Curcumin ingestion and exercise training improve vascular endothelial function in postmenopausal women

	Akazawa Nobuhiko, Choi Youngju, Miyaki Asako, Tanabe Yoko, Sugawara Jun, Ajisaka Ryuichi, Maeda Seiji
journal or publication title	Nutrition research
volume	32
number	10
page range	795-799
year	2012-10
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URL	http://hdl.handle.net/2241/118147

1 **Curcumin ingestion and exercise training improve vascular endothelial function in**

2 **postmenopausal women**

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19 **Word counts:** 3241

20   **Abbreviations**

21   FMD; flow-mediated dilation

22    $\dot{V}O_{2peak}$; peak oxygen consumption

23   HDL cholesterol; high-density lipoprotein cholesterol

24   LDL cholesterol; low-density lipoprotein cholesterol

25   NO; nitric oxide

26   TNF-α; tumor necrosis factor-alpha

Abstract

27

28   Vascular endothelial function is declines with aging and is associated with an

29 increased risk of cardiovascular disease. Lifestyle modification, particularly aerobic exercise

30 and dietary adjustment, has a favorable effect on vascular aging. Curcumin, is a major

31 component of turmeric, with known anti-inflammatory and anti-oxidative effects. We

32 investigated the effects of curcumin ingestion and aerobic exercise training on flow-mediated

33 dilation as an indicator endothelial function in postmenopausal women. A total of 32

34 postmenopausal women were assigned to 3 groups: control, exercise, and curcumin groups.

35 The curcumin group ingested curcumin orally for 8 weeks. The exercise group underwent

36 moderate aerobic exercise training for 8 weeks. Before and after each intervention,

37 flow-mediated dilation was measured. No difference in baseline flow-mediated dilation or

38 other key dependent variables were detected among the groups. Flow-mediated dilation

39 increased significantly and equally in the curcumin and exercise groups, whereas no changes

40 were observed in the control group. Our results indicated that curcumin ingestion and aerobic

41 exercise training can increase flow-mediated dilation in postmenopausal women, suggesting

42 that both can potentially improve the age-related decline in endothelial function.

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44

45 **Key Words**: flow-mediated dilation, turmeric, physical activity, lifestyle modification,

46 menopause, women

1. Introduction

Arterial endothelial dysfunction has been associated with cardiovascular morbidity and mortality [1]. Flow-mediated dilation (FMD), which is an index of endothelial function [2], is progressively impaired with age [3,4]. In women, the age-associated decline in endothelial function is enhanced during menopause because of the estrogen deficiency [5,6], and postmenopausal women are at a higher risk of cardiovascular disease [7]. Thus, slowing the decline of endothelial function in postmenopausal women could have potential health benefits. We and other groups have reported that aerobic exercise training enhances endothelial function [8-10]. Lifestyle modification is a desirable way to prevent or treat endothelial dysfunction without the need for pharmaceutical intervention.

Vascular inflammation and oxidative stress play important roles in development of vascular endothelial dysfunction and cardiovascular disease [11]. Previous studies have demonstrated that increased production of pro-inflammatory cytokines and reactive oxygen species in the aging vessel results in endothelial dysfunction [12,13]. Therefore, following an anti-inflammatory or anti-oxidative diet may help counteract the effects of aging on blood vessel. Curcumin, a polyphenol molecule extracted from turmeric, is a commonly used spice and a yellow pigment. Curcumin regulate biochemical and molecular pathway by modulating several molecular targets including transcription factors, cytokines, enzymes, and genes regulating cell proliferation and apoptosis [14-16]. In addition to the anti-inflammatory and anti-oxidative effects of curcumin [17,18], is has been associated with the protection against cardiovascular disease [19]. However, the effect of curcumin on endothelial function remains unclear.

We hypothesized that, similar to exercise, curcumin ingestion could improve endothelial function. The objective of the present study was to determine the effect of curcumin ingestion and the effect of exercise training on endothelial function. We therefore

76 investigated endothelial function as measured by the FMD in postmenopausal women before

77 and after 8 weeks of curcumin ingestion or exercise training intervention.

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80 **2. Methods and materials**

81 **2.1 Subjects** A total of 32 healthy, sedentary postmenopausal women (amenorrhea

82 for at least 2 years) participated in the study. Subjects were assigned to one of the following

83 intervention groups: control group (n = 10), curcumin group (n = 11), and exercise training

84 group (n = 11). Subjects were nonsmokers, nonobese, and free of cardiovascular disease as

85 assessed by medical history. None of the subjects were taking cardiovascular-acting

86 medications or hormone replacement therapy. All potential risks and associated with the

87 study were explained to the subjects, and they gave their written informed consent for

88 participation in the study. All procedures were reviewed and approved by the ethical

89 committee of the University of Tsukuba.

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92 **2.2 Experimental protocol** All experiments were performed in the morning after a

93 12-h overnight fast. Subjects abstained from alcohol and caffeine for at least 12 h and did not

94 exercise for at least 24 h before beginning the experiment to avoid the potential acute effects

95 of exercise. Measurements were taken in a quiet, temperature-controlled room (24–26°C).

96 After a resting period of at least 20 min, FMD, arterial blood pressure, and blood

97 biochemistry were determined. After these measurements, peak oxygen consumption

98 ($\dot{V}O_{2peak}$) was measured during incremental cycle ergometer exercise.

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101 **2.3 Curcumin ingestion** Subjects in the curcumin group ingested 6 pills (150 mg

102 total) of curcumin per day [20,21], which supplies 25 mg of highly absorptive curcumin

103 dispersed with colloidal nanoparticles (Theracurmin; Theravalues Corporation, Tokyo) [22].

104 Supplementary curcumin was administered orally for 8 weeks. All subjects were instructed

105   not to alter their dietary habits during the intervention period.

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108   **2.4 Exercise training**   Subjects in the exercise group underwent aerobic exercise

109   training more than 3 days per week (2-3 supervised sessions and additional home-based

110   training) for 8 weeks [23]. Initially, subjects performed cycling and walking 30 min/day at a

111   relatively low intensity (60% of their individually determined maximal heart rate). As their

112   exercise tolerance improved, the intensity and duration of aerobic exercise were increased to

113   40−60 min/day at an intensity of 70−75 % of the maximal heart rate. Subjects in the control

114   and curcumin groups were instructed not to change their level of physical activity.

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117   **2.5 Measurements**

118   2.5.1 *FMD.* Brachial artery FMD was assessed noninvasively by using an ultrasound

119   system (UNEXEF18G, Unex, Nagoya, Japan) as previously described [24]. Briefly,

120   high-resolution ultrasound with a 10 MHz linear array transducer was used to obtain a

121   longitudinal image of the right brachial artery in the cubital region at the baseline and then

122   continuously from 30 s prior to 2 min or more after the release of suprasystolic pressure (50

123   mmHg above systolic blood pressure) maintained for 5 minutes of the right forearm. The

124   diameter at the same point of the artery was monitored continuously, and the maximal

125   dilatation after deflation was recorded. FMD was calculated as the percentage change in

126   brachial artery diameter in response to the forearm reactive hyperemic stimulus. FMD was

127   calculated as follows:

128   (Maximal diameter – baseline diameter) $\times$ 100/baseline diameter

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131   2.5.2 *Arterial blood pressure.* Arterial blood pressure and heart rate at rest were

132   determined in the supine position using an automated device (formPWV/ABI, Colin Medical

133   Technology, Komaki, Japan) [23].

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136   2.5.3 *Blood chemistry.* A blood sample was collected from the antecubital vein after

137   overnight fasting. Serum of cholesterol and triglyceride and plasma of glucose were

138   determined using standard enzymatic techniques [25].

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141   2.5.4 *Peak oxygen consumption.* $\dot{V}O_{2peak}$ was measured during incremental cycle

142   ergometer exercise by using online computer-assisted circuit spirometry (AE280, Minato

143   Medical Science, Osaka, Japan) as we previously reported [23]. All subjects underwent an

144   incremental exercise test (2 min at 40 W, followed by 20 W increases every 2 min) until

145   volitional exhaustion. $\dot{V}O_{2peak}$ was defined as the highest $\dot{V}O_2$ recorded during the test. Heart

146   rate and rating of perceived exertion were recorded throughout the exercise.

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149   **2.6 Statistical analyses.** The effects of each intervention on the outcomes

150   measured were determined by repeated measures analysis of variance. If a significant effect

151   was detected, specific mean comparisons were performed to determine the significance of

152   each intervention. In the case of a significant F-value, a post-hoc test (Bonferroni test) was

153   used to identify significant differences among mean values. All data are reported as means ±

154   SD. Statistical significance was set a priori at $P < 0.05$ for all comparisons.

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157   **3. Results**

158   The compliance/adherence to curcumin ingestion in the curcumin group was 97.6 ±

159   2.8%. No adverse effects of curcumin were reported. In the exercise training group, the

160   average frequency and duration of the exercise training was 4.5 ± 1.4 days/week and 48 ± 23

161   min/day. There were no drop-outs in either group.

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Table 1 shows the baseline characteristics of the study participants. There were no group differences in age, height, body weight, body mass index, total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride, glucose, or $\dot{V}O_{2peak}$ between the groups at the start of the study. HDL cholesterol levels increased significantly in the exercise group (P < 0.05). There were no significant changes in body weight, body mass index, total cholesterol, LDL cholesterol, triglyceride and glucose levels in any of the groups. $\dot{V}O_{2peak}$ in the exercise group increased significantly after the intervention (P < 0.05).

3.1 Heart rate and blood pressure

As shown in Table 2, no statistically significant differences in the baseline hemodynamic parameters at rest were detected among the groups before the intervention. After 8 weeks of intervention, systolic blood pressure decreased in the exercise and curcumin groups (P < 0.05). Heart rate and diastolic blood pressure did not change in any of the groups.

3.2 FMD

No significant difference in the baseline FMD was detected among the groups (Fig. 1). After 8 weeks of intervention, FMD increased significantly in the exercise and curcumin groups, whereas no significant change in FMD was detected in the control group. The change in FMD was significantly greater in the exercise and the curcumin groups than in the control group (Fig. 2). The differences in FMD changes between the exercise and curcumin groups were not statistically significant (Fig. 2).

4. Discussion

The present study showed that regular ingestion of curcumin or regular aerobic

192   exercise training significantly improved endothelial function. The magnitude of improvement

193   in endothelial function to the same extent, suggesting that curcumin may prevent the

194   age-associated decline in endothelial function in postmenopausal women.

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197   Curcumin, a polyphenolic derivative of turmeric, is widely cultivated in Asia and is

198   commonly used as a spice to add flavor and yellow, coloring to food. Curcumin is known to

199   anti-inflammatory and anti-oxidant effects in addition to acting as an anti-carciogenic and

200   neuroprotective agent [26-28]. Recent studies have reported a beneficial effect of curcumin

201   on the cardiovascular system, suggesting its potential as a therapeutic agent for the treatment

202   of cardiovascular disease and endothelial dysfunction [19]. In this study, we showed an

203   improvement in endothelial function after 8 weeks of the curcumin ingestion in

204   postmenopausal women. The magnitude of the improvement achieved by curcumin treatment

205   was comparable to that obtained with exercise. Therefore, regular ingestion of curcumin

206   could be a preventive measure against cardiovascular disease in postmenopausal women.

207   Furthermore, our results suggest that curcumin may be a potential alternative treatment for

208   patients who are unable to exercise.

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210

211   Our hypothesis that curcumin ingestion may improve endothelial function in a

212   similar manner as exercise was proven in the present study, as shown in the significant and

213   comparable increase in FMD after 8 weeks of curcumin ingestion and exercise training.

214   Regular aerobic exercise improves enhanced endothelial function, which has been associated

215   with increased nitric oxide (NO) bioavailability [9,29]. Therefore, the exercise-induced

216   endothelial function improvement in our study could have been mediated by an increase in

217   NO bioavailability. However, the mechanism responsible for the curcumin ingestion induced

218   improvement in endothelial function is unclear. Curcumin exerts anti-inflammatory and

219   anti-oxidative effects by inhibiting tumor necrosis factor-alpha (TNF-α) [30], suggesting that

220   its effect on endothelial function may be mediated by the suppression of inflammation and/or

221 oxidative stress via downregulation of TNF-α. However, TNF-α levels were mot assessed in

222 this study. Further studies are warranted to clarify the mechanism undeerlying the effect of

223 curcumin on endothelial function.

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225

226   In our previous study, we investigated the effect of exercise training and curcumin

227 ingestion on central arterial hemodynamics, i.e., wave reflection and central blood pressure

228 [21]. Wave reflection and central blood pressure did not improve with exercise training alone

229 or curcumin ingestion alone, whereas these parameters improved in response to the

230 combination of exercise training with curcumin ingestion. However, in the present study, we

231 investigated the effect of curcumin on endothelial function as measured by FMD, and

232 demonstrated for the first time that curcumin ingestion alone increased FMD, similar to the

233 effect of exercise demonstrated previously. The effect of the combination of exercise training

234 with curcumin ingestion on vascular endothelial function were not assessed in this study and

235 should be addressed in future studies in comparison to the effect of each agent alone.

236

237

238   The present study had some limitations. First, this study was conducted with a

239 small sample size in each group. However, the power calculation indicated that the number of

240 subjects was sufficient to establish statistical significance. Furthermore, this study focused

241 only on postmenopausal women. Thus, the findings of this study cannot be generalized to

242 other populations, such as men and young women. Second, the present study measured only

243 FMD as an index of endothelial function. We did not measure any biomarkers of

244 inflammation and oxidative stress, plasma curcumin concentration, or endothelial function

245 using different indexes. Further studies are needed to clarify the mechanism underlying the

246 effect of curcumin on vascular endothelial function. Third, analysis of the baseline

247 characteristics of the participants and the baseline FMD suggest that the subjects in the

248 exercise group showed overall better before the start of the study. Although there were no

249 significant differences in any of the variables among the groups before the intervention, small

250 differences in baseline values might have biased the results.

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252

253   In conclusion, we examined the effect of curcumin ingestion and exercise training

254 on endothelial function in postmenopausal women and found that regular curcumin ingestion

255 and exercise improve endothelial function. These findings suggest that curcumin could be

256 developed as a therapeutic strategy for the treatment of cardiovascular disease similar to

257 exercise training in postmenopausal women.

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260 **5. Acknowledgments**

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6. References

[1] Moncada S, Palmer RM, Higgs EA. Nitric oxide: physiology, pathophysiology, and pharmacology. *Pharmacol Rev* 1991;43:109-142.

[2] Thijssen DH, Black MA, Pyke KE, Padilla J, Atkinson G, Harris RA, et al. Assessment of flow-mediated dilation in humans: a methodological and physiological guideline. *Am J Physiol Heart Circ Physiol* 2011;300:H2-12.

[3] Celermajer DS, Sorensen KE, Spiegelhalter DJ, Georgakopoulos D, Robinson J, Deanfield JE. Aging is associated with endothelial dysfunction in healthy men years before the age-related decline in women. *J Am Coll Cardiol* 1994;24:471-476.

[4] Gates PE, Boucher ML, Silver AE, Monahan KD, Seals DR. Impaired flow-mediated dilation with age is not explained by L-arginine bioavailability or endothelial asymmetric dimethylarginine protein expression. *J Appl Physiol* 2007;102:63-71.

[5] Taddei S, Virdis A, Ghiadoni L, Mattei P, Sudano I, Bernini G, et al. Menopause is associated with endothelial dysfunction in women. *Hypertension* 1996;28:576-582.

[6] Gavin KM, Seals DR, Silver AE, Moreau KL. Vascular endothelial estrogen receptor alpha is modulated by estrogen status and related to endothelial function and endothelial nitric oxide synthase in healthy women. *J Clin Endocrinol Metab* 2009; 94: 3513-3520.

[7] La Vecchia C. Sex hormones and cardiovascular risk. *Hum Reprod* 1992;7:162-167.

[8] DeSouza CA, Shapiro LF, Clevenger CM, Dinenno FA, Monahan KD, Tanaka H, et al. Regular aerobic exercise prevents and restores age-related declines in endothelium-dependent vasodilation in healthy men. *Circulation* 2000;102:1351-1357.

[9] Taddei S, Galetta F, Virdis A, Ghiadoni L, Salvetti G, Franzoni F, et al. Physical activity prevents age-related impairment in nitric oxide availability in elderly athletes. *Circulation* 2000;101:2896-2901.

[10] Yoshizawa M, Maeda S, Miyaki A, Misono M, Choi Y, Shimojo N, et al. Additive beneficial effects of lactotripeptides intake with regular exercise on endothelium-dependent dilatation in postmenopausal women. *Am J Hypertens* 2010;23:368-372.

293   [11] Herrera MD, Mingorance C, Rodríguez-Rodríguez R, Alvarez de Sotomayor M.

294   Endothelial dysfunction and aging: an update. *Ageing Res Rev* 2010;9:142-152.

295   [12] Donato AJ, Black AD, Jablonski KL, Gano LB, Seals DR. Aging is associated with

296   greater nuclear NF kappa B, reduced I kappa B alpha, and increased expression of

297   proinflammatory cytokines in vascular endothelial cells of healthy humans. *Aging Cell*

298   2008;7:805-812.

299   [13] Csiszar A, Ungvari Z, Edwards JG, Kaminski P, Wolin MS, Koller A, et al.

300   Aging-induced phenotypic changes and oxidative stress impair coronary arteriolar

301   function. *Circ Res* 2002;90:1159-1166.

302   [14] Goel A, Kunnumakkara AB, Aggarwal BB. Curcumin as "Curecumin": from kitchen to

303   clinic. *Biochem Pharmacol* 2008;75:787-809.

304   [15] Gupta SC, Patchva S, Koh W, Aggarwal BB. Discovery of curcumin, a component of

305   golden spice, and its miraculous biological activities. *Clin Exp Pharmacol Physiol*

306   2012;39:283-299.

307   [16] Gupta SC, Prasad S, Kim JH, Patchva S, Webb LJ, Priyadarsini IK, et al. Multitargeting

308   by curcumin as revealed by molecular interaction studies. *Nat Prod Rep*

309   2011;28:1937-1955.

310   [17] Cho JW, Lee KS, Kim GW. Curcumin attenuate the expression of IL-1ß, IL-6, and

311   TNF-α as well as cyclin E in TNF-α-treated HaCaT cell; NF-kB and MAPKs as potential

312   upstream targets. *Int J Mol Med* 2007;19:469-474

313   [18] Quiles JL, Mesa MD, Ramírez-Tortosa CL, Aguilera CM, Battiono M, Gil A, et al.

314   Curcuma longa extract supplementation reduces oxidative stress and attenuates aortic

315   fatty streak development in rabbits. *Arterioscler Throm Vasc Biol* 2002;22:1225-1231.

316   [19] Wongcharoen W, Phrommintikul A. The protective role of curcumin in cardiovascular

317   diseases. *Int J Cardiol* 2009;133:145-151.

318   [20] Kanai M, Imaizumi A, Otsuka Y, Sasaki H, Hashiguchi M, Tsujiko K, et al.

319   Dose-escalation and pharmacokinetic study of nanoparticle curcumin, a potential

320   anticancer agent with improved bioavailability, in healthy human volunteers. *Cancer*

321   *Chemother Pharmacol* 2012;69:65-70.

322   [21] Sugawara J, Akazawa N, Miyaki A, Choi Y, Tanabe Y, Imai T, et al. Effect of
323   endurance exercise training and curcumin intake on central arterial hemodynamics in
324   postmenopausal women: pilot study. *Am J Hypertens* 2012;25:651-656.

325   [22] Sasaki H, Sunagawa Y, Takahashi K, Imaizumi A, Fukuda H, Hashimoto T, et al.
326   Innovative preparation of curcumin for improved oral bioavailability. *Biol Pharm Bull*
327   2011;34:660-665.

328   [23] Yoshizawa M, Maeda S, Miyaki A, Misono M, Choi Y, Shimojo N, et al. Additive
329   beneficial effects of lactotripeptides and aerobic exercise on arterial compliance in
330   postmenopausal women. *Am J Physiol Heart Circ Physiol* 2009;297:H1899-903

331   [24] Kawano N, Emoto M, Mori K, Yamazaki Y, Urata H, Tsuchikura S, et al. Association
332   of endothelial and vascular smooth muscle dysfunction with cardiovascular risk factors,
333   vascular complications, and subclinical carotid atherosclerosis in type 2 diabetic patients.
334   *J Atheroscler Thromb* 2011. In press.

335   [25] Miyaki A, Maeda S, Otsuki T, Ajisaka R. Plasma pentraxin 3 concentration increases in
336   endurance-trained men. *Med Sci Sports Exerc* 2011;43:12-17.

337   [26] Sharma RA, Gescher AJ, Steward WP. Curcumin: the story so far. *Eur J Cancer*
338   2005;41:1955-1968.

339   [27] Maheshwari RK, Singh AK, Gaddipati J, Srimal RC. Multiple biological activities of
340   curcumin: a short review. *Life Sci* 2006;78:2081-2087.

341   [28] Jiang J, Wang W, Sun YJ, Hu M, Li F, Zhu DY. Neuroprotective effect of curcumin on
342   focal cerebral ischemic rats by preventing blood-brain barrier damage. *Eur J Pharmacol*
343   2007;561:54-62.

344   [29] Eskurza I, Monahan KD, Robinson JA, Seals DR. Effect of acute and chronic ascorbic
345   acid on flow-mediated dilatation with sedentary and physically active human ageing. *J*
346   *Physiol* 2004;556:315-324.

347   [30] He ZY, Shi CB, Wen H, Li FL, Wang BL, Wang J. Upregulation of p53 expression in
348   patients with colorectal cancer by administration of curcumin. *Cancer Invest*
349   2011;29:208-213.

350

351 **Figure legends**

352

353 Figure 1. FMD before and after intervention. Data are expressed as means ± SD. *P < 0.05

354 before vs. after intervention.

355

356 Figure 2. Changes in FMD in response to intervention. Data are expressed as means ± SD. *P

357 < 0.05 vs. control group.

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Table1. Baseline characteristics of subjects

	Control (n = 10)		Exercise (n = 11)		Curcumin (n = 11)		P		
	Before	After	Before	After	Before	After	Group	Time	Time×Group
Age, years	64 ± 6		59 ± 5		60 ± 6		NS		
Height, cm	154 ± 6		154 ± 4		155 ± 8		NS		
Weight, kg	51 ± 2	51 ± 2	54 ± 2	54 ± 2	54 ± 3	54 ± 3	NS	NS	NS
BMI, kg/m	21.5 ± 1.0	21.6 ± 1.0	22.7 ± 1.0	22.6 ± 1.0	22.5 ± 1.0	22.7 ± 1.0	NS	NS	NS
Total Cholesterol, mmol/l	6.1 ± 0.5	6.3 ± 0.5	5.4 ± 0.6	5.7 ± 0.6	6.3 ± 0.7	6.6 ± 0.5	NS	0.005	NS
HDL Cholesterol, mmol/l	1.7 ± 0.4	1.7 ± 0.3	1.7 ± 0.3	1.9 ± 0.3*	1.6 ± 0.5	1.7 ± 0.5	NS	0.010	NS
LDL Cholesterol, mmol/l	3.8 ± 0.6	3.9 ± 0.4	3.2 ± 0.4	3.5 ± 0.6	3.8 ± 0.7	4.0 ± 0.7	NS	0.027	NS
Triglyceride, mmol/l	1.4 ± 0.6	1.3 ± 0.4	1.0 ± 0.6	0.9 ± 0.4	1.9 ± 0.9	1.7 ± 0.1	NS	NS	NS
Glucose, mmol/l	5.3 ± 0.4	5.3 ± 0.4	4.9 ± 0.4	4.9 ± 0.3	5.1 ± 1.1	5.4 ± 1.6	NS	NS	NS
$\dot{V}O_{2peak}$, ml/kg/min	22.9 ± 1.4	22.5 ± 1.1	25.3 ± 1.2	27.3 ± 1.2*	21.9 ± 0.7	21.9 ± 0.8	NS	NS	0.024

Values are means ± SD. BMI; body mass index, HDL Cholesterol; high-density lipoprotein cholesterol, LDL Cholesterol; low-density lipoprotein cholesterol, $\dot{V}O_{2peak}$; peak oxygen consumption.

*$P < 0.05$ vs. before intervention. A main time and group effect overall by repeated-measures ANOVA.

Table 2. Hemodynamics parameter before and after intervention.

	Control (n = 10)		Exercise (n = 11)		Curcumin (n = 11)		P value		
	Before	After	Before	After	Before	After	Group	Time	Time×Group
Heart rate, beats/min	62 ± 6	64 ± 11	61 ± 6	57 ± 5	61 ± 8	59 ± 7	NS	NS	NS
SBP, mmHg	112 ± 12	113 ± 11	112 ± 10	107 ± 10*	122 ± 17	116 ± 15*	NS	0.003	0.025
DBP mmHg	69 ± 5	69 ± 6	71 ± 8	69 ± 9	72 ± 12	69 ± 11	NS	NS	NS

Values are means ± SD. SBP; systolic blood pressure, DBP; diastolic blood pressure

*$P < 0.05$ vs. before intervention. A main time and group effect overall by repeated-measures ANOVA.
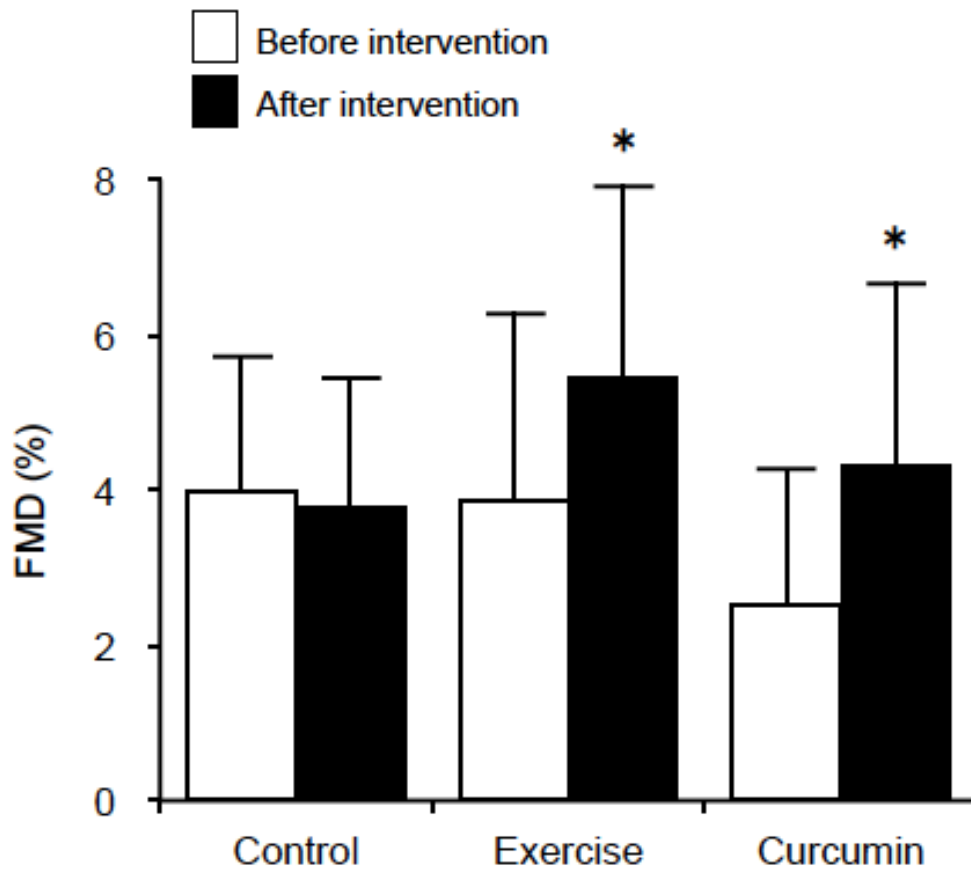
Figure 1. FMD before and after intervention. Data are expressed as means ± SD. *P < 0.05 before vs. after intervention.

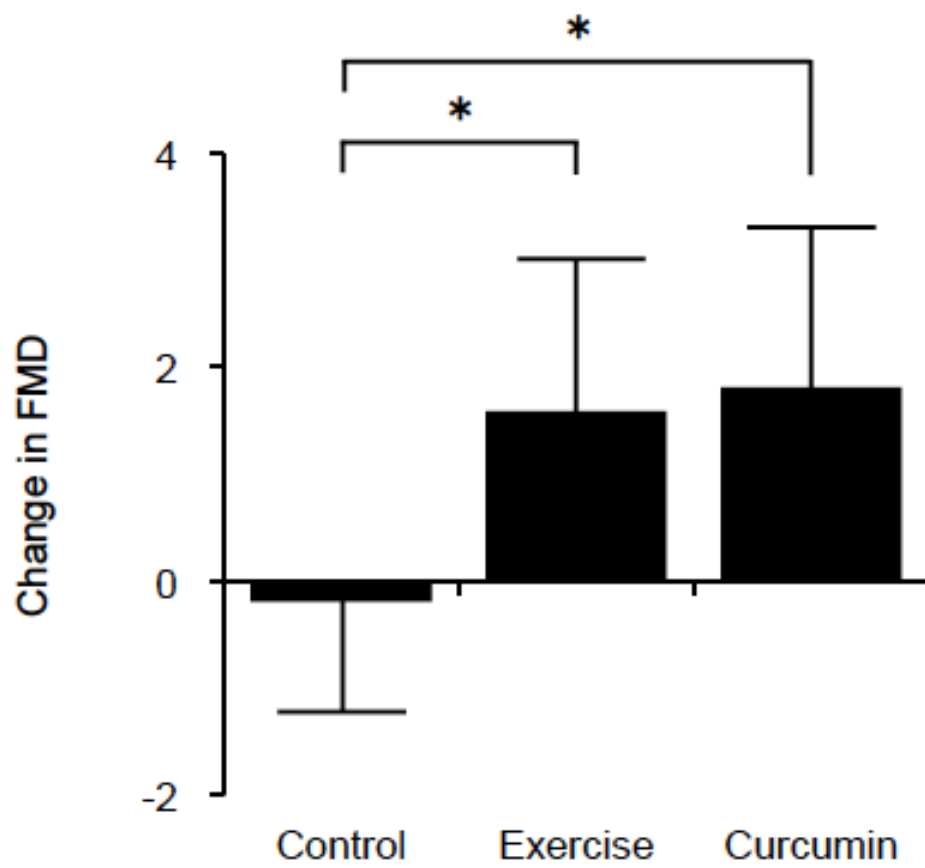Figure 2. Changes in FMD in response to intervention. Data are expressed as means ± SD. *P < 0.05 vs. control group.