

**Supplement Table 1.** Serum concentration of leptin, oxidative stress, inflammatory marker, blood pressure, and AIP of the study participants before and after 8 weeks of intervention

Variables	Crocetin group (n=23)	Placebo group (n=25)	P-value <sup>c</sup>	P-value <sup>d</sup>	P-value <sup>e</sup>
<b>hs-CRP (ng/mL)</b>					
Baseline	487.72 ± 127.23	736.60 ± 513.97	0.006	0.695	0.695
End of trial	368.09 ± 140.29	579.68 ± 257.46	0.002		
P-value <sup>a</sup>	0.0001	0.021			
Mean difference	-119.62 (83.20)	-156.91 (471.95)			
P-value <sup>b</sup>	0.0001	0.109			
<b>SOD (U/ml)</b>					
Baseline	257.52 ± 38.18	275.89 ± 35.96	0.049	0.520	0.520
End of trial	299.24 ± 29.49	268.56 ± 22.04	0.0001		
P-value <sup>a</sup>	0.001	0.716			
Mean difference	41.72 (45.72)	-7.33 (49.67)			
P-value <sup>b</sup>	0.0001	0.468			
<b>MDA (nmol/ml)</b>					
Baseline	9.74 ± 1.68	9.25 ± 1.10	0.54	0.178	0.779
End of trial	8.75 ± 1.22	9.09 ± 0.73	0.043		
P-value <sup>a</sup>	0.002	0.909			
Mean difference	-0.99 (1.83)	-0.16 (1.12)			
P-value <sup>b</sup>	0.017	0.485			
<b>CAT (Unit/mL)</b>					
Baseline	2.04 ± 0.61	2.24 ± 0.56	0.076	0.008	0.886
End of trial	1.69 ± 0.35	2.58 ± 0.65	0.0001		
P-value <sup>a</sup>	0.094	0.074			
Mean difference	-0.34 (0.81)	0.33 (0.82)			
P-value <sup>b</sup>	0.052	0.055			
<b>Leptin (ng/mL)</b>					
Baseline	2.46 ± 0.96	0.73 ± 0.59	0.0001	0.854	0.854
End of trial	0.59 ± 0.66	0.64 ± 0.52	0.38		
P-value <sup>a</sup>	0.0001	0.196			
Mean difference	-1.86 (1.185)	-0.09 (0.82)			
P-value <sup>b</sup>	0.0001	0.591			
<b>AIP</b>					
Baseline	0.78 ± 0.29	0.55 ± 0.12	0.001	0.409	0.058
End of trial	0.64 ± 0.26	0.59 ± 0.18	0.475		
P-value <sup>a</sup>	0.045	0.367			
Mean difference	-0.13 (0.25)	0.04 (0.20)			
P-value <sup>b</sup>	0.017	0.280			
<b>SBP</b>					
Baseline	13.25 ± 0.88	14.18 ± 1.54	0.013	0.096	0.096
End of trial	13.00 ± 0.86	14.31 ± 1.67	0.001		
P-value <sup>a</sup>	0.0001	0.086			
Mean difference	-0.25 (0.27)	0.13 (0.37)			
P-value <sup>b</sup>	0.0001	0.086			
<b>DBP</b>					

Baseline	8.89 ± 0.97	9.66 ± 1.13	0.013		
End of trial	8.60 ± 0.83	9.64 ± 1.06	0.0001	0.218	
P-value <sup>a</sup>	0.004	0.943			
Mean difference	-0.24 (0.35)	-0.01 (0.29)			0.218
P-value <sup>b</sup>	0.003	0.789			

SOD superoxide dismutase, CAT catalase, MDA malondialdehyde, hs-CRP high-sensitivity C-reactive protein, AIP the Atherogenic Index of Plasma, SBP systolic blood pressure, DBP diastolic blood pressure

\* Mean (SD)

P-value<sup>a</sup> P values denote the significance of within-group changes with (P< 0.05), paired t-test (for normal distribution data) and Wilcoxon test (for non-normal distribution data)

P-value <sup>b</sup> P values denote the significance of within-group mean difference, one sample test was used

P-value <sup>c</sup> P values denote the significance of between-group differences with (P< 0.05, Mann–Whitney U test (for all variables)

P-value <sup>d</sup> P values denote the significance of between-group differences with (P< 0.05), We used analysis of covariance (ANCOVA) to control confounders and baseline values such as age, gender, education, duration of disease, smoking, physical activity, history of disease, blood pressure, diabetes mellitus, dietary intake of energy, carbohydrate, protein, fat, BMI, W/H ratio and leptin, hs CRP, SOD at baseline)

P-value <sup>e</sup> P values denote the significance of the between-group mean difference with (P< 0.05), We used analysis of covariance (ANCOVA) to control confounders and baseline values such as age, gender, education, duration of disease, smoking, physical activity, history of disease, blood pressure, diabetes mellitus, dietary intake of energy, carbohydrate, protein, fat, BMI, W/H ratio and leptin, hs CRP, SOD at baseline)

**SupplementTable 2.** Basic anthropometric indices of patients with coronary artery disease

Variables	Crocetin group (n=23)	Placebo group (n=25)	P-value <sup>c</sup>	P-value <sup>d</sup>	P-value <sup>e</sup>
<b>Weight (kg)</b>					
Baseline	81.17 ± 10.42	77.70 ± 9.46	0.341	0.195	0.014
End of trial	80.29 ± 10.32	77.68 ± 9.22	0.522	0.356	
P-value <sup>a</sup>	0.0001	0.5			
Mean difference	-0.87±0.68	-0.02±1.002			
P-value <sup>b</sup>	0.0001	0.921			
<b>WC (cm)</b>					
Baseline	92.60 ± 7.98	92.28 ± 8.71	0.853	0.480	0.08
End of trial	91.33 ± 8.30	91.78 ± 8.48	0.951	0.593	
P-value <sup>a</sup>	0.0001	0.016			
Mean difference	-1.269±0.813	-0.5±1.02			
P-value <sup>b</sup>	0.0001	0.022			
<b>HC (cm)</b>					
Baseline	104.53 ± 8.60	101.12 ± 6.43	0.132	0.123	0.107
End of trial	104 ± 8.77	101.04 ± 6.15	0.179	0.172	
P-value <sup>a</sup>	0.001	0.723			
Mean difference	-0.526±0.662	-0.08±1.115			
P-value <sup>b</sup>	0.001	0.723			
<b>BMI (kg/m<sup>2</sup>)</b>					
Baseline	28.07 ± 1.87	27.14 ± 2.70	0.13	0.228	0.017
End of trial	27.76 ± 1.81	27.15 ± 2.76	0.18	0.441	
P-value <sup>a</sup>	0.0001	0.435			
Mean difference	-0.306±0.255	0.008±0.338			
P-value <sup>b</sup>	0.0001	0.903			
<b>WHR</b>					
Baseline	0.88 ± 0.05	0.91 ± 0.05	0.104	0.403	0.861
End of trial	0.87 ± 0.05	0.90 ± 0.04	0.05	0.360	
P-value <sup>a</sup>	0.0001	0.058			
Mean difference	-0.008±0.006	-0.004±0.011			
P-value <sup>b</sup>	0.0001	0.058			

BMI body mass index, HC hip circumference, WC waist circumference, WHR waist/hip ratio

\* Mean (SD)

P-value<sup>a</sup> indicate the significance of within-group changes, with P < 0.05. Analyses were conducted using the paired t-test for normally distributed data and the Wilcoxon test for non-normally distributed data.

P-value <sup>b</sup> indicates the significance of within-group mean difference, one sample test was used.

P-value <sup>c</sup> indicates the significance of between-group differences with P< 0.05, Independent Samples t-test for normal distribution data, and Mann–Whitney U test for non-normal distribution data.

P-value <sup>d</sup> indicates the significance of between-group differences, with P < 0.05. We used analysis of covariance (ANCOVA) to control confounders and baseline values such as age, gender, education, physical activity, smoking status, blood pressure, and dietary intake (energy, carbohydrates, protein, fat), as well as baseline value of leptin, high-sensitivity C-reactive protein (hs-CRP), and superoxide dismutase (SOD).

P-value <sup>e</sup> indicates the significance of between-group mean differences, with P < 0.05. We used analysis of covariance (ANCOVA) to control confounders and baseline values such as age, gender, education, physical

activity, smoking status, blood pressure, and dietary intake (energy, carbohydrates, protein, fat), as well as baseline value of leptin, high-sensitivity C-reactive protein (hs-CRP), and superoxide dismutase (SOD).

**Supplement Table 3.** Energy and macronutrient intake of patients with coronary artery disease

Variables	Crocetin group (n=23)	Placebo group (n=25)	P-value <sup>c</sup>	P-value <sup>d</sup>	P-value <sup>e</sup>
<b>Energy</b> (kcal/day)					
Baseline	2623.86 ± 265.32	2478.07 ± 303.10	0.067	0.027	0.012
End of trial	2511.55 ± 295.32	2465.07 ± 288.64	0.812	0.332	
P-value <sup>a</sup>	0.0001	0.231			
Mean difference	-112.303±69.829	-13.004±68.941			
P-value <sup>b</sup>	0.0001	0.231			
<b>Protein</b> (g/d)					
Baseline	70.24 ± 11.70	68.10 ± 9.41	0.541	0.315	0.002
End of trial	65.85 ± 11.81	67.78 ± 9.32	0.375	0.886	
P-value <sup>a</sup>	0.0001	0.242			
Mean difference	-4.393±3.436	-0.322±1.758			
P-value <sup>b</sup>	0.0001	0.242			
<b>Carbohydrate</b> (g/d)					
Baseline	385.10 ± 42.96	365.47 ± 44.65	0.177	0.047	0.268
End of trial	367.23 ± 46.44	359.99 ± 52.09	0.984	0.415	
P-value <sup>a</sup>	0.0001	0.183			
Mean difference	-17.869±10.699	-5.474±20.481			
P-value <sup>b</sup>	0.0001	0.183			
<b>Fat</b> (g/d)					
Baseline	89.16 ± 6.76	82.64 ± 11.29	0.014	0.005	0.336
End of trial	86.57 ± 8.68	82.00 ± 10.89	0.117	0.08	
P-value <sup>a</sup>	0.002	0.225			
Mean difference	-2.583±3.424	-0.638±2.563			
P-value <sup>b</sup>	0.002	0.225			

\* Mean (SD)

P-value<sup>a</sup> indicates the significance of within-group changes, with P < 0.05. Analyses were conducted using the paired t-test for normally distributed data and the Wilcoxon test for non-normally distributed data.

P-value <sup>b</sup> indicates the significance of within-group mean difference, one sample test was used.

P-value <sup>c</sup> indicates the significance of between-group differences with P< 0.05, Independent Samples t-test for normal distribution data, and or Mann–Whitney U test for non-normal distribution data.

P-value <sup>d</sup> indicates the significance of between-group differences, with P < 0.05. We used analysis of covariance (ANCOVA) to control confounders and baseline values such as age, gender, education, physical activity, smoking status, blood pressure, disease history, disease duration, and WHR, as well as baseline value of leptin, high-sensitivity C-reactive protein (hs-CRP), and superoxide dismutase (SOD).

P-value <sup>e</sup> indicates the significance of between-group mean differences, with P < 0.05. We used analysis of covariance (ANCOVA) to control confounders and baseline values such as age, gender, education, physical activity, smoking status, blood pressure, disease history, disease duration, and WHR, as well as baseline value of leptin, high-sensitivity C-reactive protein (hs-CRP), and superoxide dismutase (SOD).

**Table 4.** Serum concentration of leptin, oxidative stress, inflammatory marker, blood pressure, and AIP of the study participants before and after 8 weeks of intervention

Variables	Crocetin group (n=23)	Placebo group (n=25)	P-value <sup>c</sup>	P-value <sup>d</sup>	P-value <sup>e</sup>
<b>hs-CRP (ng/mL)</b>					
Baseline	487.72 ± 127.23	736.60 ± 513.97	0.006		
End of trial	368.09 ± 140.29	579.68 ± 257.46	0.002	0.695	
P-value <sup>a</sup>	0.0001	0.021			
Mean difference	-119.62 (83.20)	-156.91 (471.95)			0.695
P-value <sup>b</sup>	0.0001	0.109			
<b>SOD (U/ml)</b>					
Baseline	257.52 ± 38.18	275.89 ± 35.96	0.049		
End of trial	299.24 ± 29.49	268.56 ± 22.04	0.0001	0.520	
P-value <sup>a</sup>	0.001	0.716			
Mean difference	41.72 (45.72)	-7.33 (49.67)			0.520
P-value <sup>b</sup>	0.0001	0.468			
<b>MDA (nmol/ml)</b>					
Baseline	9.74 ± 1.68	9.25 ± 1.10	0.54		
End of trial	8.75 ± 1.22	9.09 ± 0.73	0.043	0.178	
P-value <sup>a</sup>	0.002	0.909			
Mean difference	-0.99 (1.83)	-0.16 (1.12)			0.779
P-value <sup>b</sup>	0.017	0.485			
<b>CAT (Unit/mL)</b>					
Baseline	2.04 ± 0.61	2.24 ± 0.56	0.076		
End of trial	1.69 ± 0.35	2.58 ± 0.65	0.0001	0.008	
P-value <sup>a</sup>	0.094	0.074			
Mean difference	-0.34 (0.81)	0.33 (0.82)			0.886
P-value <sup>b</sup>	0.052	0.055			
<b>Leptin (ng/mL)</b>					
Baseline	2.46 ± 0.96	0.73 ± 0.59	0.0001		
End of trial	0.59 ± 0.66	0.64 ± 0.52	0.38	0.854	
P-value <sup>a</sup>	0.0001	0.196			
Mean difference	-1.86 (1.185)	-0.09 (0.82)			0.854
P-value <sup>b</sup>	0.0001	0.591			
<b>AIP</b>					
Baseline	0.78 ± 0.29	0.55 ± 0.12	0.001		
End of trial	0.64 ± 0.26	0.59 ± 0.18	0.475	0.409	
P-value <sup>a</sup>	0.045	0.367			
Mean difference	-0.13 (0.25)	0.04 (0.20)			0.058
P-value <sup>b</sup>	0.017	0.280			
<b>SBP</b>					
Baseline	13.25 ± 0.88	14.18 ± 1.54	0.013		
End of trial	13.00 ± 0.86	14.31 ± 1.67	0.001	0.096	
P-value <sup>a</sup>	0.0001	0.086			
Mean difference	-0.25 (0.27)	0.13 (0.37)			0.096
P-value <sup>b</sup>	0.0001	0.086			
<b>DBP</b>					

Baseline	8.89 ± 0.97	9.66 ± 1.13	0.013		
End of trial	8.60 ± 0.83	9.64 ± 1.06	0.0001	0.218	
P-value <sup>a</sup>	0.004	0.943			
Mean difference	-0.24 (0.35)	-0.01 (0.29)			0.218
P-value <sup>b</sup>	0.003	0.789			

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P-value <sup>d</sup> P values denote the significance of between-group differences with (P< 0.05), We used analysis of covariance (ANCOVA) to control confounders and baseline values such as age, gender, education, duration of disease, smoking, physical activity, history of disease, blood pressure, diabetes mellitus, dietary intake of energy, carbohydrate, protein, fat, BMI, W/H ratio and leptin, hs CRP, SOD at baseline)

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