect. Moreover, the study had not been designed for such analysis with only 1 control group dog in each diet-order group. Therefore, results generated from our study are only valid for dogs represented by our study population. It is possible that dietary replacement of LCTs with MCTs would have a beneficial effect in untreated dogs with EPI or in dogs with uncontrollable EPI.

The decision to exclude data from analysis was made before investigators were made aware of treatments (ie, unblinded) and before data analysis. Excluded data were in our opinion not representative of our study. Gastrointestinal protein loss was diagnosed by an increased fecal $\alpha_1$-proteinase inhibitor concentration in 1 EPI group dog while enrolled in our study. This test had been performed because of a low serum albumin concentration. One possible cause of the protein loss may have been intestinal lymphangiectasia, which can respond favorably to MCT supplementation.[15] The owner did not agree to further diagnostic evaluation of the protein loss because the dog did not have any clinical signs associated with the protein loss. Therefore, we could not be sure that any changes that may have been observed in this dog would have been caused by the effect of MCTs on EPI rather than on lymphangiectasia. In 1 of the EPI group dogs, serum cTLI concentration was within the reference range after the first feeding period. Therefore, the inclusion criterion of a cTLI concentration of < 2 μg/L for EPI group dogs was no longer met. Also, 1 EPI dog did not want to consume the 0% and 16% MCT diets during our study but continued to try to eat other foods intended for the other dogs in the household. Moreover, this dog had a history of small intestinal bacterial overgrowth and multiple episodes of diarrhea with a high serum folate concentration, which resolved after changing the diet. We highly suspect concurrent small intestinal bacterial overgrowth in this dog; therefore, we did not believe results from this dog to be representative of our study. One dog in the EPI group needed an unusually high amount of pancreatic enzyme per day to maintain normal stool quality. During the last 10 days of the first feeding period, the owner of the dog reduced the amount of enzymes because not enough enzyme supplement was available in the household. This dog immediately developed diarrhea. Therefore, data of the first feeding period from this dog were excluded because of insufficient enzyme treatment in the last 10 days before blood sample collection. For 1 EPI group dog, only data of the first feeding period were available because right before the beginning of the second feeding period, the dog developed intervertebral disk disease, underwent hemilaminectomy, was treated with steroids for 10 weeks, and was thus excluded from our study.

According to the analysis of data collected through questionnaires, the owners of the EPI and control group dogs did not observe any significant differences in the subjective well-being of their dogs or fecal quality among the 3 diets. More subtle alterations in fecal consistency and color may have been missed as a result of the crudeness of the 4-point scale used and the possibility of variation in interpretation.

Measurement of digestibility (3-day measurement of the amount of food intake and fecal output) was attempted. However, it was not possible to get valid results under field conditions because the owners of the dogs were not always able to collect the entire amount of stools (eg, the dog defecated in tall grass).

Of the EPI group dogs, 2 had dietary intolerance, which did not, however, seem to be related to the addition of MCTs to the diet because no apparent dose-response relationship was found. One of these 2 EPI group dogs was reported as not doing well while consuming the 16% MCT diet, and the other EPI group dog was reported as not doing well while consuming the 0% and 35% MCT diets. Therefore, it is unlikely that any of the problems these dogs had were caused by the addition of MCTs to the diet alone.

Most routine measurements of serum biochemical variables in EPI group dogs in our study were within the reference range, which is consistent with a previous report.[1] The experimental diet did not cause any changes in most routine variables or in serum retinol, retinyl oleate, vitamin D, cTLI, cobalamin, and folate concentrations.

Serum total vitamin A concentration and vitamin A components were not significantly different between EPI and control group dogs. This is especially remarkable because at the time of baseline analysis, serum total vitamin A, retinyl palmitate, and stearate concentrations were significantly lower in EPI group dogs, compared with control group dogs. During our study when the EPI and control group dogs were consuming the same diet, no differences were detectable. Serum reference range values for vitamin A components in dogs have not previously been established, but the well-managed EPI group dogs in our study did not appear to have vitamin A malabsorption. The 35% MCT diet did result in an increase serum concentration of vitamin A components and total vitamin A concentrations, even though the vitamin A content of the 35% MCT diet was 29% lower, compared with the vitamin A content in the 0% MCT diet. Thus, these differences in serum vitamin A concentrations after feeding the different diets might have been even more apparent if the vitamin A content of the diets had been the same. The increase in serum vitamin A concentration after feeding the 35% diet may have been caused by a higher percentage of saturated fatty acids in the MCT diet because MCTs had mainly been exchanged for unsaturated linoleic acid ($C_{18:2}$; **Appendix 2**). Wilson et al[16] showed that feeding the Erhardt diet (a diet that is rich in saturated fatty acids and that leads to an increase in serum cholesterol concentrations) in 2 dogs resulted in a dramatic increase in serum concentrations of retinyl esters in the lipoprotein fraction of the serum (7-fold in the low-density lipoprotein fraction and 44-fold in the very low-density and high-density lipoprotein fractions). Another interesting finding of our study, which confirms the findings of Wilson et al,[16] concerns the peculiarity of the metabolism of vitamin A esters in dogs. In other species such as humans, rabbits, and rats, plasma and serum retinyl ester concentrations are negligible after withholding food for hours.[16] However, in canine plasma, considerable amounts of retinyl esters remained measurable when food had been withheld from dogs.[16] This was also true in our study. Melchior et al[17] showed that dietary retinyl esters are taken up into chylomicrons in the canine small intestine. The liver then extracts the retinyl esters effectively from these chylomicrons, and the retinyl esters are excreted by the liver as retinyl ester containing lipoproteins.[17] To date, the impact and importance of this

peculiarity of the canine metabolism of retinyl esters are unknown, but it is thought to be the reason for the considerable increase in serum retinyl ester concentrations found in dogs after withholding food for a prolonged time.[16]

In other species, serum retinol concentration is used to assess vitamin A status. Results of our study indicate that serum retinol concentration may not be sufficient to assess vitamin A status in dogs. Serum retinol concentrations were not significantly different between EPI and control group dogs, but the retinyl stearate and retinyl palmitate concentrations were significantly different between these 2 groups. Another interesting finding in our study is the higher concentration of retinyl stearate, compared with retinyl palmitate, in both EPI and control group dogs. This may have been caused by the special ability of chain elongation of saturated fatty acids in dogs.

In human patients with EPI who are treated with a pancreatic enzyme supplement, subnormal serum vitamin D concentrations were found in 10 out of 15 patients.[18] In our study, subnormal serum vitamin D concentrations did not appear to be a substantial problem but may be a problem in dogs with untreated or uncontrolled EPI.

In our study, EPI group dogs had a significantly lower baseline serum concentration of vitamin D, compared with control group dogs. However, only 2 EPI group dogs had values that were slightly below the reference range. During the study, although all dogs were consuming the same experimental diets, this difference in serum concentrations of vitamin D between control and EPI group dogs diminished.

In both EPI and control group dogs, serum vitamin E concentrations increased after feeding the 35% MCT diet, even though the vitamin E content of the 35% MCT diet was 41% lower, compared with the vitamin E content in the 0% MCT diet. The differences in serum vitamin E concentrations after feeding the different diets might have been even more apparent if the vitamin E content of the diets had been the same. A small portion of dietary α-tocopherol can be absorbed directly into the portal blood just like MCTs, and it has been suspected that the addition of MCTs to the diet may increase the absorption of α-tocopherol proportionally.[19] In healthy rats, increased vitamin E absorption and increased plasma tocopherol concentrations were observed after the addition of MCTs to the diet (vitamin E absorption with the addition of MCTs was 79 ± 9%, compared with 26 ± 16% with the addition of LCTs).[12,20] At the beginning of our study, serum vitamin E concentrations were below the lower limit of the reference range (≤ 5 μg/mL) in 4 dogs (mean, 4.32 ± 0.62 μg/mL). Serum vitamin E concentration decreased even further after use of the diet without MCTs (3.98 ± 1.42 μg/mL). In contrast, addition of MCTs to the diet led to an increase in serum vitamin E concentration (6.67 ± 0.83 μg/mL) in these 4 dogs to values within the reference range. These findings support the contention that MCTs in the diet increase α-tocopherol absorption.

Humans with EPI have been reported to have low serum concentrations of cholesterol.[7] Pancreatic enzyme supplementation of these patients causes increased cholesterol absorption and decreased cholesterol synthesis, but serum cholesterol concentrations do not normalize.[7] In the EPI group of our study, cholesterol malabsorption was suspected, but in dogs treated with enzyme supplement, this could not be confirmed. On the contrary, even baseline serum cholesterol concentrations were higher in EPI group dogs than in control group dogs. During our study, serum cholesterol concentrations in EPI group dogs were higher than in control group dogs for all 3 diets, but the difference reached significance only with the 35% MCT diet. Both diets containing MCTs led to an increase in serum cholesterol concentration in the EPI group dogs. It has previously been reported for dogs that the dietary addition of the MCTs $C_{12:0}$ and $C_{14:0}$ appears to especially increase serum cholesterol concentrations, compared with LCTs and shorter-chain MCTs, such as $C_{8:0}$ or $C_{10:0}$.[21] Moreover, saturated fatty acids in the diet also increase serum cholesterol concentrations.[22] As previously stated, experimental diets with MCTs in our study contained a higher percentage of saturated fatty acids than the 0% MCT diet, perhaps explaining the increase in serum cholesterol concentrations.

Simpson and Doxey[23] observed decreased serum triglyceride concentrations in dogs with EPI, compared with clinically normal control group dogs, at 3 hours after eating, which appeared to be a reflection of the fat malassimilation present in dogs with EPI.[23] In our study, all serum samples were obtained after withholding food for 12 hours. Serum triglyceride concentrations were not significantly different in EPI group dogs, compared with control group dogs, but serum triglyceride concentrations are highly dependent on food uptake. Even though no significant difference was found in serum triglyceride concentrations among the diets, we did observe an increase in serum triglyceride concentrations with an increase in the MCT content of the diet in EPI group dogs. This may have been the result of increased absorption or decreased clearance of triglycerides in the serum.

Even though baseline serum palmitic acid ($C_{16:0}$) and $C_{18:2(n-6)}$ concentrations were slightly lower in EPI group dogs, no significant difference was found in fatty acid concentrations between EPI and healthy control group dogs during our study. However, we did observe differences among the different diets. The concentration of the different fatty acids in serum as part of total serum triglyceride concentration is dependent on the concentration of specific fatty acids in the diet and on the species-specific ability for fatty acid chain desaturation and elongation. Even though the content of $C_{16:0}$ fatty acids was 13% in all of the diets, the serum concentration of $C_{16:0}$ was significantly increased after feeding the 35% MCT diet in both the EPI and control group dogs. This could be explained by chain elongation of $C_{12:0}$ and $C_{14:0}$ fatty acids to $C_{16:0}$. The frequency of chain elongation may be increased by the addition of MCTs to the diet. The different concentrations of serum linoleic acid ($C_{18:2[n-6]}$) after feeding the experimental diets are probably a result of different MTC concentrations in those diets. But this does not necessarily mean that EPI or feeding an MCT diet causes deficiency of linoleic acid. No known reference range values exist for serum concentrations of linoleic

acid, but dietary recommendations are that at least 1% linoleic acid is provided in total energy requirements to prevent fatty acid deficiency.[24] In our study, linoleic acid content was higher than the recommendation of 1% in all 3 diets, suggesting that none of these dogs were deficient in linoleic acid.

The finding that serum amylase activities in EPI group dogs, both before and during our study, were significantly lower than in healthy control group dogs (while serum lipase activities were within the reference range in both groups) is concordant with results described by Simpson and Doxey.[25] Serum lipase activities that are within the reference range in the EPI group dogs of our study may be the result of extrapancreatic lipases, such as gastric or intestinal lipase.

As expected, the cTLI concentration was significantly lower in EPI group dogs than in control group dogs at the beginning of and throughout our study. The significantly lower mean cTLI concentrations in the control group dogs after feeding the 35% MCT diet, compared with the 16% MCT diet, was caused by 2 high measurements of cTLI concentrations after feeding the 16% MCT diet. Another high serum cTLI concentration was found in a control group dog after feeding the 0% MCT diet (this was observed in 1 of the 2 dogs that had a high serum cTLI concentration when fed the 16% MCT diet), which did however result in a significant difference in serum cTLI concentrations between groups. In all 3 instances of high serum cTLI concentrations, values were within the reference range (5 to 35 μg/L) when measurements were repeated approximately 2 weeks later. In these 3 instances of high serum cTLI concentrations, the values were above the currently recommended cutoff for pancreatitis of 50 μg/L. In dogs that had the increased serum cTLI concentration after feeding both the 0% and 16% MCT diets, abdominal ultrasonography revealed calcified areas in the parenchyma of the pancreas. None of these dogs had a history of clinical pancreatitis. However, subclinical pancreatitis may have been present in these dogs. It is intriguing to speculate that the 35% MCT diet containing less LCT may have been beneficial in these dogs with subclinical pancreatitis. However, such speculation remains to be evaluated. Before and throughout our study, serum cobalamin concentrations in EPI group dogs were significantly less than that in control group dogs. Dogs with EPI frequently have low serum cobalamin concentrations that remain low even after treatment with a pancreatic enzyme supplement.[26] Addition of MCTs to the diet does not influence serum cobalamin concentration because cobalamin absorption is not dependent on fat absorption but on proteases for the digestion of the so-called R-protein and intrinsic factor, which are both mainly produced by the exocrine pancreas.

Serum albumin concentration was not significantly different between EPI and control group dogs. The significant decrease of serum albumin in control group dogs after feeding the 35% MCT diet appeared to be the result of 2 low values (2.8 and 3.1 g/dL). An effect of the 35% MCT diet cannot be totally excluded because both low values were measured during the first feeding period, when both dogs received the 35% MCT diet. Serum albumin concentrations after the other 2 feeding periods were within the reference range for both groups of dogs. We speculate that the significance of this result was caused by the small sample size of 6 dogs in the control group and not by a true effect of MCT on serum albumin concentrations in healthy dogs. However, this speculation needs to be confirmed by further studies.

Overall, the purpose of our study was to evaluate the effect of dietary replacement of LCTs with different concentrations of MCTs in dogs with well-managed EPI. We determined that replacement of LCTs with MCTs in the diet led to an increase in serum concentrations of cholesterol and certain fat-soluble vitamins in our study population. The clinical usefulness of diets containing MCTs for dogs with well-managed EPI cannot be conclusively determined at this point because we do not know whether high serum cholesterol and fat-soluble vitamin concentrations were essential in our group of dogs and because no detectable effect on the subjective well-being of dogs was found. We found that diets containing MCTs were well tolerated in our study. An aversion to MCTs as described by other authors in cats was not observed in our study.[27] In all EPI group dogs, the serum cobalamin concentration was decreased independently from the MCT content of the diet. Cobalamin is essential for proper cell function in many organs, and a decrease in serum cobalamin concentration indicates depletion of cobalamin body stores.It is therefore necessary to measure serum cobalamin concentrations in dogs with EPI. Instances in which serum cobalamin concentrations are found to be low supplementation would appear to be indicated.[1] Results of our study indicate that MCTs do have an effect on lipid and lipophilic nutrient absorption, but no evidence exists on the effects on overall health or condition in dogs with successfully treated EPI.

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[b]Williams DA. *Studies on the diagnosis and pathophysiology of exocrine pancreatic insufficiency.* PhD Thesis. Department of Medicine, University of Liverpool, Liverpool, England, 1985.

[c]Milkbone, Ralston Purina Co, St Louis, Mo (now Nestlé Purina Co, St Louis, Mo).

[d]PetTabs vitamin tablet, Pfizer, Lincoln, Neb.

[e]PetForm vitamin mixture, Lloyd Inc, Shenandoah, Iowa.

[f]Pancrezyme, Daniels Pharmaceuticals, St Petersburg, Fla (now King Pharmaceuticals, Bristol, Tenn).

[g]Experimental diets specifically produced for this study, Ralston Purina Co, St Louis, Mo.

[h]Body condition scoring table for cats and dogs, Ralston Purina Co, St Louis, Mo.

[i]Hitachi 911 analyzer, Roche, Indianapolis, Ind.

[j]Lipase assay, Diagnostic Chemicals Ltd, Oxford, Conn.

[k]Supelco Hypersil silica column, 5 μm, 4.6 × 250 nm, Sigma-Aldrich Inc, St Louis, Mo.

[l]UV/Vis 486 detector, Waters Corp, Milford, Mass.

[m]DL-α-tocopherol, Fluka Biochemicals, Buchs, Switzerland.

[n]Millenium software package, Waters Corp, Milford, Mass.

[o]LIAISON 25-hydroxy vitamin D assay kit, DiaSorin, Stillwater, Minn.

[p]IMMULITE, Diagnostics Products Corp, Los Angeles, Calif.

[q]KTLD1 TLI assay kit, Diagnostics Products Corp, Los Angeles, Calif.

[r]HPLC with two 510 pumps, 486 detector, 717 Plus autosampler, Waters Corp, Milford, Mass.

[s]Retinal acetate (R4632), Sigma-Aldrich Inc, St Louis, Mo.

[t]Symmetry $C_{18}$ column, 5 μm, 6 × 250 nm, Waters Corp, Milford, Mass.

[u]Millenium 32 software package, Waters Corp, Milford, Mass.
[v]Retinol (R7632), Sigma-Aldrich Inc, St Louis, Mo.
[w]Retinyl palmitate (R3375), Sigma-Aldrich Inc, St Louis, Mo.
[x]Hewlett Packard (now Agilent), Wilmington, Del.
[y]Carbowax-PEG column, Restek Corp, Bellefonte, Pa.
[z]HP chemstation, Hewlett Packard, Wilmington, Del.
[aa]Fatty acid standards, NuCheck Prep Inc, Elysian, Minn.

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## Appendix 1

Feeding order groups of dogs in the study.

| Feeding order of diets A, B, and C* | No. of dogs† | Breeds | Age (y) | Sex |
|---|---|---|---|---|
| Dogs with exocrine pancreatic insufficiency | | | | |
| ABC | 4 | 1 SS, 3 GSD | 1–6 | 2 FS, 1 MN, 1 M |
| ACB | 4 | 3 GSD, 1 LR | 1–11 | 4 FS |
| BAC | 4 | 1 WC, 2 GSD, 1 CS | 1 to 8 | 2 FS, 2 MN |
| BCA | 4 | 2 GSD, 2 WC | 2–5 | 2 MN, 1 M, 1 FS |
| CAB | 4 | 1 LR-GSD crossbred, 2 GSD, 1 Tervuren | 2–8 | 1 F, 2 FS, 1 MN |
| CBA | 4 | 3 GSD, 1 Collie | 1–4 | 1 MN, 2 FS, 1 M |
| Control group dogs | | | | |
| ABC | 1 | Mix breed | 3 | FS |
| ACB | 1 | LR | 2 | FS |
| BAC | 1 | White GSD | 3 | FS |
| BCA | 1 | Boxer | 3 | FS |
| CAB | 1 | LR | 6 | FS |
| CBA | 1 | WC | 5 | M |

*Diet A contained 0% medium chain triglycerides (MCTs), diet B contained 16% MCTs, and diet C contained 35% MCTs. †Dogs were randomized into feeding order groups by use of a replicated Latin-square design based on the order of enrollment into the study.

GSD = German Shepard Dog. SS = Springer Spaniel. LR = Labrador Retriever. WC = Welsh Corgi. CS = Cocker Spaniel. FS = Female spayed. F = Female sexually intact. MN = Male neutered. M = Male sexually intact.

*Appendix 2 appears on the next page*

## Appendix 2

Mean (± SD) analysis variables of the 3 experimental diets (0%, 16%, and 35%) MCTs of the total fat content).

| | Diets* as a percentage of total fat content | | |
|---|---|---|---|
| **Variables** | **0% MTC** | **16% MTC** | **35% MTC** |
| Calories (kcal/g) | 4.56 ± 0.12 | 4.54 ± 0.15 | 4.52 ± 0.11 |
| Ash (%) | 5.55 ± 0.05 | 5.44 ± 0.04 | 5.53 ± 0.63 |
| Moisture (%) | 10.61 ± 0.84 | 10.41 ± 0.86 | 10.36 ± 0.71 |
| Protein (%) | 25.77 ± 0.23 | 25.53 ± 0.31 | 25.73 ± 0.67 |
| Total dietary fiber (%) | 7.07 ± 0 | 5.66 ± 0 | 6.85 ± 0 |
| Fiber, crude (%) | 1.74 ± 0.63 | 1.34 ± 0.01 | 1.26 ± 0.11 |
| Insoluble dietary fiber (%) | 6.34 ± 0 | 5.66 ± 0 | 6.85 ± 0 |
| Soluble fiber (%) | 0.74 ± 0 | < 0.500 | < 0.50 |
| Vitamin A (IU /kg) | 32,187.5 ± 0 | 24,030.4 ± 0 | 23,148.5 ± 0 |
| Vitamin D (IU /g) | 3.75 ± 0 | 2.73 ± 0 | 2.96 ± 0 |
| Vitamin E (mg/100 g) | 6.37 ± 0 | 5.59 ± 0 | 3.81 ± 0 |
| Total fat (g/100 g) | 10.57 ± 0.29 | 10.77 ± 0.12 | 9.87 ± 0.40 |
| Monounsaturated fat (g/100 g) | 2.67 ± 0.17 | 2.19 ± 0.11 | 1.45 ± 0.11 |
| Saturated fat (g/100 g) | 2.00 ± 0.10 | 4.12 ± 0.09 | 6.16 ± 0.24 |
| Fat (%) | 11.23 ± 0.29 | 11.27 ± 0.32 | 10.60 ± 0.60 |
| Caproic ($C_{6:0}$; %) | < 0.10 | 0.11 ± 0.01 | 0.16 ± 0.09 |
| Caprylic ($C_{8:0}$; %) | < 0.10 | 1.72 ± 0.07 | 3.86 ± 0.06 |
| Capric ($C_{10:0}$; %) | < 0.10 | 1.50 ± 0.04 | 3.34 ± 0.07 |
| Lauric ($C_{12:0}$; %) | 0.12 ± 0.03 | 12.47 ± 0.21 | 28.10 ± 0.26 |
| Myristic ($C_{14:0}$; %) | 0.39 ± 0.01 | 5.40 ± 0.10 | 11.80 ± 0 |
| Palmitic ($C_{16:0}$; %) | 13.20 ± 0.36 | 12.63 ± 0.21 | 12.67 ± 0.23 |
| Palmitoleic ($C_{16:1}$; %) | 0.51 ± 0.10 | 0.40 ± 0.06 | 0.41 ± 0.06 |
| Margaric ($C_{17:0}$; %) | 0.20 ± 0.01 | 0.16 ± 0.01 | 0.13 ± 0.01 |
| Stearic ($C_{18:0}$; %) | 4.83 ± 0.21 | 4.29 ± 0.09 | 3.94 ± 0.07 |
| Other cis isomers ($C_{18:1}$; %) | < 0.10 | 0.10 ± 0 | < 0.10 |
| †Oleic ($C_{18:1C}$; %) | 23.83 ± 0.64 | 19.67 ± 0.49 | 14.87 ± 0.42 |
| †Vaccenic ($C_{18:1C}$; %) | 1.34 ± 0.12 | 0.98 ± 0.07 | 0.50 ± 0.04 |
| †Elaidic ($C_{18:1T}$; %) | 0.37 ± 0.04 | 0.25 ± 0.07 | 0.28 ± 0.04 |
| Linoleic ($C_{18:2}$; %) | 47.93 ± 1.01 | 35.43 ± 0.93 | 18.10 ± 0.52 |
| Trans Isomers ($C_{18:2}$; %) | 0.32 ± 0.06 | 0.20 ± 0.03 | < 0.10 |
| Linolenic ($C_{18:3}$; %) | 4.79 ± 0.43 | 3.15 ± 0.30 | 0.77 ± 0.08 |
| Arachidic ($C_{20:0}$; %) | 0.35 ± 0.01 | 0.29 ± 0.01 | 0.21 ± 0.01 |
| Eicosenoic ($C_{20:1}$; %) | 0.46 ± 0.04 | 0.33 ± 0.03 | 0.12 ± 0.01 |
| Arachidonic ($C_{20:4}$; %) | 0.11 ± 0.02 | 0.11 ± 0.01 | 0.11 ± 0.02 |
| Behenic ($C_{22:0}$; %) | 0.31 ± 0.02 | 0.22 ± 0.03 | 0.12 ± 0.02 |
| Lignoceric ($C_{24:0}$; %) | 0.19 ± 0.02 | 0.17 ± 0.03 | 0.16 ± 0.03 |
| Unknowns (%) | 0.57 ± 0.08 | 0.36 ± 0.04 | 0.18 ± 0.06 |
| Total saturated fatty acids (%) | 19.59 ± 0.57 | 38.95 ± 0.53 | 64.49 ± 0.39 |
| Total MCTs (%) | 0.12 ± 0.03 | 15.79 ± 0.30 | 35.47 ± 0.45 |

*Before investigators were made aware of treatments (ie, unblinded), the 0% MCT diet was referred to as diet A, the 16% MCT diet as diet B, and the 35% MCT diet as diet C.

†C = Cis. T = Trans-fatty acids

Fatty acids listed only when ≥ 0.1% of total fat content.