

Supplementary Table S3—Mean ± SEM serum biochemical data prior to (week 0) and following 4 weeks of dosing (week 4) for the dogs of Table S1.

| | RR/Units | Placebo | | 1 mg/kg | | 2 mg/kg | | 4 mg/kg | | 12 mg/kg | |
|------------------|------------------|-----------|-----------|------------|--------------------------|-----------|------------------------|-----------|-----------------------------|-----------|---------------------------|
| | | Week 0 | Week 4 | Week 0 | Week 4 | Week 0 | Week 4 | Week 0 | Week 4 | Week 0 | Week 4 |
| TP | 50-74 g/L | 58.8±0.6 | 57.8±1.3 | 59.0±0.6 | 56.5±0.5 | 59.0±0.7 | 55.5±1.9 | 58.0±1.8 | 53.8±1.7^a | 59.5±0.3 | 56.5±0.7 |
| Albumin | 27-44 g/L | 34.3±0.3 | 33.8±0.3 | 34.0±0.4 | 33.5±0.3 | 34.5±0.3 | 33.3±0.6 | 32.8±1.1 | 32.0±0.4 | 36.0±0.4 | 35.0±0.4 |
| Globulin | 16-36 g/L | 24.5±0.7 | 24.0±1.2 | 25.0±0.4 | 23.0±0.4 | 24.5±0.9 | 22.3±1.7 | 25.3±1.1 | 21.8±1.7 ^a | 23.5±0.3 | 21.5±0.3 |
| AST | 15-66 U/L | 27±2 | 22±2 | 28±3 | 28±3 ^a | 25±2 | 23±2 | 29±1 | 25±2 | 25±3 | 21±2 |
| ALT | 12-118 U/L | 39±12 | 154±127 | 30±3 | 34±4 | 26±3 | 28±4 | 25±2 | 25±1 | 28±3 | 29±2 |
| ALP | 5-131 U/L | 51±15 | 62±24 | 34±6 | 38±5 | 59±12 | 81±19 | 45±3 | 89±23 | 51±8 | 179±52^a |
| GGTP | 1-12 U/L | 2.8±0.5 | 3.8±1.1 | 2.3±0.3 | 2.5±0.3 | 2.8±0.5 | 2.5±0.3 | 1.8±0.3 | 2.5±0.3 | 3.0±0.4 | 3.0±0.4 |
| Bilirubin | 0.0-5.1 µmol/L | 3.7±0.4 | 2.9±0.2 | 4.0±0.6 | 3.4±0.2 | 4.3±0.2 | 2.8±0.1 ^a | 3.3±0.4 | 2.5±0.2 | 4.4±0.5 | 2.2±0.1 ^a |
| BUN | 2.1-11.1 mmol/L | 6.3±0.3 | 6.2±0.4 | 7.1±0.7 | 5.7±0.5 | 6.1±0.3 | 4.6±0.2 | 7.3±0.5 | 7.3±1.7 | 6.2±0.4 | 5.5±0.4 |
| Cr | 44-141 µmol/L | 71±7 | 72±3 | 79±2 | 80±3 | 69±3 | 73±5 | 77±4 | 104±26 | 73±5 | 76±3 |
| P | 0.81-1.94 mmol/L | 1.37±0.12 | 1.44±0.07 | 1.37±0.07 | 1.44±0.17 | 1.32±0.11 | 1.21±0.06 | 1.51±0.11 | 1.58±0.13 | 1.43±0.06 | 1.33±0.12 |
| Ca | 2.23-2.85 mmol/L | 2.53±0.03 | 2.43±0.03 | 2.48±0.05 | 2.45±0.03 | 2.60±0.00 | 2.45±0.03 | 2.53±0.05 | 2.43±0.05 | 2.58±0.03 | 2.43±0.03 |
| Mg | 0.7-1.3 mmol/L | 0.8±0.0 | 0.8±0.0 | 0.8±0.0 | 0.8±0.0 | 0.8±0.0 | 0.8±0.0 | 0.7±0.0 | 0.8±0.0 | 0.7±0.0 | 0.7±0.0 |
| Na | 139-154 mmol/L | 147.5±0.3 | 148.0±0.4 | 148.25±0.5 | 148.5±0.5 | 148.8±0.5 | 147.5±1.0 ^a | 148.3±0.3 | 148.0±0.4 | 148.0±0.7 | 148.3±1.4 |
| K | 3.6-5.5 mmol/L | 4.1±0.1 | 4.3±0.1 | 4.4±0.1 | 4.1±0.0 ^a | 4.2±0.1 | 4.2±0.1 | 4.2±0.1 | 4.2±0.1 | 4.3±0.0 | 4.2±0.1 |
| Cl | 102-120 mmol/L | 114.3±1.1 | 113.8±1.0 | 116.5±0.7 | 115.5±0.9 | 115.0±0.0 | 114.0±0.7 | 115.8±0.5 | 115.3±0.5 | 115.3±0.8 | 114.8±1.4 |
| Glu | 3.9-7.7 mmol/L | 5.2±0.3 | 5.3±0.4 | 5.1±0.1 | 5.1±0.1 | 4.8±0.2 | 4.9±0.2 | 4.6±0.3 | 5.2±0.2 | 4.9±0.2 | 5.4±0.3 |
| Chol | 2.38-10.0 mmol/L | 6.55±0.32 | 6.35±0.43 | 5.85±0.16 | 5.18±0.17 | 6.28±0.54 | 5.40±0.44 ^a | 5.85±0.36 | 5.18±0.30 | 6.50±0.40 | 6.15±0.47 |
| TG | 0.33-3.32 mmol/L | 0.76±0.04 | 0.92±0.15 | 0.83±0.12 | 0.52±0.04 ^a | 0.83±0.08 | 0.55±0.05 ^a | 0.85±0.20 | 0.48±0.07 | 0.87±0.13 | 0.86±0.21 |
| Amylase | 290-1125 U/L | 474±29 | 419±42 | 500±26 | 407±44 | 415±15 | 384±9 | 565±47 | 482±52 | 391±18 | 347±11 |
| PSL | 24-140 U/L | 44±9 | 49±10 | 62±15 | 60±15^a | 45±5 | 47±6 | 54±9 | 52±10 ^a | 46±8 | 45±8 ^a |
| CPK | 59-895 U/L | 90±9 | 94±8 | 147±54 | 96±11 | 130±41 | 102±21 | 132±16 | 87±4 | 123±16 | 105±12 |

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Ca, calcium; Chol, cholesterol; Cl, chloride; CPK, creatine phosphokinase; Cr, creatinine; GGTP, gamma-glutamyl transpeptidase; Glu, glucose; K, potassium; Mg, magnesium; Na, sodium; P, phosphorus; PSL, pancreatic sensitive lipase; RR, reference range; TG, triglycerides; TP, total protein; U/L, units per liter

^a Mean change in a parameter from Week 0 (7 days prior to treatment initiation) to the end of the dosing period (end of Week 4) in one or more of the CBD dose groups (1, 2, 4, or 12 mg/kg) was significantly different from the mean change in the placebo group over the same time period (Generalized estimating equation with alpha level set at p<0.05, two-tailed, and adjustments made for multiple comparisons). Of the parameters that achieved statistical significance relative to placebo, only for three parameters did an individual subject (and in all cases only one subject) fall outside of the RR at Week 4: TP (4 mg/kg), ALP (12 mg/kg) and PSL (1 mg/kg) – all bolded. Moreover, only for ALP, did the mean group value fall outside of the RR. For all other parameters for which statistical significance was achieved, individual subjects all fell within the RR at Week 4.