

**Table 1. Clinical trials of Berberine in treating cardiovascular and metabolic diseases**

<b>Authors</b>	<b>Testing scheme</b>	<b>Sample size (treatment/control)</b>	<b>Diagnosis</b>	<b>Duration (wks)</b>	<b>Intervention</b>		<b>Outcomes</b>	<b>Main results</b>
Chang et al. [351]	R, PaC, OP, MC	80 (41/39)	NAFLD	16	1.5 g/d+LSI	LSI	BW, BMI, WC, FPG, P-LPG, P-LSI, HOMA-IR, TC, TG, LDL-C, HDL-C, ApoA, ApoB, ApoE, AST, ALT, $\gamma$ GT	Statistically significant reduction in anthropometric parameters, levels of glucose and lipid metabolism markers and liver enzyme serum levels
Cicero et al. [352]	SB	20	Moderate hyperlipidemia and cvd risk ranged 10-20%	4	0.5 g/d	-	TC, LDL-C, HDL-C, Non-HDL-C, TG, ApoB, ApoA	Significant improvement in all lipid metabolism markers evaluated
Derosa et al. [353]	R,DB,PC,MC	141 (71/70)	Hypercholesterolemia and low cvd risk	24 (12 weeks treatment; 8 weeks washout; 12 weeks treatment)	1.0 g/d	Placebo	BW, BMI, FPG, TC, LDL-C, HDL-C, TG	No statistically significant reduced body weight and FBG after 24 weeks treatment. TC, LDL-C and TG levels significantly decreased after each 12 weeks treatment, but increased during the washout period. HDL-C levels increased during treatment and decreased during

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Di et al. [354]	R, SB	57 (27/30)	T2DM	16	1.0 g/d <i>Berberis aristata</i> extract (85% berberine) plus 0.21 g/d <i>Silybum marianum</i> extract (>60% flavolignans)	1.176 g/d FPG, HbA1c, TC, LDL-C, TG, AST, ALT	washout period Statistically significant reduction in blood levels of AST, ALT and glucose and lipids metabolism markers.
Kong et al. [23]	R, PC	43 (32/11)	Hypercholesterolemia	12	1.0 g/d Placebo	TC, LDL-C, HDL-C, TG	Significant reduced levels of TC, TG and LDL-C; HDL-C levels remained unchanged
Kong et al. [355]	R	40 (24/16)	Hypercholesterolemia	8	1.0 g/d Simvastatin (0.2 g/d)	TC, LDL-C, TG, HDL	Statistically significant reduced TC, LDL-C and TG levels
Meng et al. [356]	R	130 (61/69)	ACS	4	0.9 g/d -	TC, TG, LDL-C, HDL-C, FPG, hsCRP, IL-6, MCP-1, ICAM-1, VCAM-1, MMP-9, SAA	Reduced blood levels of lipids and inflammatory markers
Wang et	R	25 (14/11)	Healthy subjects	4	1.2 g/d -	SBP, DBP, PP,	Significant reduction in

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al. [112]						TC, TG, LDL-C, HDL-C, FPG, hsCRP, FMD, NMD, CD31 <sup>+</sup> /CD42 <sup>-</sup> microparticles	blood pressure profile, TC, LDL-C, TG, FPG and circulating levels CD31 <sup>+</sup> /CD42 <sup>-</sup> microparticles. Significant improvement in endothelial function	
Yan et al. [359]	R, PaC, OP, MC	155 (55/100)	NAFLD	16	1.5 g/d + LSI	LSI; LSI + pioglitazone (0.15 g/d)	BW, BMI, WC, FPG, P-LPG, P-LSI, HOMA-IR, TC, TG, LDL-C, HDL-C, ApoA, ApoB, ApoE, AST, ALT, $\gamma$ GT	Statistically significant reduction in anthropometric parameters, levels of glucose and lipids metabolism markers, liver enzyme serum levels and hepatic fat content
Zhang et al. [360]	R,DB,PC,MC	106 (57/49)	T2DM and dyslipidemia	12	1.0 g/d	Placebo	HbA1c, FPG, P-LBG, TG, TC, HDL-C, LDL-C, SBP, DBP, HOMA-IR	Significant reduced levels of blood glucose and lipids and blood pressure. Statistically significant improvement of insulin-resistance
Zhang et al. [325]	R	97 (50/47)	T2DM	8	1.0 g/d	Metformin (1.5 g/d); rosiglitazone	FPG, HbA1c, TG, FSI, InsR, ALT, $\gamma$ -GT	Reduced levels of FPG, HbA1c (comparable with metformin and

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					(4.0 g/d)		rosiglitazone), TG, ALT, $\gamma$ -GT and FSI. On the other hand, increased expression levels of InsR, with a negative correlation between FPG and InsR.
		35	T2DM or IFG and HCV or HBV	8	1.0 g/d	-	FPG, TG, ALT, AST Reduced levels of glucose and lipid metabolism biomarkers; reduced AST and ALT levels
Yin et al. [361]	R	36 (18/18)	T2DM	12	1.5 g/d	Metformin (1.5 g/d)	HbA1c, FPG, TG, TC, HDL-C, LDL-C Significant decreased blood levels of glucose and lipids. Berberine and metformin exhibited identical efficacy in regulating the glucose metabolism; Berberine is more effective than metformin in lipids metabolism regulation
		48	T2DM	12	Berberine (1.5 g/d) added to previous T2DM treatment	HbA1c, FPG, PBG, TG, TC, HDL-C, LDL-C, C-peptide	Initial lowering effect in glucose and lipids levels. No changes in metabolic parameters were observed between weeks 5 and 13. However, increased fasting

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							and postprandial C-peptide levels were reported	
Hu et al. [362]		7	Obesity	12	1.5 g/d	-	BW, BMI, WHR, Body fat, TC, TG	Mild body weight loss and significant reduced blood lipids levels
Gu et al. [363]	R,DB,PC,MC	60 (30/30)	T2DM	12	1.0 g/d	Placebo	BW, BMI, WHR, SBP, DBP, FPG, P-LPG, HbA1c, TG, TC, HDL-C, LDL-C, FSI, P-LSI, HOMA-IR, FFAs	Significant improvement in glucose and lipid profile and insulin-sensitivity regulation by FFAs metabolism down-regulation.
Zeng et al. [364]	R, PC, SB	156 (79/77)	Chronic CHF and > 90 VPCs and/or nonsustained VT	8	1.2 to 2.0 g/d	Placebo	6-minute walk test, LVEF, frequency and complexity of VPCs, quality of life	Significant improvement in cardiac function and exercise capacity. Long-term follow-up mortality was significantly decreased. No side effects were observed

**Abbreviations:** ACS, Acute coronary syndrome; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; AUC, Area under the curve; BMI, Body mass index; BW, Body weight; CHF, Congestive heart failure; DB, Double-blind; DBP, Diastolic blood pressure; FFAs, Free Fatty Acids; FMD, Flow-mediated vasodilation; FPG, Fasting plasma glucose; FSI, Fasting serum insulin; HbA1c, Glycated haemoglobin; HBV, Hepatitis B virus; HCV, Hepatitis C virus; HDL-C, High-density lipoprotein cholesterol; HOMA-IR, Homeostasis model assessment-insulin resistance; hsCRP, High-sensitivity C-reactive protein; ICAM-1,

Intercellular adhesion molecule-1; **IFG**, Impaired fasting glucose; **IL-6**, Interleukin-6; **InsR**, Insulin receptor; **IR**, Insulin-resistance; **LDL-C**, Low-density lipoprotein cholesterol; **LSI**, Life style intervention; **LVEF**, Left ventricular ejection fraction; **MC**, Multiple-center; **MCP-1**, Monocyte chemoattractant protein-1; **MMP-9**, Metalloproteinase-9; **NAFLD**, Nonalcoholic fatty liver disease; **NMD**, Nitroglycerine-mediated vasodilation; **OP**, Open-label; **PaC**, Parallel-controlled; **PBG**, postprandial blood glucose; **PC**, Placebo-controlled; **PCOS**, Polycystic ovary syndrome; **P-LPG**, Post-load plasma glucose; **P-LSI**, Post-load serum insulin; **PP**, Pulse pressure; **R**, Randomised; **SAA**, Serum amyloid A; **SB**, Single-blind; **SBP**, Systolic blood pressure; **T2DM**, Type 2 diabetes mellitus; **TC**, Total cholesterol; **TG**, Triglyceride; **VCAM-1**, Vascular cell adhesion molecule-1; **VPCs**, Ventricular premature complexes; **VT**, Ventricular tachycardia; **WHR**, Waist-to-hip ratio;  **$\gamma$ -GT**,  $\gamma$ -glutammate transpeptidase.