Supplementary Material

Supplementary Table 1 Included study quality assessment judgment and support for the judgment

	Tre dome on t	Support for judgment			
Entry	Judgment (Yes/No)	Location in the article or	Comment of		
	(1es/ No)	"Quote"	author		
Soleimani <i>et al</i> ^[29]					
Eligibility criteria	Yes	"We included patients aged 18	Eligibility criteria		
specified	165	to 80 years old"	were specified.		
Random		Randomization section in the	Subjects were		
allocation	Yes	article.	randomly		
anocation		urticie.	allocated.		
Concealed	Yes	Randomization section in the	Concealment was		
allocation	163	article.	maintained.		
Groups similar at			Groups were		
baseline	Yes	Table 1 in the article.	similar at		
buseine			baseline.		
		" was a prospective	Subjects were		
Subject blinding	Yes	randomized, double-blind,	blinded and the		
Subject billianing		placebo controlled	procedures were		
		clinical trial."	informed.		
		" was a prospective	Therapist were		
Therapist	Yes	randomized, double-blind,	blinded and the		
blinding	165	placebo controlled	procedures were		
		clinical trial."	informed.		
			No details of		
Assessor blinding	No	Not applicable.	assessor blinding		
			are provided.		
Less than 15%	Yes	Figure 1 in the article.	Data from more		
dropouts	100	116 are 1 in the article.	than 85% of the		

			subjects initially allocated to
			groups is
			available.
Intention-to-treat analysis	Yes	"The analyses were carried out based on the intention-to-treat principle."	Intention-to-treat analysis method was used.
Between-group statistical comparison	Yes	Statistical methods section in the article.	Between-group statistical analysis were performed, and results are reported.
Point measures and variability	Yes	Table 2 and table 3 in the article.	Data of point measure and measure of variability for at least one key outcome is reported.
Soleimani <i>et al</i> ^[30]		T'1 D' 1 0 1	
Eligibility criteria specified	Yes	Trial Design and Study Participants section in the article.	Eligibility criteria were specified.
Random allocation	Yes	Randomization section in the article.	Subjects were randomly allocated.
Concealed allocation	Yes	Randomization section in the article.	Concealment was maintained.
Groups similar at baseline	Yes	Table 1 in the article.	Groups were similar at baseline.

Subject blinding Therapist blinding	Yes	"It was a randomized, double-blinded, placebo-controlled clinical trial." "It was a randomized, double-blinded, placebo-controlled clinical trial."	Subjects were blinded and the procedures were informed. Therapist were blinded and the procedures were informed.
Assessor blinding	No	Not applicable.	No details of assessor blinding are provided.
Less than 15% dropouts	Yes	Figure 1 in the article.	Data from more than 85% of the subjects initially allocated to groups is available.
Intention-to-treat analysis	Yes	Not applicable.	As no drop-out was observed, the intention-to-treat analysis method was used as default method.
Between-group statistical comparison	Yes	Statistical Methods section in the article.	Between-group statistical analysis were performed, and results are reported.
Point measures and variability	Yes	Table 2 in the article.	Data of point measure and measure of

variability for at least one key outcome is reported.

Tajabadi-Ebrahimi et al^[31]

Eligibility criteria specified	Yes	"Patients with T2DM, overweight (BMI \geq 25) aged"	Eligibility criteria were specified.
Random	Yes	"Computer-generated random numbers were used for	•
allocation	165	random assignment."	allocated.
Concealed allocation	Yes	"Randomization and allocation were concealed from the researcher"	Concealment was maintained.
Croums similar at			Groups were
Groups similar at baseline	Yes	Table 1 in the article.	similar at
baseinie			baseline.
		"Placebos (starch) were similar	Subjects were
Subject blinding	Yes	in color, shape, size and	blinded and the
Subject billianing	165	package to the synbiotic	procedures were
		capsules"	informed.
		" study was a randomized	Therapist were
Therapist	Yes	double-blind placebo-	blinded and the
blinding		controlled trial"	procedures were
			informed.
A 11: 1:	N.T.	NI	No details of
Assessor blinding	No	Not applicable.	assessor blinding
			are provided.
Less than 15%	Voc	Figure 1 in the outists	Data from more
dropouts	Yes	Figure 1 in the article.	than 85% of the
			subjects initially

			allocated to
			groups is
			available.
Intention-to-treat		"The intention-to-treat (ITT)	Intention-to-treat
analysis	Yes	analysis of the primary study	analysis method
ariarysis		end-point was done"	was used.
			Between-group
Between-group		Chatistical mathods socian in	statistical analysis
statistical	Yes	Statistical methods section in	were performed,
comparison		the article.	and results are
			reported.
			Data of point
			measure and
D		TI 1 0 1 11 4 1 1	measure of
Point measures	Yes	Table 3 and table 4 in the	variability for at
and variability		article.	least one key
			outcome is
			reported.
Raygan et al ^[32]			•
Eligibility criteria		"Inclusion criteria were as	Eligibility criteria
specified	Yes	follows: patients with"	were specified.
•		"Randomization was	Subjects were
Random	Yes	conducted using computer-	randomly
allocation		generated random numbers."	allocated.
		"Randomization and allocation	
Concealed	Yes	were concealed from the	Concealment was
allocation		investigators"	maintained.
		8	Groups were
Groups similar at	Yes	Table 1 in the article.	similar at
baseline		The Time with the control of the con	baseline.
			Edocinic.

Subject blinding	Yes	"Color, shape, size, and package of placebos and probiotics capsules were identical"	blinded and the procedures were informed.
Therapist blinding	Yes	"This study was a randomized, double-blind, placebocontrolled trial"	Therapist were blinded and the procedures were informed. No details of
Assessor blinding	No	Not applicable.	assessor blinding are provided. Data from more
Less than 15% dropouts	Yes	Figure 1 in the article.	than 85% of the subjects initially allocated to groups is available.
Intention-to-treat analysis	Yes	"The analyses were repeated using intention-to-treat (ITT) protocol."	analysis method was used.
Between-group statistical comparison	Yes	Statistical methods and sample size section in the article.	Between-group statistical analysis were performed, and results are reported.
Point measures and variability	Yes	Table 3 in the article.	Data of point measure and measure of variability for at least one key

	outcome	is
	reported.	
9 se	Eligibility of were specifi	
e	Subjects randomly	were
	allocated.	
e	Concealmen	nt was
	maintained	
	Groups	were
	similar	at
	baseline.	
e	maintained	•

Subjects

were

Farrokhian $et~al^{[33]}$ Eligibility criteria Yes kg/m2) and obese specified reported. Farrokhian $et~al^{[33]}$ Eligibility criteria were specified

individuals ..."

Random
Yes

Randomization section in the randomly allocated.

Concealed

Randomization section in the Concealment was

Concealed Yes allocation article. Randomization section in the Concealment was allocation article.

Groups similar at
Yes Table 1 in the article. similar at baseline
baseline.

Subject blinding Yes "Placebos (starch) were similar blinded and the in color, shape, size, and ..." procedures were

informed. Therapist were

Therapist
Yes randomized, double-blind, blinding
placebo-controlled trial ..."

The current study was a blinded and the procedures were informed.

Assessor blinding No Not applicable. No details of assessor blinding are provided.

Data from more than 85% of the

Less than 15% Yes Figure 1 in the article.

dropouts allocated to

ropouts allocated to groups is available.

Intention-to-treat		"The intention-to-treat (ITT)	Intention-to-treat
	Yes	analysis of the primary study	analysis method
analysis		end-point was conducted"	was used.
			Between-group
Between-group		Statistical methods section in	statistical analysis
statistical	Yes	the article.	were performed,
comparison		the article.	and results are
			reported.
			Data of point
			measure and
Point measures		Table 3 and table 4 in the	measure of
	Yes	article.	variability for at
and variability		article.	least one key
			outcome is
			reported.
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The quality of included studies was evaluated using PEDro scale. PEDro: physiotherapy evidence database.

Supplementary Table 2 Result of sensitivity analysis

Study excluded	I ²	Mean difference	95% CI	p-value
	value	estimate		
Glucose level				
Overall	0%	-23.86	-34.92 to -12.80	< 0.001
Raygan et al ^[32]	0%	-24.52	-38.18 to -10.86	< 0.001
Soleimani <i>et al</i> ^[29]	0%	-21.72	-35.05 to -8.40	0.001
Soleimani <i>et al</i> ^[30]	0%	-27.14	-39.91 to -14.37	< 0.001
Tajabadi-Ebrahimi $et\ al^{[31]}$	0%	-22.29	-33.92 to -10.66	< 0.001
Insulin level				
Overall	64%	-5.02	-7.67 to -2.37	< 0.001
Raygan et al ^[32]	51%	-5.99	-8.67 to -3.32	< 0.001
Soleimani <i>et al</i> ^[29]	18%	-3.87	-5.84 to -1.90	< 0.001
Soleimani <i>et al</i> ^[30]	75%	-4.84	-8.46 to -1.21	0.009
Tajabadi-Ebrahimi <i>et al</i> ^[31]	74%	-5.43	-9.19 to -1.67	0.005
HOMA-IR score				
Overall	78%	-1.82	-3.29 to -0.35	0.015
Raygan et al ^[32]	81%	-2.30	-4.19 to -0.41	0.017
Soleimani <i>et al</i> ^[29]	24%	-1.04	-1.91 to -0.18	0.017
Soleimani <i>et al</i> ^[30]	85%	-1.70	-3.57 to 0.16	0.074
Tajabadi-Ebrahimi <i>et al</i> ^[31]	82%	-2.20	-4.28 to -0.13	0.037
QUICKI score				
Overall	85%	0.02	0.01 to 0.04	0.002
Raygan et al ^[32]	88%	0.03	0.01 to 0.04	0.006
Soleimani <i>et al</i> ^[29]	3%	0.01	0.01 to 0.02	< 0.001
Soleimani <i>et al</i> ^[30]	90%	0.02	0.00 to 0.04	0.024
Tajabadi-Ebrahimi <i>et al</i> ^[31]	88%	0.03	0.01 to 0.05	0.012
Total antioxidant capacity	level			
Overall	0%	92.55	40.87 to 144.22	< 0.001
Farrokhian <i>et al</i> ^[33]	0%	115.16	54.68 to 175.64	< 0.001

Raygan et al ^[32]	15%	90.61	33.26 to 147.96	0.002
Soleimani <i>et al</i> ^[29]	13%	87.11	24.09 to 150.13	0.007
Soleimani <i>et al</i> ^[30]	0%	78.19	19.90 to 136.48	0.009
Glutathione level				
Overall	53%	40.55	-3.32 to 84.42	0.070
Farrokhian <i>et al</i> ^[33]	19%	59.79	17.60 to 101.98	0.005
Raygan <i>et al</i> ^[32]	68%	40.48	-20.89 to 101.84	0.196
Soleimani <i>et al</i> ^[29]	68%	44.93	-13.21 to 103.06	0.130
Soleimani <i>et al</i> ^[30]	0%	18.17	-15.25 to 51.58	0.287
Malondialdehyde level				
Overall	27%	-0.48	-0.70 to -0.25	< 0.001
Farrokhian <i>et al</i> ^[33]	51%	-0.46	-0.75 to -0.18	0.001
Raygan et al ^[32]	42%	-0.52	-0.78 to -0.27	< 0.001
Soleimani <i>et al</i> ^[29]	0%	-0.42	-0.65 to -0.18	< 0.001
Soleimani <i>et al</i> ^[30]	48%	-0.52	-0.80 to -0.24	< 0.001
high sensitivity C-reactive	protein	level		
Overall	59%	-2.24	-3.48 to -1.00	< 0.001
Farrokhian <i>et al</i> ^[33]	69%	-2.05	-3.54 to -0.55	0.007
Raygan et al ^[32]	0%	-2.91	-3.87 to -1.95	< 0.001
Soleimani <i>et al</i> ^[29]	73%	-2.29	-3.92 to -0.65	0.006
Soleimani <i>et al</i> ^[30]	43%	-1.81	-3.12 to -0.49	0.007
Nitric oxide level				
Overall	56%	6.45	2.09 to 10.81	0.004
Farrokhian <i>et al</i> ^[33]	0%	5.24	2.15 to 8.34	< 0.001
Raygan et al ^[32]	69%	5.62	-1.93 to 13.17	0.145
Soleimani et al ^[29]	62%	7.29	2.67 to 11.90	0.002
Soleimani <i>et al</i> ^[30]	58%	7.56	2.80 to 12.31	0.002
Total cholesterol level				
Overall	0%	-3.43	-10.46 to 3.61	0.340
Raygan et al ^[32]	0%	-1.63	-9.96 to 6.70	0.701
Soleimani <i>et al</i> ^[29]	0%	-5.60	-14.25 to 3.06	0.205

Soleimani <i>et al</i> ^[30]	0%	-2.89	-10.50 to 4.71	0.456
Tajabadi-Ebrahimi <i>et al</i> ^[31]	0%	-3.82	-11.84 to 4.19	0.350
Triglycerides level				
Overall	0%	-4.26	-15.26 to 6.74	0.448
Raygan <i>et al</i> ^[32]	0%	-4.14	-16.03 to 7.75	0.495
Soleimani <i>et al</i> ^[29]	0%	-9.92	-25.15 to 5.32	0.202
Soleimani <i>et al</i> ^[30]	0%	-2.21	-14.54 to 10.11	0.725
Tajabadi-Ebrahimi <i>et al</i> ^[31]	0%	-2.80	-14.90 to 9.31	0.651
Low-density lipoprotein le	evel			
Overall	0%	-4.62	-10.66 to 1.42	0.134
Raygan et al ^[32]	0%	-2.58	-10.01 to 4.85	0.496
Soleimani <i>et al</i> ^[29]	0%	-5.90	-12.95 to 1.16	0.101
Soleimani <i>et al</i> ^[30]	0%	-4.84	-11.30 to 1.62	0.142
Tajabadi-Ebrahimi <i>et al</i> ^[31]	0%	-4.93	-12.00 to 2.15	0.172
Very low-density lipoprote	ein leve	1		
Overall	0%	-0.83	-3.03 to 1.37	0.461
Raygan et al ^[32]	0%	-0.80	-3.18 to 1.58	0.510
Soleimani <i>et al</i> ^[29]	0%	-1.95	-4.99 to 1.10	0.210
Soleimani <i>et al</i> ^[30]	0%	-0.43	-2.90 to 2.05	0.736
Tajabadi-Ebrahimi <i>et al</i> ^[31]	0%	-0.54	-2.96 to 1.89	0.664
High-density lipoprotein l	evel			
Overall	28%	1.83	0.29 to 3.36	0.020
Raygan <i>et al</i> [32]	52%	1.83	0.06 to 3.60	0.042
Soleimani <i>et al</i> ^[29]	50%	2.04	0.16 to 3.92	0.034
Soleimani <i>et al</i> ^[30]	0%	2.35	0.67 to 4.02	0.006
Tajabadi-Ebrahimi <i>et al</i> ^[31]	0%	1.02	-0.78 to 2.82	0.265
Total cholesterol : High-de	nsity lip	poprotein ratio		
Overall	0%	-0.25	-0.45 to -0.04	0.020
Raygan et al ^[32]	0%	-0.29	-0.57 to 0.00	0.050
Soleimani <i>et al</i> ^[30]	0%	-0.25	-0.47 to -0.04	0.020
Tajabadi-Ebrahimi <i>et al</i> ^[31]	0%	-0.19	-0.47 to 0.10	0.193

HOMA-IR: Homeostatic model assessment for insulin resistance; HOMA-B: Homeostasis model assessment of β -cell function; QUICKI: Quantitative insulinsensitivity check index.

Supplementary Table 3 Result of sub-group analysis

Triple pro	biotics alone	Triple pro	biotics with	P value*	
therapy		prebiotics t	prebiotics therapy		
MD	I ² value	MD	I ² value	-	
-25.45	0%	-20.84	25%	0.70	
-5.34	87%	-4.73	0%	0.86	
-2.18	91%	-1.39	46%	0.67	
0.03	94%	0.02	30%	0.48	
102.68	0%	81.75	55%	0.69	
37.35	0%	47.18	84%	0.86	
-0.54	74%	-0.45	0%	0.72	
-1.28	15%	-3.13	0%	0.02	
5.79	4%	7.22	77%	0.78	
-3.18	0%	-3.84	0%	0.93	
0.31	0%	-11.79	0%	0.30	
-5.30	0%	-3.58	0%	0.78	
0.08	0%	-2.31	0%	0.30	
1.57	0%	2.17	75%	0.70	
	therapy MD -25.45 -5.34 -2.18 0.03 102.68 37.35 -0.54 -1.28 5.79 -3.18 0.31 -5.30 0.08	therapy MD I² value -25.45 0% -5.34 87% -2.18 91% 0.03 94% 102.68 0% 37.35 0% -0.54 74% -1.28 15% 5.79 4% -3.18 0% 0.31 0% -5.30 0% 0.08 0%	therapy prebiotics for the product of the	MD I² value MD I² value -25.45 0% -20.84 25% -5.34 87% -4.73 0% -2.18 91% -1.39 46% 0.03 94% 0.02 30% 102.68 0% 81.75 55% 37.35 0% 47.18 84% -0.54 74% -0.45 0% -1.28 15% -3.13 0% 5.79 4% 7.22 77% -3.18 0% -3.84 0% 0.31 0% -11.79 0% -5.30 0% -3.58 0% 0.08 0% -2.31 0%	

^{*}Significance between sub-groups. MD: Mean difference; HOMA-IR: Homeostatic model assessment for insulin resistance; QUICKI: Quantitative insulin-sensitivity check index; TAC: Total antioxidant capacity; GSH: Glutathione; MDA: Malondialdehyde; hs-CRP: High sensitivity C-reactive protein; NO: Nitric oxide; TC:

Total cholesterol; TG: Triglycerides; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein; HDL: High density lipoprotein.