

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

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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

27 **Abstract**

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

47 **1. Introduction**

48 Arterial endothelial dysfunction has been associated with cardiovascular morbidity
49 and mortality [1]. Flow-mediated dilation (FMD), which is an index of endothelial function
50 [2], is progressively impaired with age [3,4]. In women, the age-associated decline in
51 endothelial function is enhanced during menopause because of the estrogen deficiency [5,6],
52 and postmenopausal women are at a higher risk of cardiovascular disease [7]. Thus, slowing
53 the decline of endothelial function in postmenopausal women could have potential health
54 benefits. We and other groups have reported that aerobic exercise training enhances
55 endothelial function [8-10]. Lifestyle modification is a desirable way to prevent or treat
56 endothelial dysfunction without the need for pharmaceutical intervention.

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

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73 We hypothesized that, similar to exercise, curcumin ingestion could improve
74 endothelial function. The objective of the present study was to determine the effect of
75 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 ($\dot{V}O_{2\text{peak}}$) 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 $(\text{Maximal diameter} - \text{baseline diameter}) \times 100 / \text{baseline diameter}$

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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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2.5.3 *Blood chemistry.* A blood sample was collected from the antecubital vein after overnight fasting. Serum of cholesterol and triglyceride and plasma of glucose were determined using standard enzymatic techniques [25].

2.5.4 *Peak oxygen consumption.* $\dot{V}O_{2peak}$ was measured during incremental cycle ergometer exercise by using online computer-assisted circuit spirometry (AE280, Minato Medical Science, Osaka, Japan) as we previously reported [23]. All subjects underwent an incremental exercise test (2 min at 40 W, followed by 20 W increases every 2 min) until volitional exhaustion. $\dot{V}O_{2peak}$ was defined as the highest $\dot{V}O_2$ recorded during the test. Heart rate and rating of perceived exertion were recorded throughout the exercise.

2.6 Statistical analyses. The effects of each intervention on the outcomes measured were determined by repeated measures analysis of variance. If a significant effect was detected, specific mean comparisons were performed to determine the significance of each intervention. In the case of a significant F-value, a post-hoc test (Bonferroni test) was used to identify significant differences among mean values. All data are reported as means \pm SD. Statistical significance was set a priori at $P < 0.05$ for all comparisons.

3. Results

The compliance/adherence to curcumin ingestion in the curcumin group was $97.6 \pm 2.8\%$. No adverse effects of curcumin were reported. In the exercise training group, the average frequency and duration of the exercise training was 4.5 ± 1.4 days/week and 48 ± 23 min/day. There were no drop-outs in either group.

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

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174 3.1 Heart rate and blood pressure

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

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181 3.2 FMD

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

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190 4. Discussion

191 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-carcinogenic 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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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 not assessed in
222 this study. Further studies are warranted to clarify the mechanism underlying the effect of
223 curcumin on endothelial function.

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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.

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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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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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265 **6. References**

- 266 [1] Moncada S, Palmer RM, Higgs EA. Nitric oxide: physiology, pathophysiology, and
267 pharmacology. *Pharmacol Rev* 1991;43:109-142.
- 268 [2] Thijssen DH, Black MA, Pyke KE, Padilla J, Atkinson G, Harris RA, et al. Assessment of
269 flow-mediated dilation in humans: a methodological and physiological guideline. *Am J*
270 *Physiol Heart Circ Physiol* 2011;300:H2-12.
- 271 [3] Celermajer DS, Sorensen KE, Spiegelhalter DJ, Georgakopoulos D, Robinson J,
272 Deanfield JE. Aging is associated with endothelial dysfunction in healthy men years
273 before the age-related decline in women. *J Am Coll Cardiol* 1994;24:471-476.
- 274 [4] Gates PE, Boucher ML, Silver AE, Monahan KD, Seals DR. Impaired flow-mediated
275 dilation with age is not explained by L-arginine bioavailability or endothelial asymmetric
276 dimethylarginine protein expression. *J Appl Physiol* 2007;102:63-71.
- 277 [5] Taddei S, Virdis A, Ghiadoni L, Mattei P, Sudano I, Bernini G, et al. Menopause is
278 associated with endothelial dysfunction in women. *Hypertension* 1996;28:576-582.
- 279 [6] Gavin KM, Seals DR, Silver AE, Moreau KL. Vascular endothelial estrogen receptor
280 alpha is modulated by estrogen status and related to endothelial function and endothelial
281 nitric oxide synthase in healthy women. *J Clin Endocrinol Metab* 2009; 94: 3513-3520.
- 282 [7] La Vecchia C. Sex hormones and cardiovascular risk. *Hum Reprod* 1992;7:162-167.
- 283 [8] DeSouza CA, Shapiro LF, Clevenger CM, Dinunno FA, Monahan KD, Tanaka H, et al.
284 Regular aerobic exercise prevents and restores age-related declines in
285 endothelium-dependent vasodilation in healthy men. *Circulation* 2000;102:1351-1357.
- 286 [9] Taddei S, Galetta F, Virdis A, Ghiadoni L, Salvetti G, Franzoni F, et al. Physical activity
287 prevents age-related impairment in nitric oxide availability in elderly athletes. *Circulation*
288 2000;101:2896-2901.
- 289 [10] Yoshizawa M, Maeda S, Miyaki A, Misono M, Choi Y, Shimojo N, et al. Additive
290 beneficial effects of lactotripeptides intake with regular exercise on
291 endothelium-dependent dilatation in postmenopausal women. *Am J Hypertens*
292 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-1 β , 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.
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351 **Figure legends**

352

353 Figure 1. FMD before and after intervention. Data are expressed as means \pm SD. *P < 0.05
354 before vs. after intervention.

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356 Figure 2. Changes in FMD in response to intervention. Data are expressed as means \pm SD. *P
357 < 0.05 vs. control group.

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Table 1. 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.

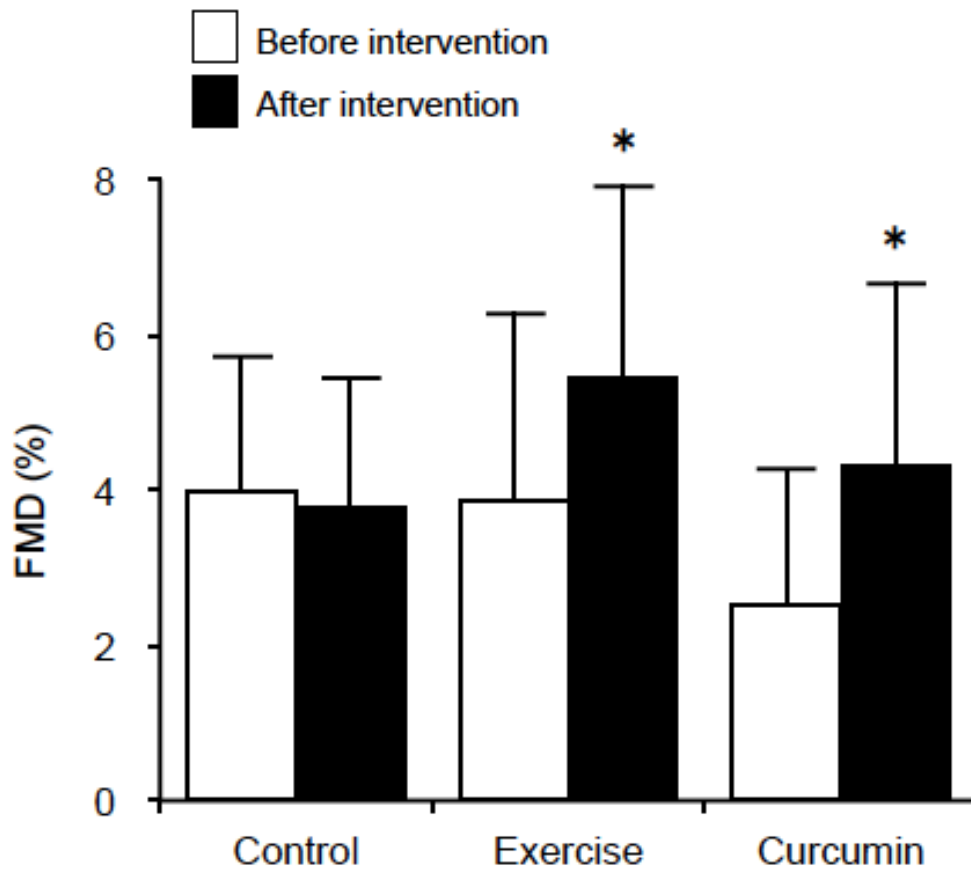


Figure 1. FMD before and after intervention. Data are expressed as means \pm SD. *P < 0.05 before vs. after intervention.

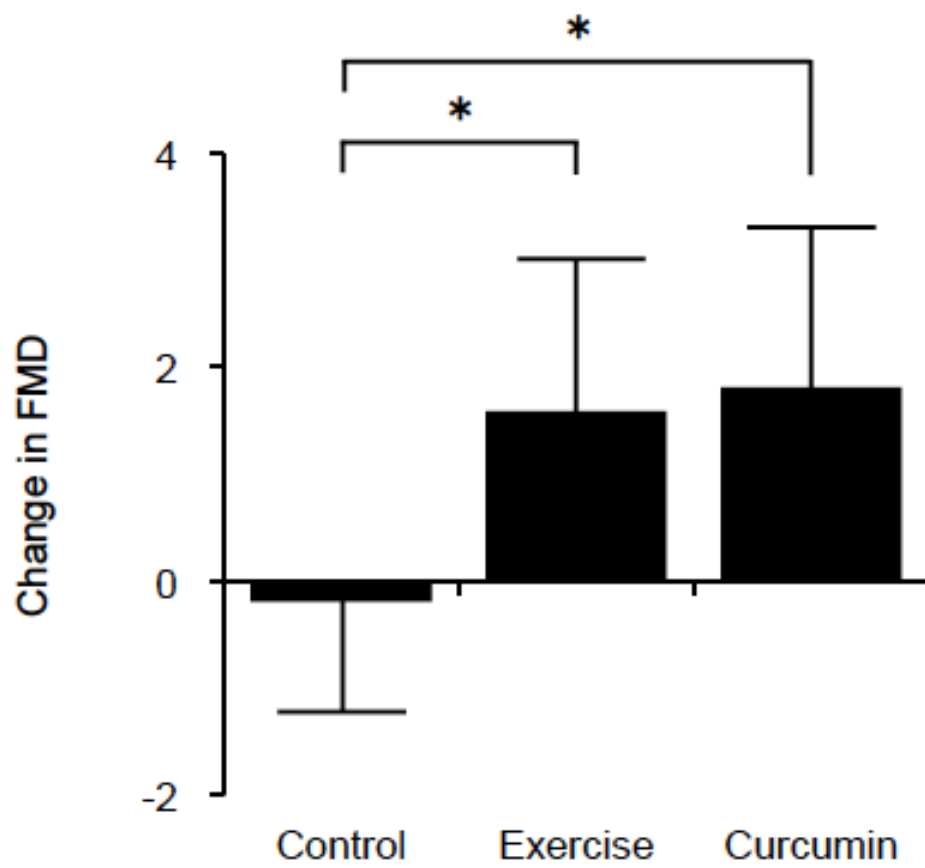


Figure 2. Changes in FMD in response to intervention. Data are expressed as means \pm SD. *P < 0.05 vs. control group.