

1 **Appendix/Supplemental Tables**

2 **Supplemental Table 1-1.** The results of the safety evaluation (physical examination)

	Unit		Scr		4w		8w		12w		<i>P</i> value			
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Scr	4w	8w	12w
Body weight	kg	Acacia group (n = 33)	66.5	11.5	66.1	10.8	66.4	11.0	66.4	10.9	0.664	0.546	0.625	0.569
		Placebo group (n = 31)	67.9	14.3	68.1	14.3	68.0	14.4	68.2	14.7				
BMI	kg/m ²	Acacia group (n = 33)	24.2	3.4	24.1	3.2	24.1	3.2	24.1	3.2	0.902	0.742	0.840	0.822
		Placebo group (n = 31)	24.3	4.0	24.4	4.1	24.3	4.1	24.4	4.3				
Body fat percentage	%	Acacia group (n = 33)	26.1	8.6	25.8	8.3	25.9	7.9	25.9	8.0	0.693	0.821	0.764	0.692
		Placebo group (n = 31)	25.3	7.6	26.3	9.9	25.3	8.1	25.1	8.4				
Pulse rate	bpm	Acacia group (n = 33)	73.7	12.3	73.1	10.6	71.0	10.7	70.2	10.7	0.878	0.201	0.130	0.011*
		Placebo group (n = 31)	74.1	10.0	76.8	12.6	75.4	12.3	78.4	13.8				
Body temperature	°C	Acacia group (n = 33)	34.7	1.8	33.7	0.9	33.9	0.7	33.9	0.7	0.858	0.361	0.204	0.816
		Placebo group (n = 31)	34.8	1.6	33.5	0.6	33.7	0.6	33.9	0.7				

3 The data are presented as the number of subjects, or the mean and standard deviation (SD).

4 *: *P* < 0.05 vs. the placebo group.

5 **Supplemental Table 1-2.** The results of the safety evaluation (urinalysis)

	Reference range		Scr		4w		8w		12w		<i>P</i> value			
			Within the reference range	Outside the reference range	Within the reference range	Outside the reference range	Within the reference range	Outside the reference range	Within the reference range	Outside the reference range	Scr	4w	8w	12w
Protein	—	Acacia group (n = 33)	30	3	29	4	29	4	26	7	1.000	0.729	0.729	0.769
		Placebo group (n = 31)	28	3	26	5	26	5	22	8				
Glucose	—	Acacia group (n = 33)	33	0	33	0	33	0	33	0	N.A.	0.484	0.484	N.A.
		Placebo group (n = 31)	31	0	30	1	30	1	30	0				
Urobilinogen	±	Acacia group (n = 33)	33	0	33	0	32	1	33	0	N.A.	N.A.	0.607	N.A.
		Placebo group (n = 31)	31	0	31	0	29	2	30	0				
Bilirubin	—	Acacia group (n = 33)	33	0	33	0	33	0	33	0	N.A.	N.A.	N.A.	N.A.
		Placebo group (n = 31)	31	0	31	0	31	0	30	0				
pH	5.0-7.5	Acacia group (n = 33)	33	0	32	1	33	0	33	0	0.231	1.000	N.A.	0.476
		Placebo group (n = 31)	29	2	31	0	31	0	29	1				
Occult blood	—	Acacia group (n = 33)	30	3	31	2	32	1	31	2	1.000	1.000	0.607	1.000
		Placebo group (n = 31)	29	2	30	1	29	2	28	2				
Ketone bodies	—	Acacia group (n = 33)	33	0	32	1	33	0	33	0	N.A.	1.000	0.484	0.476
		Placebo group (n = 31)	31	0	31	0	30	1	29	1				

6 N.A.: Not Available

7 **Supplemental Table 1-3.** The results of the safety evaluation (blood test)

	Reference range	Unit	Scr		4w		8w		12w		P value				
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Scr	4w	8w	12w	
Leukocyte count	3300-9000	/μL	Acacia group (n = 33)	5690.9	1530.0	5690.9	1488.8	5275.8	1203.6	5336.4	1657.9	0.804	0.412	0.168	0.254
			Placebo group (n = 31)	5600.0	1385.6	5422.6	1058.8	5722.6	1360.1	5816.7	1647.6				
Erythrocyte count	Men: 430-570	×10 ⁴ /μL	Acacia group (n = 33)	467.6	35.9	462.0	39.4	457.9	36.4	459.6	35.5	0.124	0.042*	0.046*	0.054
	Women: 380-500		Placebo group (n = 31)	482.3	39.1	482.1	38.0	477.8	41.7	479.0	42.8				
Hemoglobin	Men: 13.5-17.5	g/dL	Acacia group (n = 33)	14.7	1.0	14.4	1.2	14.3	1.1	14.4	1.1	0.077	0.026*	0.018*	0.033*
	Women: 11.5-15.0		Placebo group (n = 31)	15.2	1.3	15.1	1.4	15.0	1.4	15.1	1.5				
Hematocrit Value	Men: 39.7-52.4	%	Acacia group (n = 33)	44.5	2.7	44.6	3.3	44.7	3.1	44.8	3.0	0.069	0.029*	0.033*	0.065
	Women: 34.8-45.0		Placebo group (n = 31)	45.9	3.0	46.5	3.5	46.5	3.5	46.4	3.9				
Platelet count	14.0-34.0	×10 ⁴ /μL	Acacia group (n = 33)	27.0	4.9	26.1	4.8	25.6	4.8	25.6	5.2	0.283	0.269	0.391	0.315
			Placebo group (n = 31)	25.7	5.3	24.8	4.6	24.5	5.2	24.4	4.7				

MCV	85-102	fL	Acacia group (n = 33)	95.5	4.4	96.8	4.3	97.9	4.6	97.7	4.4	0.800	0.895	0.809	0.688
			Placebo group (n = 31)	95.2	4.7	96.6	6.1	97.5	6.2	97.2	6.0				
MCH	28.0-34.0	pg	Acacia group (n = 33)	31.4	1.6	31.3	1.6	31.2	1.6	31.3	1.5	0.827	0.701	0.498	0.590
			Placebo group (n = 31)	31.5	2.0	31.5	2.2	31.5	2.2	31.6	2.3				
MCHC	30.2-35.1	%	Acacia group (n = 33)	32.9	0.9	32.3	1.0	31.9	0.9	32.1	1.0	0.564	0.424	0.134	0.097
			Placebo group (n = 31)	33.1	1.1	32.5	1.0	32.3	1.0	32.5	1.0				
Percentage of neutrophils	40.0-75.0	%	Acacia group (n = 33)	58.2	10.0	58.7	10.1	55.6	8.3	57.6	8.3	0.994	0.859	0.166	0.199
			Placebo group (n = 31)	58.2	8.7	58.4	6.4	58.3	6.4	60.1	7.0				
Percentage of lymphocytes	18.0-49.0	%	Acacia group (n = 33)	33.8	9.5	32.8	9.4	35.5	8.4	33.8	8.3	0.988	0.808	0.257	0.320
			Placebo group (n = 31)	33.8	7.8	33.3	5.9	33.4	5.6	31.9	6.2				
Percentage of monocytes	2.0-10.0	%	Acacia group (n = 33)	5.1	1.0	5.6	1.2	5.3	0.9	5.2	0.9	0.309	0.747	0.291	0.893
			Placebo group (n = 31)	5.3	1.0	5.5	0.9	5.6	1.2	5.2	1.2				

Percentages of eosinophils	0.0-8.0	%	Acacia group (n = 33)	2.3	1.3	2.3	1.2	3.1	1.9	2.8	1.7	0.488	0.973	0.048*	0.146
			Placebo group (n = 31)	2.1	1.6	2.3	1.4	2.2	1.5	2.2	1.4				
Percentages of basophils	0.0-2.0	%	Acacia group (n = 33)	0.6	0.4	0.5	0.4	0.5	0.3	0.6	0.4	0.762	0.756	0.885	0.243
			Placebo group (n = 31)	0.5	0.3	0.6	0.3	0.5	0.3	0.5	0.4				
Neutrophils	-	/μL	Acacia group (n = 33)	3409.1	1388.6	3441.5	1382.0	2980.7	987.9	3154.1	1369.0	0.793	0.396	0.126	0.228
			Placebo group (n = 31)	3323.8	1183.1	3195.5	838.6	3368.5	1010.8	3558.1	1251.7				
Lymphocytes	-	/μL	Acacia group (n = 33)	1830.9	424.0	1780.9	444.9	1828.5	440.3	1723.3	407.0	0.953	0.953	0.610	0.472
			Placebo group (n = 31)	1837.0	402.3	1774.9	349.4	1883.8	421.9	1797.5	405.2				
Monocytes	-	/μL	Acacia group (n = 33)	289.6	96.9	310.4	81.6	279.4	84.7	281.1	114.5	0.787	0.442	0.095	0.415
			Placebo group (n = 31)	295.6	80.4	296.0	66.9	316.4	90.4	305.7	123.9				
Eosinophils	-	/μL	Acacia group (n = 33)	131.0	77.2	128.6	63.1	160.6	91.7	146.8	95.5	0.429	0.906	0.116	0.395
			Placebo group (n = 31)	113.9	94.7	126.4	89.1	123.3	95.3	126.1	96.5				

Basophils	-	/μL	Acacia group (n = 33)	30.3	20.2	28.2	17.1	26.7	14.2	31.1	15.5	0.902	0.708	0.349	0.681
			Placebo group (n = 31)	29.7	18.6	29.8	17.3	30.5	18.4	29.3	19.2				
AST (GOT)	10-40	U/L	Acacia group (n = 33)	22.4	7.0	22.0	5.6	23.4	6.4	21.9	5.1	0.183	0.172	0.401	0.043*
			Placebo group (n = 31)	24.6	5.9	24.1	6.6	25.0	8.4	26.4	11.4				
ALT (GPT)	5-45	U/L	Acacia group (n = 33)	21.8	14.7	20.2	10.6	22.7	13.4	20.5	10.7	0.563	0.263	0.677	0.196
			Placebo group (n = 31)	24.0	15.7	24.4	18.2	24.5	19.2	25.8	20.3				
γ-GT (γ-GTP)	Men: ≤80	U/L	Acacia group (n = 33)	43.2	34.3	43.9	35.2	48.3	44.6	49.6	51.9	0.860	0.939	0.609	0.885
	Women: ≤30		Placebo group (n = 31)	45.0	43.4	43.2	36.8	42.9	38.6	47.8	48.5				
ALP	100-325	U/L	Acacia group (n = 33)	214.4	60.8	208.4	60.2	208.2	62.0	207.9	62.6	0.449	0.814	0.625	0.563
			Placebo group (n = 31)	203.5	53.2	212.0	62.2	201.0	55.5	199.2	54.5				
LD (LDH)	120-240	U/L	Acacia group (n = 33)	199.3	33.0	195.4	30.5	199.2	32.3	199.0	31.0	0.122	0.168	0.191	0.383
			Placebo group (n = 31)	187.8	25.0	185.3	27.5	189.6	25.1	192.7	24.6				

LAP	Men: 45-81	U/L	Acacia group (n = 33)	55.6	11.1	56.8	11.8	57.2	12.7	57.3	14.4	0.898	0.813	0.674	0.802
	Women: 37-61		Placebo group (n = 31)	55.3	12.4	56.1	11.6	55.8	12.7	56.4	12.8				
Total bilirubin	0.2-1.2	mg/dL	Acacia group (n = 33)	0.8	0.4	0.9	0.4	0.8	0.3	0.8	0.3	0.508	0.837	0.096	0.364
			Placebo group (n = 31)	0.9	0.3	0.9	0.4	0.9	0.2	0.9	0.3				
Direct bilirubin	0.0-0.2	mg/dL	Acacia group (n = 33)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.633	0.620	0.350	0.751
			Placebo group (n = 31)	0.1	0.1	0.1	0.0	0.1	0.1	0.1	0.1				
Indirect bilirubin	0.2-1.0	mg/dL	Acacia group (n = 33)	0.7	0.4	0.8	0.3	0.7	0.2	0.7	0.3	0.511	0.886	0.098	0.344
			Placebo group (n = 31)	0.8	0.2	0.8	0.3	0.8	0.2	0.8	0.2				
Cholinesterase (ChE)	Men: 234-493	U/L	Acacia group (n = 33)	358.9	69.8	344.5	71.5	343.6	70.0	345.4	68.1	0.690	0.978	0.943	0.776
	Women: 200-452		Placebo group (n = 31)	352.3	61.7	345.0	59.5	342.4	64.1	340.5	67.5				
Total protein	6.7-8.3	g/dL	Acacia group (n = 33)	7.1	0.3	7.1	0.4	7.1	0.4	7.1	0.4	0.253	0.556	0.319	0.489
			Placebo group (n = 31)	7.2	0.4	7.2	0.3	7.2	0.5	7.2	0.5				

Urea nitrogen	8.0-20.0	mg/dL	Acacia group (n = 33)	14.0	3.7	14.0	3.4	14.9	3.6	14.3	3.1	0.720	0.797	0.882	0.690
			Placebo group (n = 31)	14.3	3.0	14.3	3.3	15.0	3.7	14.6	3.2				
Creatinine	Men: 0.61-1.04	mg/dL	Acacia group (n = 33)	0.8	0.1	0.8	0.1	0.8	0.1	0.8	0.1	0.225	0.390	0.332	0.145
	Women: 0.47-0.79		Placebo group (n = 31)	0.8	0.2	0.8	0.2	0.8	0.2	0.8	0.2				
Uric acid	Men: 3.8-7.0	mg/dL	Acacia group (n = 33)	5.8	1.6	5.9	1.4	5.9	1.5	5.9	1.5	0.540	0.540	0.840	0.958
	Women: 2.5-7.0		Placebo group (n = 31)	5.6	1.2	5.7	1.4	5.8	1.4	5.9	1.5				
CK	Men: 60-270	U/L	Acacia group (n = 33)	139.9	106.2	123.7	62.5	141.6	87.4	132.4	61.4	0.917	0.424	0.270	0.718
	Women: 40-150		Placebo group (n = 31)	137.2	99.7	111.7	56.3	121.1	55.2	140.3	107.2				
Sodium	137-147	mEq/L	Acacia group (n = 33)	140.8	1.6	140.9	1.6	141.5	1.5	141.0	1.6	0.770	0.405	0.939	0.363
			Placebo group (n = 31)	140.6	1.4	140.5	2.1	141.5	1.6	141.4	1.6				
Potassium	3.5-5.0	mEq/L	Acacia group (n = 33)	4.2	0.5	4.1	0.5	3.9	0.3	4.0	0.4	0.645	0.980	0.788	0.814
			Placebo group (n = 31)	4.2	0.4	4.1	0.4	4.0	0.4	3.9	0.4				

Chloride	98-108	mEq/L	Acacia group (n = 33)	101.4	1.5	101.4	2.0	101.9	1.2	101.7	1.8	0.182	0.434	0.061	0.174
			Placebo group (n = 31)	100.8	1.6	101.0	1.7	101.0	2.3	101.0	2.2				
Calcium	8.4-10.4	mg/dL	Acacia group (n = 33)	9.4	0.3	9.3	0.3	9.3	0.3	9.3	0.4	0.237	0.855	0.331	0.682
			Placebo group (n = 31)	9.4	0.3	9.3	0.3	9.4	0.4	9.3	0.3				
Inorganic phosphorus	2.5-4.5	mg/dL	Acacia group (n = 33)	3.3	0.4	3.7	0.6	3.7	0.5	3.6	0.5	0.056	0.046*	0.045*	0.318
			Placebo group (n = 31)	3.1	0.5	3.4	0.5	3.4	0.5	3.4	0.5				
Serum iron	Men: 50-200	µg/dL	Acacia group (n = 33)	104.5	36.3	105.2	36.2	105.2	37.2	101.7	33.0	0.193	0.965	0.693	0.576
	Women: 40-180		Placebo group (n = 31)	116.6	37.2	104.8	37.7	108.9	39.1	106.8	39.1				
Serum amylase	40-122	U/L	Acacia group (n = 33)	71.2	17.0	69.7	15.4	72.1	20.6	70.1	16.1	0.261	0.179	0.311	0.304
			Placebo group (n = 31)	76.9	22.8	76.0	21.5	77.8	23.7	75.5	24.4				
Total cholesterol	120-219	mg/dL	Acacia group (n = 33)	218.4	34.0	212.7	31.5	213.4	30.6	210.0	32.4	0.809	0.915	0.800	0.664
			Placebo group (n = 31)	216.0	42.6	211.7	43.7	211.1	42.0	214.2	42.6				

HDL cholesterol	Men: 40-85	mg/dL	Acacia group (n = 33)	64.0	16.8	62.2	15.4	62.5	15.5	61.9	14.8	0.973	0.905	0.803	0.641
	Women: 40-95		Placebo group (n = 31)	64.1	13.8	61.7	16.0	63.5	16.5	63.6	14.2				
LDL cholesterol	65-139	mg/dL	Acacia group (n = 33)	134.7	30.5	129.9	28.3	131.1	26.5	128.8	27.8	0.508	0.560	0.448	0.764
			Placebo group (n = 31)	128.8	39.5	124.9	39.5	124.6	40.0	126.2	39.1				
Triglyceride	30-149	mg/dL	Acacia group (n = 33)	105.1	50.0	103.6	58.5	106.6	61.6	108.7	60.2	0.099	0.075	0.204	0.139
			Placebo group (n = 31)	130.1	68.5	140.7	101.4	135.1	110.4	137.3	89.6				
Glucose	70-109	mg/dL	Acacia group (n = 33)	88.5	8.5	92.4	12.5	92.2	13.4	92.5	10.9	0.509	0.328	0.828	0.969
			Placebo group (n = 31)	90.3	12.2	102.4	56.8	93.0	14.2	92.3	14.1				
Glycoalbumin	12.3-16.5	%	Acacia group (n = 33)	13.5	1.1	14.1	1.5	14.0	1.5	13.9	1.4	0.283	0.581	0.589	0.343
			Placebo group (n = 31)	13.9	1.8	14.3	2.2	14.2	2.4	14.4	2.5				

8 The data are presented as the number of subjects, or the mean and standard deviation (SD).

9 *: $P < 0.05$ vs. the placebo group.