

**Supplementary Table 1.** Information stated in the consent document.

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- 1 the name of the study and the fact that it has been reviewed by the bioethics committee of Hokkaido Information University and has been approved by the president
  - 2 name, affiliation, and contact information of the investigator, consultation service for the study, and the medical institution cooperating with the study
  - 3 purpose and method of the trial
  - 4 expected effects (physician comments can be obtained through periodic blood tests, etc.) and expected disadvantages (the burden of eating the test food every day, the burden of writing in the daily diary, the time restriction of regular visits, the burden of taking blood samples and various tests, etc.) of trial participation
  - 5 ability to withdraw from the trial at any time
  - 6 no consequences for failing to participate or withdrawing from the trial
  - 7 methods of confidentiality of subjects and anonymizing, storing, and disposing of samples and information
  - 8 matters concerning compensation in the event of adverse health effects requiring treatment
  - 9 matters concerning the bearing of expenses pertaining to the examination
  - 10 research funding sources and conflicts of interest
  - 11 method for disclosing information on tests
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**Supplementary Table 2.** The secondary endpoints assessed in the SM DNA and placebo groups.

	Placebo (n = 22-23)	SM DNA (n = 26)	Group	p value*				
				Two-way ANOVA				
				Period effect	Treatment effect	Interaction		
<b>FIB-4 index</b>								
Basal	0.96 ± 0.41	1.15 ± 0.32	0.069	†	0.004	#	0.900	0.843
Δ4wk	-0.04 ± 0.18	-0.07 ± 0.22	0.681					
Δ8wk	0.05 ± 0.15	0.05 ± 0.33	0.934					
Δ12wk	0.03 ± 0.18	0.04 ± 0.22	0.881					
<b>NAFLD fibrosis score</b>								
Basal	-3.02 ± 1.04	-2.47 ± 0.70	0.035	#	0.010	#	0.385	0.586
Δ4wk	-0.04 ± 0.53	-0.17 ± 0.29	0.264					
Δ8wk	0.17 ± 0.52	0.03 ± 0.53	0.372					
Δ12wk	0.09 ± 0.59	0.07 ± 0.35	0.894					
<b>TP (g/dL)</b>								
Basal	7.55 ± 0.30	7.46 ± 0.36	0.347		0.058	†	0.429	0.604
Δ4wk	-0.08 ± 0.24	-0.06 ± 0.22	0.707					
Δ8wk	-0.05 ± 0.31	0.00 ± 0.28	0.557					
Δ12wk	-0.17 ± 0.37	-0.07 ± 0.26	0.275					
<b>Alb (g/dL)</b>								
Basal	4.58 ± 0.23	4.62 ± 0.19	0.545		0.464		0.560	0.865
Δ4wk	0.00 ± 0.17	0.02 ± 0.13	0.655					
Δ8wk	0.00 ± 0.15	0.03 ± 0.15	0.435					
Δ12wk	-0.02 ± 0.20	-0.01 ± 0.15	0.782					
<b>A/G ratio</b>								
Basal	1.56 ± 0.21	1.65 ± 0.20	0.162		0.254		0.630	0.095 †
Δ4wk	0.04 ± 0.11	0.05 ± 0.09	0.874					
Δ8wk	0.03 ± 0.11	0.03 ± 0.09	0.769					
Δ12wk	0.08 ± 0.10	0.03 ± 0.09	0.082	†				
<b>Fasting blood glucose (mg/dL)</b>								
Basal	94.09 ± 11.33	95.31 ± 11.62	0.712		0.061	†	0.656	0.468
Δ4wk	-1.35 ± 7.27	0.15 ± 5.65	0.421					
Δ8wk	0.86 ± 6.40	0.65 ± 6.57	0.912					
Δ12wk	-1.61 ± 6.84	-0.19 ± 6.81	0.472					
<b>HbA1c (%)</b>								
Basal	5.37 ± 0.37	5.47 ± 0.35	0.338		0.003	#	0.880	0.027 #

	$\Delta 4\text{wk}$	0.08	$\pm$	0.12	0.12	$\pm$	0.14	0.278				
	$\Delta 8\text{wk}$	0.17	$\pm$	0.22	0.21	$\pm$	0.15	0.513				
	$\Delta 12\text{wk}$	0.16	$\pm$	0.25	0.05	$\pm$	0.18	0.071	†			
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Insulin ( $\mu\text{U/mL}$ )												
	Basal	7.04	$\pm$	4.29	6.32	$\pm$	3.79	0.533	0.154	0.080	†	
	$\Delta 4\text{wk}$	-1.10	$\pm$	3.29	0.12	$\pm$	2.53	0.151				
	$\Delta 8\text{wk}$	-0.60	$\pm$	2.84	0.14	$\pm$	1.49	0.276				
	$\Delta 12\text{wk}$	-1.93	$\pm$	3.85	-0.05	$\pm$	3.61	0.084	†			
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HOMA-IR												
	Basal	1.68	$\pm$	1.21	1.50	$\pm$	0.92	0.553	0.097	†	0.073	†
	$\Delta 4\text{wk}$	-0.29	$\pm$	0.76	0.03	$\pm$	0.59	0.106				
	$\Delta 8\text{wk}$	-0.13	$\pm$	0.67	0.05	$\pm$	0.41	0.287				
	$\Delta 12\text{wk}$	-0.50	$\pm$	1.04	-0.01	$\pm$	0.89	0.083	†			
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T-Cho (mg/dL)												
	Basal	229.91	$\pm$	32.98	238.96	$\pm$	29.38	0.315	0.534	0.814	0.642	
	$\Delta 4\text{wk}$	6.35	$\pm$	23.61	4.73	$\pm$	21.05	0.801				
	$\Delta 8\text{wk}$	7.36	$\pm$	15.00	3.77	$\pm$	17.67	0.456				
	$\Delta 12\text{wk}$	1.13	$\pm$	20.53	3.62	$\pm$	16.50	0.641				
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HDL-Cho (mg/dL)												
	Basal	65.00	$\pm$	13.68	69.19	$\pm$	20.07	0.404	0.825	0.117	0.307	
	$\Delta 4\text{wk}$	-0.30	$\pm$	6.18	-0.38	$\pm$	6.13	0.964				
	$\Delta 8\text{wk}$	1.50	$\pm$	6.09	-1.62	$\pm$	5.95	0.080	†			
	$\Delta 12\text{wk}$	1.35	$\pm$	7.58	-1.23	$\pm$	6.83	0.216				
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LDL-Cho (mg/dL)												
	Basal	141.61	$\pm$	28.99	146.50	$\pm$	31.19	0.574	0.178	0.960	0.469	
	$\Delta 4\text{wk}$	8.74	$\pm$	19.41	7.46	$\pm$	17.38	0.809				
	$\Delta 8\text{wk}$	6.73	$\pm$	14.71	3.88	$\pm$	16.39	0.534				
	$\Delta 12\text{wk}$	1.39	$\pm$	17.91	4.85	$\pm$	14.45	0.459				
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TG (mg/dL)												
	Basal	107.09	$\pm$	45.68	118.35	$\pm$	56.44	0.450	0.190	0.871	0.484	
	$\Delta 4\text{wk}$	4.09	$\pm$	30.24	1.88	$\pm$	41.94	0.836				
	$\Delta 8\text{wk}$	11.27	$\pm$	40.64	7.92	$\pm$	41.19	0.779				
	$\Delta 12\text{wk}$	-3.65	$\pm$	26.17	4.31	$\pm$	40.33	0.423				
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Hs-CRP (mg/dL)	n=17			n=21								
	Basal	0.06	$\pm$	0.05	0.06	$\pm$	0.06	0.845	0.884	0.888	0.212	
	$\Delta 4\text{wk}$	0.01	$\pm$	0.05	0.01	$\pm$	0.05	0.955				
	$\Delta 8\text{wk}$	-0.01	$\pm$	0.03	0.01	$\pm$	0.05	0.082	†			
	$\Delta 12\text{wk}$	0.00	$\pm$	0.06	-0.01	$\pm$	0.05	0.449				

TNF- $\alpha$ (pg/mL)								
	Basal	3.03	$\pm$	1.28	2.73	$\pm$	0.64	0.300
	$\Delta$ 8wk	0.15	$\pm$	1.80	-0.07	$\pm$	0.64	0.555
	$\Delta$ 12wk	1.02	$\pm$	2.35	0.76	$\pm$	0.51	0.573
IL1- $\beta$ (pg/mL)								
	Basal	1.43	$\pm$	0.95	1.18	$\pm$	0.29	0.207
	$\Delta$ 8wk	0.13	$\pm$	1.84	-0.25	$\pm$	0.20	0.303
	$\Delta$ 12wk	0.30	$\pm$	2.12	-0.16	$\pm$	0.14	0.270
IL-6 (pg/mL)								
	Basal	1.94	$\pm$	2.77	5.56	$\pm$	22.06	0.439
	$\Delta$ 8wk	0.29	$\pm$	0.84	-3.09	$\pm$	16.61	0.345
	$\Delta$ 12wk	0.20	$\pm$	0.50	-2.71	$\pm$	14.89	0.355
Adiponectin ( $\mu$ g/mL)								
	Basal	8.70	$\pm$	2.90	9.15	$\pm$	3.61	0.633
	$\Delta$ 4wk	-0.04	$\pm$	0.68	-0.06	$\pm$	0.74	0.913
	$\Delta$ 8wk	0.19	$\pm$	0.91	0.18	$\pm$	1.07	0.985
	$\Delta$ 12wk	0.05	$\pm$	0.85	0.17	$\pm$	0.92	0.635
Leptin (ng/mL)								
	Basal	19.59	$\pm$	11.38	18.38	$\pm$	8.39	0.672
	$\Delta$ 4wk	1.31	$\pm$	4.69	2.01	$\pm$	4.02	0.580
	$\Delta$ 8wk	0.76	$\pm$	4.82	3.09	$\pm$	4.88	0.104
	$\Delta$ 12wk	0.10	$\pm$	6.92	1.93	$\pm$	5.51	0.309
Weight (kg)								
	Basal	66.37	$\pm$	7.48	65.55	$\pm$	11.91	0.777
	$\Delta$ 4wk	0.11	$\pm$	0.86	-0.12	$\pm$	0.66	0.282
	$\Delta$ 8wk	0.26	$\pm$	1.24	-0.35	$\pm$	0.61	0.044
	$\Delta$ 12wk	0.33	$\pm$	1.21	-0.27	$\pm$	0.97	0.058
Body fat percentage (%)								
	Basal	34.29	$\pm$	6.79	34.37	$\pm$	5.40	0.961
	$\Delta$ 4wk	-0.02	$\pm$	0.96	-0.27	$\pm$	0.90	0.350
	$\Delta$ 8wk	-0.04	$\pm$	1.00	-0.11	$\pm$	0.67	0.773
	$\Delta$ 12wk	-0.36	$\pm$	1.25	-0.35	$\pm$	0.97	0.984
BMI ( $\text{kg}/\text{m}^2$ )								
	Basal	25.60	$\pm$	2.02	25.47	$\pm$	2.03	0.817
	$\Delta$ 4wk	0.03	$\pm$	0.35	-0.06	$\pm$	0.26	0.296
	$\Delta$ 8wk	0.09	$\pm$	0.48	-0.14	$\pm$	0.25	0.053
	$\Delta$ 12wk	0.13	$\pm$	0.47	-0.10	$\pm$	0.39	0.071

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Values are presented as the mean  $\pm$  standard deviation.

\**P* values were determined by independent sample *t*-tests; †, *P*<0.1 #, *P*<0.05.

**Supplementary Table 3.** Effects of the SM DNA on the parameters assessed through the VAS questionnaire.

		Placebo (n = 22-23)	SM DNA (n = 26)	Group	p value*		
					Period effect	Two-way ANOVA	
						Treatment effect	Interaction
Lassitude (mm)							
	Basal	51.87 ± 26.05	61.23 ± 20.87	0.169	0.992	0.081 †	0.544
	4wk	61.70 ± 23.68	58.54 ± 21.72	0.629			
	8wk	58.14 ± 28.01	61.96 ± 22.26	0.601			
	12wk	61.57 ± 26.62	60.88 ± 23.48	0.925			
Mental stress (mm)							
	Basal	56.65 ± 24.48	58.58 ± 22.27	0.774	0.740	0.719	0.795
	4wk	63.39 ± 27.07	62.88 ± 22.76	0.944			
	8wk	60.55 ± 26.78	60.50 ± 23.12	0.995			
	12wk	61.91 ± 23.95	63.69 ± 24.88	0.800			
Skin stains (mm)							
	Basal	39.35 ± 22.50	50.62 ± 26.27	0.116	0.025 #	0.717	0.201
	4wk	43.30 ± 21.90	54.15 ± 24.72	0.113			
	8wk	43.09 ± 23.40	55.23 ± 25.37	0.094 †			
	12wk	52.04 ± 25.69	56.19 ± 26.56	0.582			
Wrinkles of the skin (mm)							
	Basal	45.61 ± 22.89	51.77 ± 25.90	0.385	0.979	0.492	0.483
	4wk	51.30 ± 22.54	58.65 ± 24.19	0.279			
	8wk	49.00 ± 21.84	61.54 ± 22.42	0.057 †			
	12wk	52.57 ± 23.68	59.92 ± 21.18	0.257			
Dull skin (mm)							
	Basal	43.57 ± 19.99	56.00 ± 21.63	0.043 #	0.616	0.589	0.918
	4wk	48.65 ± 19.23	57.54 ± 22.14	0.143			
	8wk	47.77 ± 21.79	58.50 ± 22.43	0.101			
	12wk	51.78 ± 23.01	59.85 ± 22.19	0.218			
Sticky skin (mm)							
	Basal	59.48 ± 26.70	69.81 ± 20.28	0.131	0.486	0.285	0.140
	4wk	68.61 ± 22.13	70.54 ± 17.80	0.737			
	8wk	60.36 ± 20.58	72.00 ± 16.07	0.033 #			
	12wk	66.43 ± 23.87	69.69 ± 18.93	0.597			
Dry skin (mm)							

Basal	42.13	$\pm$	25.46	56.65	$\pm$	20.59	0.032	#	0.929	0.554	0.333
4wk	47.22	$\pm$	24.07	55.73	$\pm$	23.33	0.215				
8wk	48.18	$\pm$	26.22	56.19	$\pm$	23.77	0.273				
12wk	45.43	$\pm$	22.08	59.77	$\pm$	21.76	0.027	#			
<b>Breakouts·Acne (mm)</b>											
Basal	61.83	$\pm$	33.51	71.69	$\pm$	26.25	0.262		0.057	†	0.906
4wk	72.35	$\pm$	25.37	80.65	$\pm$	17.53	0.196				
8wk	64.14	$\pm$	26.14	75.38	$\pm$	22.76	0.118				
12wk	66.17	$\pm$	27.10	78.35	$\pm$	19.08	0.080	†			
<b>Skin condition (mm)</b>											
Basal	43.35	$\pm$	23.97	61.31	$\pm$	19.53	0.006	#	0.674	0.004	#
4wk	53.22	$\pm$	20.33	60.27	$\pm$	17.32	0.196				
8wk	54.09	$\pm$	25.79	62.27	$\pm$	18.69	0.224				
12wk	51.52	$\pm$	19.64	65.00	$\pm$	17.24	0.014	#			

Values are presented as the mean  $\pm$  standard deviation.

\*P values were determined by independent sample t-tests; †, P<0.1 #, P<0.05.

**Supplementary Table 4.** Effect of SM DNA on secondary endpoints in males and females obtained after subgroup analysis based on the gender of the participants.

	male						female							
	Placebo (n = 7)			SM DNA (n = 7)			p value*	Placebo (n = 15- 16)			SM DNA (n = 19)			
Lassitude (mm)														
Basal	48.00	±	21.48	61.57	±	25.35	0.301	53.56	±	28.29	61.11	±	19.76	
4wk	64.57	±	26.20	59.57	±	20.39	0.697	60.44	±	23.28	58.16	±	22.72	
8wk	63.43	±	29.27	60.14	±	25.56	0.827	55.67	±	28.09	62.63	±	21.65	
12wk	57.71	±	26.47	64.43	±	31.43	0.673	63.25	±	27.38	59.58	±	20.72	
Mental stress (mm)														
Basal	70.57	±	21.09	61.57	±	25.05	0.481	50.56	±	23.90	57.47	±	21.80	
4wk	70.86	±	21.51	69.57	±	23.56	0.917	60.13	±	29.20	60.42	±	22.60	
8wk	66.43	±	25.24	61.43	±	26.69	0.725	57.80	±	27.88	60.16	±	22.47	
12wk	62.14	±	24.28	65.71	±	28.26	0.804	61.81	±	24.61	62.95	±	24.31	
Skin stains (mm)														
Basal	44.14	±	25.18	66.43	±	23.04	0.110	37.25	±	21.76	44.79	±	25.47	
4wk	44.14	±	25.76	69.43	±	22.82	0.076	42.94	±	20.91	48.53	±	23.47	
8wk	40.00	±	26.96	70.43	±	15.69	0.024	44.53	±	22.43	49.63	±	26.25	
12wk	49.43	±	25.04	74.29	±	21.30	0.069	53.19	±	26.70	49.53	±	25.58	
Wrinkles of the skin (mm)														
Basal	57.57	±	23.46	68.14	±	22.97	0.411	40.38	±	21.27	45.74	±	24.77	
4wk	57.14	±	16.03	69.43	±	22.49	0.264	48.75	±	24.89	54.68	±	24.14	
8wk	50.14	±	24.26	71.14	±	15.39	0.077	48.47	±	21.51	58.00	±	23.87	
12wk	57.00	±	19.25	74.43	±	21.56	0.137	50.63	±	25.71	54.58	±	18.86	
Dull skin (mm)														
Basal	53.00	±	20.68	67.71	±	23.49	0.237	39.44	±	18.84	51.68	±	19.82	
4wk	57.29	±	16.29	69.71	±	22.54	0.260	44.88	±	19.66	53.05	±	20.79	
8wk	42.29	±	25.28	70.00	±	14.41	0.027	50.33	±	20.41	54.26	±	23.65	
12wk	49.14	±	22.77	74.86	±	21.36	0.050	52.94	±	23.76	54.32	±	20.29	
Sticky skin (mm)														
Basal	43.86	±	22.15	72.71	±	20.60	0.027	#	66.31	±	26.19	68.74	±	20.63
4wk	52.43	±	22.96	72.57	±	21.02	0.113	75.69	±	18.22	69.79	±	17.04	
8wk	51.57	±	18.29	71.71	±	13.71	0.038	64.47	±	20.86	72.11	±	17.21	
12wk	49.86	±	27.45	64.14	±	23.84	0.319	73.69	±	18.70	71.74	±	17.08	
Dry skin (mm)														
Basal	42.00	±	25.41	48.29	±	24.96	0.649	42.19	±	26.32	59.74	±	18.54	
4wk	47.71	±	27.66	69.14	±	18.57	0.115	47.00	±	23.32	50.79	±	23.35	
8wk	42.43	±	25.93	60.43	±	27.37	0.231	50.87	±	26.81	54.63	±	22.92	

12wk	42.29	±	24.98	66.71	±	24.86	0.092	†	46.81	±	21.42	57.21	±	20.64	0.154
<b>Breakouts·Acne (mm)</b>															
Basal	52.14	±	28.01	53.57	±	27.49	0.925		66.06	±	35.64	78.37	±	23.02	0.246
4wk	57.14	±	24.50	70.29	±	21.81	0.310		79.00	±	23.42	84.47	±	14.52	0.424
8wk	50.14	±	26.58	65.57	±	24.92	0.284		70.67	±	24.05	79.00	±	21.48	0.295
12wk	54.86	±	27.81	70.57	±	23.34	0.275		71.13	±	26.11	81.21	±	17.08	0.197
<b>Skin condition (mm)</b>															
Basal	44.14	±	28.23	62.86	±	20.76	0.183		43.00	±	22.87	60.74	±	19.62	0.019 #
4wk	47.29	±	23.19	61.86	±	16.54	0.201		55.81	±	19.17	59.68	±	18.01	0.543
8wk	46.86	±	28.50	66.71	±	18.70	0.149		57.47	±	24.72	60.63	±	18.92	0.675
12wk	54.43	±	24.60	70.71	±	20.45	0.203		50.25	±	17.84	62.89	±	16.00	0.034 #

Values are presented as the mean ± standard deviation.

\*P values were determined by independent sample t-tests; †, P<0.1 #, P<0.05.