Received: 27 August 2020 | Revised: 5 November 2020 | Accepted: 13 December 2020

DOI: 10.1002/ptr.7000

RESEARCH ARTICLE

WILEY

The effect of barberry (*Berberis vulgaris*) consumption on flow-mediated dilation and inflammatory biomarkers in patients with hypertension: A randomized controlled trial

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Hypertension is considered as an important cardiovascular risk factor and evidence suggests that hypertension and endothelial dysfunction reinforce each other. Polyphenol-rich foods, such as barberry can reduce the risk of cardiovascular disease. Our aim was to investigate the effects of barberry consumption on vascular function and inflammatory markers in hypertensive subject. In this randomized controlled parallel trial, 84 hypertensive subjects of both genders (aged 54.06 ± 10.19 years; body mass index 28.02 ± 2.18 kg/m^2) were randomly allocated to consume barberry (10 g/day dried barberry) or placebo for 8 weeks. Before and after the intervention, changes in brachial flow-mediated dilation (FMD) and plasma macrophage/monocyte chemo-attractant protein-1 (MCP-1), vascular cellular adhesion molecule-1, and intracellular adhesion molecule-1 (ICAM-1) were measured. An intention-to-treat analysis was performed. Compared to placebo (n = 42), barberry consumption (n = 42) improved FMD (B [95% CI] was 6.54% [4.39, 8.70]; p < .001) and decreased plasma ICAM-1 (B [95% CI] was −1.61 ng/ml [−2.74, −0.48]; p = .006). MCP-1 was significantly lower in the barberry group compared with the placebo group (B [95% CI] was −37.62 pg/ml [−72.07, −3.17]; p = .033). Our results indicate that barberry consumption improves FMD and has a beneficial effect on plasma ICAM-1 and MCP-1 in hypertensive patients. This trial was registered at the Iranian Registry of Clinical Trial (IRCT) with number IRCT20160702028742N8.

KEYWORDS
barberry, *Berberis vulgaris*, flow-mediated dilation, FMD, hypertension, inflammation

1 | INTRODUCTION

Hypertension is a common and important cardiovascular risk factor that imposes a great burden on the healthcare system (Carretero & Oparil, 2000). Endothelial dysfunction, a change in vascular endothelium that occurs before the development of adverse cardiovascular disease (CVD) events appears to have a complex association with hypertension, and evidence suggests that hypertension and endothelial dysfunction reinforce each other (Dharmashankar & Widlansky, 2010). Endothelial dysfunction is readily measurable using both invasive and noninvasive methods and is a prognostic predictor of future CVDs (McMackin & Vita, 2005; Vita & Keaney Jr., 2002). Flow-mediated dilation (FMD), that is, measurement of the brachial artery diameter before and after an increase in shear stress-induced by reactive hyperemia is most frequently used to evaluate endothelial function in the clinical setting.

Inflammation appears to contribute to the development of vascular endothelial disorders (Ong et al., 2012). Low-grade inflammation in vascular endothelium is involved in the progression of atherosclerosis, as well as other cardiovascular risk factors including hypertension

(De Ciuceis et al., 2005; Savoia & Schiffrin, 2006, 2007). Adhesion and chemo-attractant molecules are expressed on endothelial cells and are involved in the recruitment of inflammatory monocytes into the vascular wall to initiate atherosclerosis. In this process, macrophage/monocyte chemo-attractant protein-1 (MCP-1), vascular cellular adhesion molecule-1 (VCAM-1), and intracellular adhesion molecule-1 (ICAM-1) play an important role (Libby, 2006). Each of these has a plasma soluble form, which can serve as a surrogate marker for their increased expression on vascular endothelial cells, and reflect inflammation and activation of endothelial cells. Brachial artery vasodilator function has been shown to correlate negatively with ICAM-1 (Vita et al., 2004) and VCAM-1 (Chen et al., 2015).

Researches show that polyphenol-rich foods, in addition to their antioxidant properties, also reduce the risk of CVD by regulating inflammation, immunity, and vasodilation (Tangney & Rasmussen, 2013). Berries and their main bioactive constituents have been identified as candidates to improve cardiovascular risk factors. Berry products contain distinguished polyphenol constituents. The Berry fruits family is rich in polyphenols such as procyanidins, quercetin, phenolic acids, and especially anthocyanins (Maatta-Riihinen, Kamal-Eldin, Mattila, Gonzalez-Paramas, & Torronen, 2004). Growing evidence highlights the beneficial effect of specific berries and their bioactive compounds that improve endothelial function (Curtis et al., 2019; Istas et al., 2019; Jeong et al., 2014; Johnson et al., 2015; Stull et al., 2015). However, studies of berries with concerning to cardiovascular health are mainly limited to a few berries such as cranberry, blueberry and chokeberry.

Berberis vulgaris commonly known as barberry is a berry fruit with high polyphenol content. The fruits of barberry have a sour taste and contain malic acid, tartaric acid, and citric acid. The barberry's fruits, flowers, and seeds contain significant amounts of phenolic compounds including anthocyanin and carotenoid pigments, pectin, oleoresin, vitamin C, and organic acids such as chelidonic acid, resin, and tannin (Kalmarzi et al., 2019). The effect of barberry consumption on endothelial function or vascular inflammatory markers has not previously been studied. Furthermore, no study has been performed on hypertensive patients and previous studies on the effects of barberry have been performed on subjects with metabolic syndrome (Mohammadi et al., 2014; Zilaee et al., 2014) or patients with diabetes (Lazavi et al., 2018; Shidfar et al., 2012). Regarding that the consumption of foods rich in polyphenols may have beneficial effects on endothelial function and by considering barberry as a rich source of phenolic compounds, in this study, the effect of barberry consumption on endothelial function was studied. In addition, considering the potential impact of vascular inflammatory factors on endothelial function, its effect on vascular inflammatory markers was also investigated.

2 | MATERIALS AND METHODS

2.1 | Participants

In this clinical study, we recruited men and women subjects with hypertension on stable medication. Volunteers among patients with a former history of hypertension who had a medical record in the academic hospital (Rajaei Cardiovascular, Medical & Research Center, Tehran, Iran) and were regularly visited in the hospital clinics every 6 months if they met the eligibility criteria recruited. Besides, by placing an advertisement in the hospital, other volunteers who are referred to the hospital if they meet the eligibility criteria are also included.

The inclusion criteria were subjects with previous history of hypertension who were already taking antihypertensive medications for >3 months, willingness to participate in the study, age between 20 and 65 years, having body mass index (BMI) < 30, and not-taking vitamins or minerals supplements during the past 2 weeks. Exclusion criteria were unwillingness to continue participation, any change in medication regimen during follow up, having inflammatory, autoimmune, or chronic kidney disease stage 4 or 5. Patients were allowed to withdraw from the study whenever they want.

The protocol conducted in this trial was in compliance with the Helsinki Declaration and the trial has received ethical approval from the Ethics Committee of National Nutrition and Food Technology Research Institute (NNFTRI), Shahid Beheshti University of Medical Sciences, Tehran, Iran (the ethical committee code was IR.SBMU.NNFTRI.REC.1398.046) and written informed consent was obtained from all participants. The NNFTRI provided financial support for the current project. This clinical trial was registered at the Iranian Registry of Clinical Trial (IRCT) with number IRCT20160702028742N8.

2.2 | Study design

This was an 8-week, prospective, single-blinded, parallel assigned, randomized controlled clinical trial. The participants were recruited from November 2019 to January 2020. Participants were blinded to the type of product they were given, but the main investigator who assigned participants to barberry or placebo groups was not blinded. The cardiologist and study staff confirmed eligibility criteria in patients, and the first appointment was arranged. In the first visit, the proposals of the research project fully were explained and written consent was obtained. A general information questionnaire, including anthropometrics, demographic information, disease history, the type and dosage of their medications, the smoking status and physical activity questionnaire were completed from each patient.

Then, participants were randomly allocated to either the barberry or the placebo group. Barberry and placebo in powder form were given to patients in small wrappers. Placebo and barberry powdered products delivered to participants in undetectable non-transparent wrappers. The placebo powder (PP) contained 9 g maltodextrin, 1 g citric acid, 1 g milled sucrose, and edible red color, and the barberry powder (BP) contained 10 g milled dried barberry and 1 g of milled sucrose). All dried barberry was obtained from the local market. To determine the total polyphenol content of the barberry, ethanol extract of dried barberry was prepared and then the total polyphenols were determined by the Folin–Ciocalteu spectrophotometric method (Zovko Koncic, Kremer, Karlovic, & Kosalec, 2010). Total polyphenol

content of the barberry used in the current study was 11.96 mg gallic acid equivalents per gram of dried food weight. Participants received 60 wrappers, each containing barberry or placebo powder for daily use. The daily amount of 10 g of barberry was selected based on a previous study by Shidfar et al. (2012) in which daily consumption of barberry extract obtained from 10 g of barberry was investigated. All participants were called biweekly to assess their compliance.

Participants were instructed to maintain their current dietary habits, physical activity levels, and the same type/dose of oral medication during this trial period.

2.3 | Randomization

Patients were randomly allocated to the barberry or placebo group. Block randomization with a block size of 4 was used with a 1:1 randomization between the two groups in each block, that is, each block consisted of two subjects for the barberry group and two subjects for the placebo group. The predetermined allocation sequence of each block was based on a sequence generated by using a random number table. Group allocation was accomplished by the patients' selection and opening of sealed envelopes containing a block.

2.4 | Biochemical assays

A 10-ml venous blood sample obtained in a 12-hr fasting state by the hospital lab technician and stored in a heparinized tube at the beginning and the end of the study. The platelet free plasma was separated by centrifugation (4,000 rpm for 20 min) and samples were stored at −80°C. For analysis, samples were thawed at room temperature and marker levels were measured with commercially available ELISA kits (R&D Systems for ICAM-1 and VCAM-1 and BioLegend, for MCP-1).

2.5 | Flow-mediated dilation

All brachial artery FMD measurement was performed by study radiologist (SA) by the method as previously described (Khandouzi, Zahedmehr, Mohammadzadeh, Sanati, & Nasrollahzadeh, 2019). The measurement was started after an overnight fasting state and at least 10 min rest. The patients were laid in the supine position in a quiet, temperature-controlled room, with the right arm in a comfortable position for imaging the brachial artery. Ultrasound imaging of the brachial artery was obtained with a non-automatic (manual) device using the iU22 xMATRIX color Doppler system with a 12-MHz linear array transducer (Philips Medical Systems, Canada, Product number: 795050). The scans were performed with a 3.5 MHz linear transducer. The brachial artery was scanned in a longitudinal section 2 cm above the antecubital fossa. The diameters of the vessel were measured from the anterior to the posterior interface between media and adventitia at a fixed distance from an anatomical marker. A baseline rest image was acquired and the arterial diameter was measured. A forearm blood-pressure cuff was placed distal to the antecubital fossa and inflated to at least 50 mmHg above systolic pressure for 5 min, followed by release. Ninety seconds after deflation of the cuff, a second scan was performed. Percentage FMD (%FMD) was calculated as $(d2 - d1)/d1 \times 100$ (d1: the brachial artery diameter at baseline; d2: brachial artery diameter after 90 s of cuff release). The radiologist was blinded to the patients' treatment group.

2.6 | Statistical analysis

The study sample size was calculated using FMD as the main outcome variable. A previous study, in which the effect of dietary intake of a polyphenol-rich juice (blackcurrant juice drink) was evaluated on FMD, generated an effect size, Cohen's *d* of 0.65 (Khan et al., 2014). Therefore, to detect an effect size of 0.65 at the 5% level of significance and with 80% power, 39 participants were needed in each arm of the two-arm trial. Allowing for an attrition rate of 10%, a total of 86 participants were screened at baseline.

All analyses were conducted using intention-to-treat. The baseline carry forward method was used to manage missing data. Data were analyzed using SPSS software (version 21.0, SPSS Inc., Chicago, IL). Data normality was determined by the Shapiro–Wilk test. To show the quantitative data, the mean and standard deviations used and to show the qualitative data frequency and percent used. Between-group differences were tested using independent *t*-test and chi-square (χ^2) test for quantitative and qualitative parameters. Changes from baseline values were analyzed by paired *t*-test. The 8-week values of FMD and inflammatory biomarkers were analyzed using analysis of covariance (ANCOVA) test with baseline values as a covariate. The Pearson correlation coefficient is used to measure the strength of a linear association between two variables.

3 | RESULTS

Among the 84 participants who entered, 78 subjects completed the study (39 in the barberry and 39 in the placebo group), with 6 dropouts arising from refusing to continue weeks after consumption, missing telephone responses, side effects (Figure 1). Patient compliance was good throughout the treatment period, and participants consumed more than 80% of the packages delivered to them.

As shown in Table 1, the baseline characteristics of the patients were not different between intervention and control groups. The mean age of the final participants was 54.12 ± 10.32. The age of the participants ranged from 21 to 65 years. About 45% of patients were male and 33% had a history of diabetes mellitus. All patients were prescribed different antihypertensive drugs.

All the treatments were well tolerated and only two potential side effects were reported throughout the study: two of the participants in the barberry group reported mild diarrhea; one volunteer in the placebo group reported bloating.

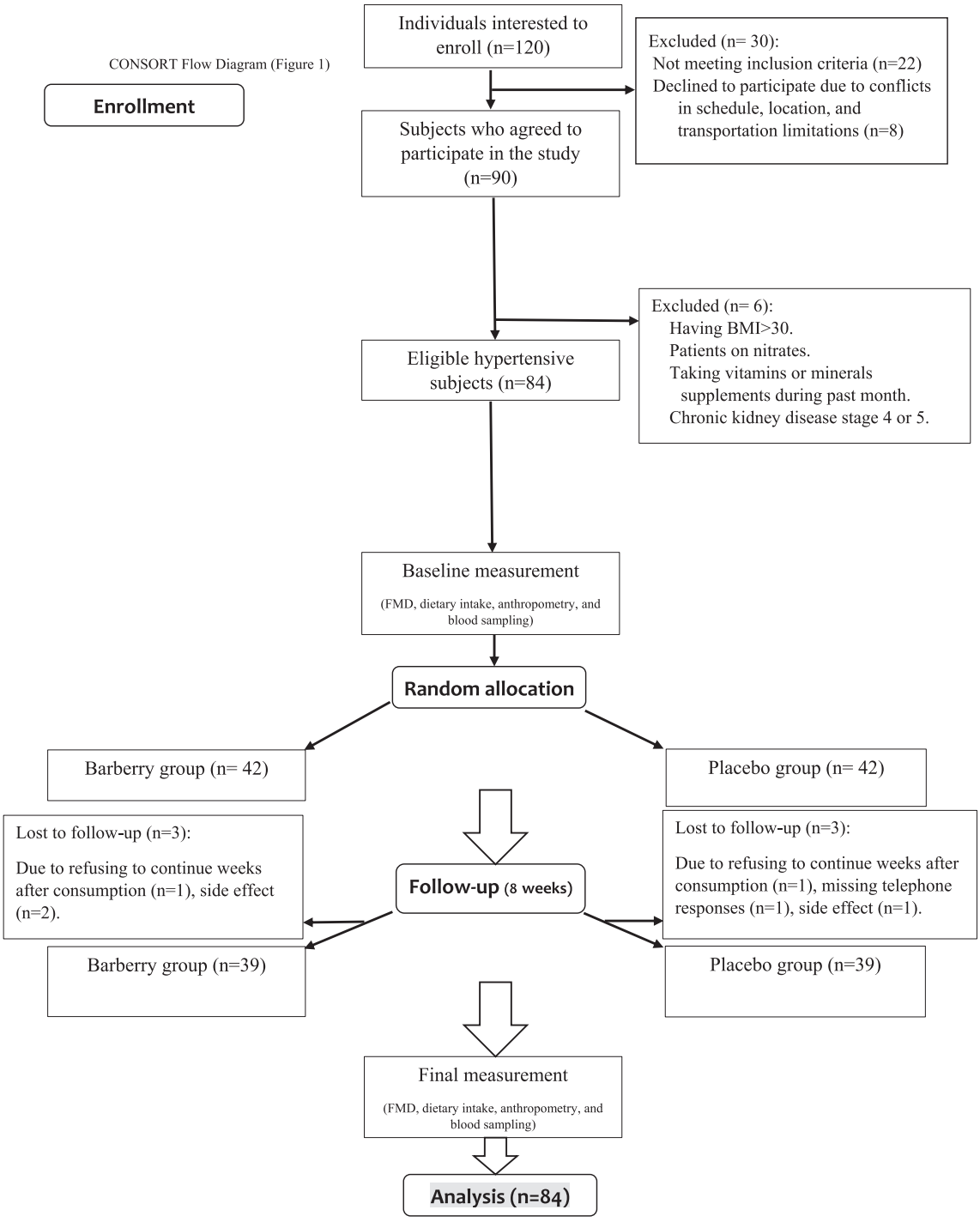

FIGURE 1 CONSORT flow diagram

Participants' body weight, BMI, and physical activity were similar between the two groups at the baseline and after 8 weeks (Table 2).

Brachial artery diameter and FMD were similar between the two groups at baseline. Baseline and 8-week values of brachial artery diameter were 4.53 ± 0.78 and 4.47 ± 0.81 mm. FMD was significantly increased in the barberry compared to placebo group (B [95% CI] was 6.54% [4.39, 8.70]; $p < .001$ and power = 1) (Table 3). We assessed the intra-observer variability of FMD measurement by measuring FMD of five participants at two different times. The mean and standard deviation of repeated measurements were 3.45 ± 0.91 and 3.73 ± 0.89 with a significant correlation coefficient ($r = 0.93$; $p < .001$) and the mean difference of 0.28 ± 0.32. This intra-observer variation was less than our founded effect of barberry on FMD.

As shown in Table 3, the plasma level of ICAM-1 was significantly reduced in the barberry group compared to the control group (B [95% CI] was −1.61 ng/ml [−2.74, −0.48]; $p = .006$ and power = 0.80).

TABLE 1 Baseline characteristics of the participants

Variable	Barberry group (n = 42)	Placebo group (n = 42)	p-value[a]
Age (years)	53.62 ± 10.34	54.50 ± 10.13	.69
Sex (male)	22 (52.4%)	16 (38.1%)	.18
Diabetes mellitus	14 (33.3%)	14 (33.3%)	1
Smoking	15 (35.7%)	12 (28.6%)	.48
Biguanides	13 (31.0%)	12 (28.6%)	.81
Insulin or insulin stimulatory drugs	5 (11.9%)	2 (4.0%)	.12
ACEI or ARB	23 (54.8%)	22 (52.4%)	.82
BB	20 (47.6%)	17 (40.5%)	.51
CCB	8 (19.0%)	6 (14.3%)	.55
Thiazide diuretics	4 (9.5%)	6 (14.3%)	.50
Loop diuretics	3 (7.1%)	1 (2.4%)	.30
Other drugs	10 (23.8%)	11 (26.2%)	.80

Note: Data represented as mean ± *SD* or frequency (percent).
Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, β-blocker; CCB, calcium channel blocker.
[a]Data were compared using independent *t* test or chi-square (χ^2) test.

TABLE 2 Body weight and physical activity of the participant at the baseline and after 8 weeks

Variable	Time	Barberry group (n = 42)	Placebo group (n = 42)	p-value[a]
Weight (kg)	Baseline	79.91 ± 13.52	75.42 ± 10.05	.08
	After 8 weeks	79.71 ± 13.27	75.46 ± 9.93	.10
BMI (kg/m^2)	Baseline	28.21 ± 2.03	27.83 ± 2.32	.42
	After 8 weeks	28.16 ± 1.96	27.85 ± 2.30	.51
Physical activity (MET-hr/day)	Baseline	27.0 ± 3.85	26.61 ± 3.62	.64
	After 8 weeks	27.38 ± 3.95	26.76 ± 3.90	.47

Note: All values are means ± *SD*.
[a]Data were compared using independent *t* test.

TABLE 3 Measures of vascular function and inflammatory markers

	Placebo group (n = 42)[a]		Barberry group (n = 42)[a]		B (95% confidence interval)[b]	p-value[c]	Estimated effect size[d]
Variable	Baseline	After 8 weeks	Baseline	After 8 weeks			
Brachial artery diameter (mm)	4.54 ± 0.81	4.46 ± 0.80	4.52 ± 0.76	4.49 ± 0.83	0.04 (– 0.11, 0.18)	.60	0.003
FMD (mm)	0.38 ± 0.29	0.37 ± 0.23	0.37 ± 0.28	0.65 ± 0.31	0.28 (0.19, 0.38)	<.001	0.29
FMD (%)	8.96 ± 7.18	8.49 ± 5.01	8.76 ± 6.98	14.93 ± 7.53	6.54 (4.39, 8.70)	<.001	0.31
ICAM-1 (ng/ml)	30.82 ± 4.29	31.49 ± 4.37	30.53 ± 5.32	29.58 ± 6.58	–1.61 (–2.74, –0.48)	.006	0.09
VCAM-1 (ng/ml)	26.52 ± 1.76	26.77 ± 1.86	25.90 ± 2.16	26.13 ± 3.17	–0.04 (–0.82, 0.74)	.91	0
MCP-1 (pg/ml)	192.70 ± 83.78	242.23 ± 109.54	226.25 ± 130.15	231.65 ± 125.37	–37.62 (–72.07, – 3.17)	.033	0.05

Abbreviations: FMD, flow-mediated dilation; ICAM-1, intercellular adhesion molecule 1; MCP-1, monocyte chemoattractant protein 1; VCAM-1, vascular cell adhesion molecule 1.
[a]Values are mean ± *SD*.
[b]Beta values (B) represents the difference between the means of the groups.
[c]The 8-week values were analyzed using ANCOVA test with baseline values as a covariate.
[d]Partial Eta squared.

TABLE 4 The correlation between changes in FMD and inflammatory markers

		Δ ICAM-1	Δ VCAM-1	Δ MCP-1
Δ FMD	*r*	−0.30	0.008	−0.10
	p-value	.005	.94	.34

Note: The correlations were analyzed using Pearson correlation test.
Δ indicates change from baseline values.
Abbreviations: FMD, flow-mediated dilation; ICAM-1, intercellular adhesion molecule 1; MCP-1, monocyte chemoattractant protein 1; VCAM-1, vascular cell adhesion molecule 1.

MCP-1 was significantly lower in the barberry group compared to the placebo group (B [95% CI] was −37.62 pg/ml [−72.07, −3.17]; p = .033 and power = 0.57). The intervention had no effect on VCAM-1 plasma values.

To explore the relationship between the FMD results and plasma vascular inflammation biomarkers, the correlation was analyzed. The changes in FMD measured after an 8-week intervention were negatively correlated with the corresponding changes in plasma ICAM-1 (r = −0.30; p = .005). No significant correlations were found between the FMD results and plasma VCAM-1 or MCP-1 (r = 0.008; p = .94 and r = −0.10; p = .34, respectively) (Table 4).

4 | DISCUSSION

This clinical trial examined the effect of barberry (*B. vulgaris*) consumption on FMD and inflammatory biomarkers in patients with hypertension. We found that barberry consumption significantly improved the vascular endothelial function assessed by FMD. The observed absolute change of 6.54% in FMD in the barberry compared to placebo group could have potential clinical relevance. The results from meta-analyses have shown that FMD is inversely associated with future CVD events (Matsuzawa, Kwon, Lennon, Lerman, & Lerman, 2015; Ras, Streppel, Draijer, & Zock, 2013). In an analysis by Ras et al. (2013) in which 23 studies were included in the meta-analysis, the pooled overall CVD risk was 0.92 per 1% higher FMD. In addition to improved FMD, barberry consumption also decreased the circulating level of ICAM-1, and also improved MCP-1 levels compared to the placebo group. The observed improvement in the level of inflammatory factors may have contributed to FMD enhancement. The endothelium has been identified as a key regulator of endothelial function. Impaired endothelial function predisposes the vasculature to vasoconstriction and leukocyte adherence (Della Corte et al., 2016). A stable relation between clinical measures of endothelial function including FMD and circulating biomarkers of vascular inflammation such as ICAM-1 levels has been observed (Witte et al., 2003). Therefore, reduced circulating ICAM-1 levels following the consumption of barberry may have partly contributed to improving FMD in the study population as shown by the significant negative correlation between changes in plasma ICAM-1 and FMD. In contrast, we did not observe any significant change in VCAM-1. The metabolism of polyphenols in barberry may result in formation of in vivo metabolites that are primarily effective on ICAM-1 rather than VCAM-1. In this regard, it has been shown that different chemical modifications of the same flavonoid molecule can significantly alter their biological responses, in order that some chemical changes may promote changes in ICAM-1 levels but have no effect on VCAM-1 (Lotito, Zhang, Yang, Crozier, & Frei, 2011). One other reason for the lack of significant improvement in circulating VCAM-1 levels could be due to the short duration of the study. No previous study has analyzed the effects of dietary intake of barberry on vascular endothelial function or cell adhesion molecules. Consumption of barberry juice (200 ml/day, with total polyphenol content of 2,403 mg gallic acid equivalent per litter of juice) for 8 weeks led to improve some cardiovascular risk factors, including blood pressure in patients with type 2 diabetes (Lazavi et al., 2018). However, in comparison, the sample size of the present study was larger and focused specifically on endothelial function and related inflammatory factors. Since barberry is a rich source of phenolic compounds (Sarraf, Beig Babaei, & Naji-Tabasi, 2019), the effects observed in this study could be compared with those obtained in studies of similar foods with a high content of polyphenols. Regular consumption of polyphenol-rich foods has been associated with improvement in vascular function (Emamat, Tangestani, Totmaj, Ghalandari, & Nasrollahzadeh, 2020; Matute et al., 2020; Wood, Hein, Heiss, Williams, & Rodriguez-Mateos, 2019). Regarding vascular inflammatory markers, our results agree with some of the data of Monagas et al. (2009) and Kurlandsky and Stote (2006), who found a decrease in circulating ICAM-1, with no significant change in the soluble adhesion molecule VCAM-1 after the intake of polyphenol-rich foods.

Although, it is not certain whether native polyphenol compounds or the metabolites are the active components in barberry, polyphenols present in barberries may have mediated improvements in vascular function. Barberry's fruits contain significant amounts of anthocyanin (0.69 mg/g) (Sarraf et al., 2019). In a meta-analysis in which the effect of anthocyanins rich foods and extracts was evaluated on functional measures of vascular health showed that both acute and chronic anthocyanin supplementation improves vascular reactivity, measured by FMD (36). One likely mechanism may be related to the antioxidant properties of polyphenols (Khan et al., 2014; Loffredo et al., 2017). Increased oxidative stress and reduced nitric oxide (NO) bioavailability are important contributing factors in the pathogenesis of endothelial dysfunction. Reduction in oxidative stress may improve the NO level in endothelial cells and such improvement could contribute to the augmentation of FMD (Heiss, Rodriguez-Mateos, & Kelm, 2015). Barberry consumption (600 mg dried barberry/day) for 6 weeks has been shown to improve the pro-oxidant–antioxidant balance of subjects with metabolic syndrome (Mohammadi et al., 2014). Berberine, an alkaloid compound has been identified in barberry (Sarraf et al., 2019). In-vitro studies have shown that berberine ameliorates endothelial dysfunction via regulating reactive oxygen species (ROS)/NO balance (Feng et al., 2019). Berberine reduces oxidized low-density lipoprotein (oxLDL)-stimulated production of ROS in human umbilical vein endothelial cells (HUVECs) (Hsieh et al., 2007).

In the cell injury model induced by palmitic acid incubation, berberine increased endothelial nitric oxide synthase (eNOS) expression and promoted NO production in HUVECs (Zhang et al., 2013). Furthermore, the berberine may partly mediate antiinflammatory effects. Berberine has inhibited the expression of ICAM-1 and MCP-1 in cultured human aortic endothelial cells. Berberine has been reported to reduce oxLDL-induced monocyte adhesion to HUVECs via suppression of adhesion molecule expression, including VCAM-1 and ICAM-1 (Huang, Chen, Liao, Zhu, & Xue, 2016).

The present study had some limitations. An 8 weeks period provides no information about the sustainability of the observed effects. Furthermore, we did not measure metabolites of phenolic compounds in the urine or plasma, which could provide useful information about the absorption and metabolism of polyphenols (Spencer, Abd El Mohsen, Minihane, & Mathers, 2007). However, it can be assumed that barberry consumption has increased plasma levels of polyphenols. In a previous study, dietary consumption of berry products has resulted in increases in plasma polyphenols (Erlund et al., 2008). Besides, although FMD is considered to be superior to the other noninvasive endothelial function assessing techniques, its measurement is highly operator dependent and therefore can increase the possibility of type two error (Deanfield, Halcox, & Rabelink, 2007). This study also had some strength, such as its design, good completion rates, and good compliance with supplemental barberry.

5 | CONCLUSION

Our results indicate that barberry consumption improves vascular endothelial function assessed by FMD and has a beneficial effect on plasma ICAM-1 and MCP-1 in hypertensive patients. Therefore, consumption of 10 g dried barberry could be suggested to those aiming to improve their cardiovascular health. The findings suggest that further evaluation of barberry intake for cardiovascular risk reduction in a larger study may be worthwhile.

ACKNOWLEDGMENTS

The study was supported by National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Sciences, Tehran, Iran. We thank the radiology ward personnel of Shahid Rajaei Hospital. We are also grateful to the volunteers who participated in the study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Javad Nasrollahzadeh and Hadi Emamat conceptualized the study and wrote the manuscript. Hadi Emamat, Javad Nasrollahzadeh, Sanaz Asadian, and Ali Zahedmehr conducted the research. Matin Ghanavati contributed to drafting of the manuscript. All authors approved the final version of the manuscript.

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How to cite this article: Emamat H, Asadian S, Zahedmehr A, Ghanavati M, Nasrollahzadeh J. The effect of barberry (*Berberis vulgaris*) consumption on flow-mediated dilation and inflammatory biomarkers in patients with hypertension: A randomized controlled trial. *Phytotherapy Research*. 2021;35: 2607–2615. https://doi.org/10.1002/ptr.7000