Vasorelaxant and blood pressure lowering effects of *alchemilla vulgaris*: A comparative study of methanol and aqueous extracts

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ABSTRACT

Background: In the last decade, a growing interest particularly in determining the cardiovascular effects of herbal extracts took place among researchers. Objective: Herein, we aimed to investigate the microvascular and blood pressure lowering effects of two differently processed extracts of the same herb, *Alchemilla vulgaris* (Rosaceaea), which was revealed to contain high levels of vasoactive compounds. **Materials and Methods:** For the purpose, endothelium intact rat mesenteric arteries were mounted in a myograph system and contracted with prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$: 3×10^{-5} M) or potassium chloride (K^+: 40 mM). Then, aqueous and methanol extracts were added at 0.01–10 mg/ml concentrations in a cumulative manner. **Results:** Both extracts produced relaxations in $PGF_{2\alpha}$ (3×10^{-5} M) precontracted arteries which were insensitive to the inhibitors of endothelium derived vasoactive substances namely, L^G-nitro-L-arginine (10^{-4} M), ODQ (10^{-5} M) and indomethacin (10^{-5} M) or removal of endothelium. Opposite vascular effects were observed when extracts were applied in K^+ precontracted arteries. In addition, oral administration of the methanol extract of *Alchemilla vulgaris,* but not the aqueous extract, reduced blood pressure significantly in L-NAME hypertensive rats. **Conclusion:** Our results demonstrated that the methanol extract of *Alchemilla vulgaris* has more prominent and favourable vascular effects in normal and experimental hypertensive conditions reinforcing its traditional use in cardiovascular disorders, in particular hypertension. These results most likely give rise to further studies to reveal its mechanism of action and clinical value of this herb.

Key words: *Alchemilla vulgaris,* blood pressure, extract, mesenteric artery, vasodilatation

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INTRODUCTION

Hypertension is the leading cause of mortality and morbidity, especially in developing countries. In the last decade, a growing interest particularly in determining the cardiovascular effects of herbal extracts took place among researchers. In several experimental studies, the plant extracts rich in polyphenolic compounds and flavonoids were shown to induce vasorelaxant, antioxidant and hypotensive effects.[1,2]

Alchemilla vulgaris (*A. vulgaris*; lady's mantle), a member of the Rosaceaea family, has traditionally been used to treat bleeding, eczema, inflammation, diarrhoea, ulcers, skin rashes, menstruation disorders and oedema in Europe.[3,4] It is also used as herbal tea for hypertension[5,6] and as infusion for diabetes.[7] Liquid extracts of *A. vulgaris* were shown to contain flavonoid glycosides composed of quercetin derivatives[3] and gallic acid.[4] It is very well known that the amount of bioactive compounds in plant extracts is subject to change according to several factors such as growth stages, cultivation, insect invasion, season of collection and the method of extraction.[8] In order to obtain standardization in medicinal plant extracts, all these factors especially the method of extraction should be under rigorous control. Indeed, a comparative study evaluating the effects of two differently processed extracts of the same herb parallelly in *in vitro* and *in vivo* experimentation is scarcely documented so far.[9] Herein, we compared the effects of aqueous and methanol extracts of *A. vulgaris* on systolic blood pressure and isolated microvessels of rats.

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We recently determined that, the methanol and aqueous extracts of *A. vulgaris* display opposite vascular effects, i.e. relaxation versus contraction, respectively, on isolated rat thoracic aorta possibly due to their different phenolic contents. In relation, total flavonoid and quercetin amount was found much higher in the methanol extract while gallic acid in the aqueous extracts.[10] Quercetin, the most abundant flavonoid in medicinal plants, also in *A. vulgaris*, was demonstrated to improve endothelium-dependent relaxation and reduce the contractile responses in rat thoracic aortas.[11,12] It was suggested to be more potent in mesenteric vascular bed compared to aorta[13] and decrease the elevated blood pressure noticeably when given orally.[14] Hence, in this study, we first aimed to identify the effectiveness of two differently processed extracts of *A. vulgaris* in small resistance arterial tone, which contribute importantly to the modulation of blood pressure, by comparing the direct effects of methanol and aqueous extracts in isolated rat mesenteric arteries. Then, in order to clarify the possible preventive influence of *A. vulgaris* on the elevation of blood pressure, the effects of orally administered methanol and aqueous extracts were determined on systolic blood pressure in L-NAME induced hypertensive rats.

MATERIALS AND METHODS

Preparation of extracts

To obtain methanol extract, the dried aerial parts of *A. vulgaris* herb (product no: 22140), purchased from Jacob Hooy and Co. BV in the Netherlands, exhausted in Soxhlet apparatus for 18 h and lyophilized after condensation in rotavopor. For the aqueous extract, plant material let to maceration at room temperature for 24 h. Then, under reverse refrigerant water bath exhausted for 6 h and lyophilized after blowing of the water. The major vasoactive constituents in methanol and aqueous extracts of *Alchemilla vulgaris* were previously determined by HPLC-DAD analysis.[10]

Characteristics of the animals

Male Wistar albino rats with an average weight of 200-250 g (10-12 weeks) were used. The animals were obtained from Experimental Medicine and Research Institute (DETAE) of Istanbul University and all experimental procedures utilized were approved by Local Animal Experimentation Ethics Committee of Istanbul University (04/11/2010, decision no: 161). Rats were housed under standard temperature of 20°C ± 2°C and humidity of 60-70% on a 12:12 h light/dark cycle with free access to standard rat chow and tap water.

Myograph experiments

The rats were sacrificed by stunning followed by decapitation. The mesenteric arteries were carefully excised and placed in cold Krebs Ringer-bicarbonate solution of the following composition (mM): NaCl 118, KCl 4.7, KH_2PO_4 1.2, $NaHCO_3$ 25, $MgSO_4.7H_2O$ 1.2, $CaCl_2$ 2.5, glucose 10 and disodium EDTA 0.026. Mesenteric arteries were cleaned of fat and surrounding tissues under a stereomicroscope (Model 2000, Zeiss, Germany). Four mesenteric artery preparations were mounted in parallel in a multichamber wire Myograph System (Model 610M, DMT, Aarhus, Denmark). Two stainless steel wires 40μm in diameter were treaded into the lumen of mesenteric arteries and then fixed to the mounting devices of a force transducer and a micrometer. The mesenteric arteries were equilibrated for 1 h in Krebs-Ringer bicarbonate solution at 37°C and gassed with 5% CO_2 + 95% O_2 (pH = 7.4). Thereafter, mesenteric arteries were set to a normalized internal circumference L_1 ($0.9L_{100}$) in accordance to passive wall tension–internal circumference relationship under a passive transmural pressure of 100 mmHg.[15] Normalized mesenteric arteries were contracted twice with potassium chloride (K^+; 120 mM) plus noradrenaline (NA; 10^{-4} M) to check the viability and standardization of the preparations. Preparations which developed a tension less than 0.5 mN/mm were discarded. Following the standardization, concentration-response curves of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha;}$ 10^{-8}–10^{-4} M) and K^+ (10-120 mM) were obtained. The presence of functional endothelium and the vascular relaxation capacities of the vessels were checked by the cumulative administration of acetylcholine (Ach; 10^{-8}–10^{-4} M) and sodium nitroprusside (SNP; 10^{-8}–10^{-4} M) to induce relaxation on $PGF_{2\alpha}$ (3×10^{-5}M) contracted mesenteric arteries.

The direct vascular effects of *A. vulgaris* extracts were investigated in mesenteric arteries of rats precontracted with differently acting contractile agents namely; $PGF_{2\alpha}$ (3×10^{-5} M) or K^+ (40 mM). Increasing concentrations (0.01-10 mg/ml) of the extracts were administered cumulatively when the contractions to $PGF_{2\alpha}$ or K^+ reached a plateau. The role of endothelium in vascular relaxant effects of the extracts were investigated in mesenteric arteries removed of endothelium or pretreated with putative inhibitors of endothelial vasodilators such as, nitric oxide (NO) synthase inhibitor, L^G-nitro-L-arginine (L-NOARG, 10^{-4} M), guanylate cyclase inhibitor, ODQ (10^{-5} M) or cyclooxygenase inhibitor, indomethacin (10^{-5} M) for 20 min.[16]

In separate sets of experiments, the effects of both extracts on the contractile reactivity of mesenteric arteries were examined. In these experiments, concentration-response curves of $PGF_{2\alpha}$ (10^{-8}-10^{-4} M) and K^+ (10-120 mM) were obtained both in the presence and absence of the extracts and compared each other. For the purpose, mesenteric arteries were pretreated either with extracts (10 mg/ml) or vehicle (Krebs) for 20 min.

In vivo experiments

Rats were randomly divided into four groups. Group 1 served as control and received tap water for 5 weeks. Group 2, 3 and 4 received nonselective NO synthase inhibitor, L-NAME (60 mg/kg/day) for 5 weeks. Group 3 received methanol extract (300 mg/kg/day) and group 4 received aqueous extract (300 mg/kg/day)[17] for 2 weeks, starting at the 3rd week of L-NAME (60 mg/kg/day) administrations. L-NAME was freshly prepared on each day and administrated in 35-40 ml of tap water which was determined as the daily water consumed per rat in our preliminary experiments. Each extract was given orally by intragastric gavage under light ether anaesthesia. Systolic blood pressure was measured by tail-cuff (PowerLab, ADInstruments, United Kingdom) and averages of four consecutive pressure measurements were calculated.

Chemicals

All drugs used in the experiments were purchased from Sigma-Aldrich (Taufkirchen, Germany) except for ODQ (Tocris, Germany). The stock solutions of ODQ were prepared in dimethylsulfoxide whereas indomethacin was prepared in 5% (w/v) sodium bicarbonate solution. Acetylcholine and noradrenaline were dissolved in 0.001 N HCl and ascorbic acid (1 mg/ml) was added to noradrenaline solution to prevent oxidation. All other drugs as well as methanol and aqueous extracts of *A. vulgaris* were dissolved in distilled water.

Statistical analysis

Data were presented as "mean ± standard error of the mean" while "n" is the number of rats or mesenteric artery rings used in the experiments. The contractile responses to spasmogens were expressed as "mN/mm". The relaxant responses were indicated as "%" decreases while the contractile responses were expressed as "%" increases of the precontractile tone. Sensitivities of the arteries to spasmogens and dilators were calculated as the effective concentration that elicit 50% of the maximal response (pD_2) by using nonlinear regression curve fit and expressed as "–Log EC_{50}". Statistical analyses were determined by Student's paired and unpaired *t*-tests as well as by one-way analysis of variance (ANOVA) followed by Tukey Kramer *post-hoc* test where appropriate. A "$P < 0.05$" was considered statistically significant.

RESULTS

Characteristics of mesenteric arteries

The length (1.73 ± 0.02 mm) and internal diameter (280.60 ± 7.83 μm) of rat mesenteric arteries used in the experiments were all comparable within the preparations ($n = 36$). The maximal relaxant responses to Ach and SNP were determined as 93.08 ± 1.73% and 90.20 ± 1.49% ($n = 36$), respectively. In endothelium denuded rings, the maximal relaxation to Ach was abolished (8.54 ± 2.5%, $n = 12$, $P < 0.05$) whereas no change was observed in the response to SNP (90.21 ± 2.02%, $n = 12$, $P > 0.05$).

Effects of methanol and aqueous extracts

Cumulative addition of methanol and aqueous extracts (0.01-10 mg/ml) to the myograph system, produced concentration-dependent relaxations in mesenteric arteries precontracted submaximally with $PGF_{2\alpha}$ (3×10^{-5}M: 1.07 ± 0.17 mN/mm and 1.04 ± 0.15 mN/mm, $n = 8$, respectively, $P > 0.05$). The maximal relaxation responses to the methanol (E_{max}: 80.86 ±3.01%, $n = 8$) and aqueous extracts (E_{max}: 79.68 ± 4.26%, $n = 8$) of *A. vulgaris* were comparable [Figure 1a]. On the other hand, cumulative addition of the methanol extract (0.01-10mg/ml) produced concentration-dependent relaxations (E_{max}: 62.68 ± 9.29%, $n = 7$) whereas the aqueous extract induced contractions (E_{max}: 37.29 ± 6.27%, $n = 10$) in mesenteric arteries precontracted with K^+ (40 mM) [Figure 1b]. In these experiments, the precontraction level obtained with K^+ (40 mM: 1.00 ± 0.10 mN/mm, $n = 7$ and 0.79 ± 0.10 mN/mm, $n = 10$, respectively, $P > 0.05$) were comparable in mesenteric arteries.

The role of endothelium and endothelium-derived vasodilator factors

Incubation of mesenteric arteries with L-NOARG (10^{-4} M), ODQ (10^{-5} M) and indomethacin (10^{-5} M) for 20 min or removal of the endothelium, did not significantly modify the relaxation responses obtained with the methanol extract of *A. vulgaris* [Figure 2]. Similar results were obtained on the relaxation responses of the aqueous extract either in the presence of these inhibitors or after the removal of endothelium [Figure 3].

Effects of the methanol and aqueous extracts on vascular reactivity

In mesenteric arteries pretreated with methanol extract (10 mg/ml, 20 min) the maximum contractile

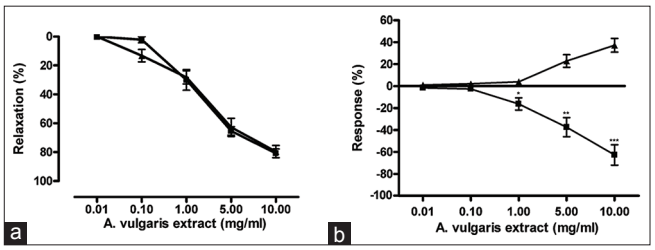

Figure 1: The effects of methanol (■) and aqueous extracts (▲) of *Alchemilla vulgaris* (0.01-10 mg/ml) on (a) $PGF_{2\alpha}$ (3×10^{-5} M) or (b) K^+ (40 mM) precontracted rat mesenteric arteries. n = 7-10. **P* < 0.05, ***P* < 0.01 and ****P* < 0.001 versus aqueous extract analysis of variance

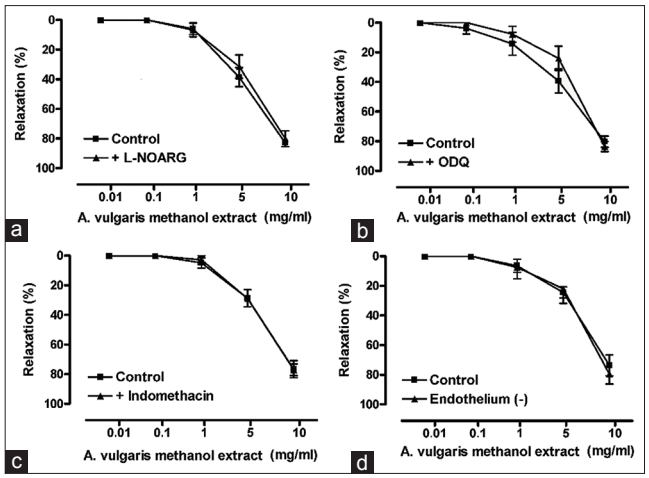

Figure 2: The effects of nitric oxide synthase inhibitor, LG-nitro-L-arginine (10-4 M), guanylate cyclase inhibitor, ODQ (10^{-5} M), cyclooxygenase inhibitor, indomethacin (10^{-5} M) or removal of endothelium on the responses induced by methanol extract of *Alchemilla vulgaris* (0.01–10 mg/ml) in rat mesenteric arteries precontracted with $PGF_{2\alpha}$ (3×10^{-5} M). n = 6–8. $P > 0.05$ versus corresponding control, paired Student's *t*-test

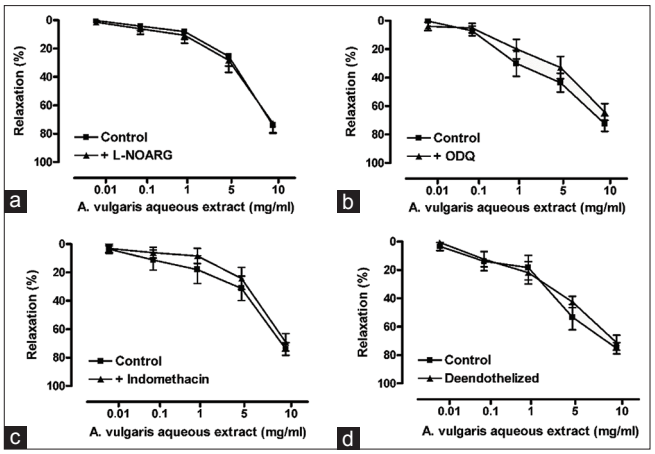

Figure 3 : The effects of nitric oxide synthase inhibitor, LG-nitro-L-arginine (10^{-4} M), guanylate cyclase inhibitor, ODQ (10^{-5} M), cyclooxygenase inhibitor, indomethacin (10^{-5} M) or removal of endothelium on the responses induced by aqueous extract of *Alchemilla vulgaris* (0.01–10 mg/ml) in rat mesenteric arteries precontracted with $PGF_{2\alpha}$ (3×10^{-5} M). n = 6–8. $P > 0.05$ versus corresponding control, paired Student's *t*-test

responses of $PGF_{2\alpha}$ and K^+ were significantly reduced. There was also a significant reduction in pD_2 value of $PGF_{2\alpha}$ but not that of K^+. On the other hand, pretreatment of the mesenteric arteries with the aqueous extract (10 mg/ml, 20 min) of *A. vulgaris* significantly decreased the maximum contractile response of $PGF_{2\alpha}$ although an increase was observed in the maximum contraction level of K^+. While, the pD_2 values of $PGF_{2\alpha}$ and K^+ were comparable [Table 1].

Effects on blood pressure levels in L-NAME-induced hypertensive rats

Daily administration of L-NAME to the rats significantly increased systolic blood pressure levels compared to the age-matched controls. Chronic treatment of rats with methanol extract (300 mg/kg/day) for 2 weeks with the continued administration of L-NAME, statistically significant decreased the blood pressure level compared to untreated L-NAME induced hypertensive rats. However, treatment with the aqueous extract (300 mg/kg/day) for 2 weeks was ineffective to decrease significantly the elevated blood pressure in L-NAME induced hypertensive rats although; a partial prevention was notable in the gradual increase of systolic blood pressure [Table 2].

Table 1: The maximum contractile response (E_{max}: mN/mm) and pD_2 values of $PGF_{2\alpha}$ and K^+ in the presence or absence of methanol (+M.E.) and aqueous (+A.E.) extracts of *A. vulgaris*

	$PGF_{2\alpha}$		K^+	
	E_{max}	pD_2	E_{max}	pD_2
Control	2.92±0.48	4.80±0.09	1.38±0.17	1.16±0.03
+M.E.(10 mg/ml)	1.39±0.43*	4.58±0.09	1.14±0.13***	1.17±0.03
Control	2.56±0.17	4.89±0.12	1.14±0.12	1.29±0.04
+A.E.(10 mg/ml)	1.67±0.41***	4.79±0.12	2.05±0.11***	1.33±0.04

*P<0.05 and ***P<0.001 versus corresponding controls, ANOVA. Data are presented as mean±SEM; n=8-10. SEM: Standard error of the mean; $PGF_{2\alpha}$: Prostaglandin $F_{2\alpha}$; *A. vulgaris: Alchemilla vulgaris*

Table 2: Blood pressure (mm/Hg) levels of control, L-NAME induced hypertensive and methanol (+M.E.) and aqueous (A.E.) extracts of *A. vulgaris* treated rats

	Blood pressure (mmHg)		
	1st week	3rd week	5th week
Control	84.44±6.38	86.07±5.52	83.04±4.62
L-NAME	94.95±5.25	139.70±5.91*	156.50±2.76*
L-NAME+M.E.	85.60±7.02	142.50±2.97*	119.60±2.50*#
L-NAME+A.E.	86.68±6.26	146.87±3.74*	138.50±2.14*

*P<0.05 versus corresponding control; #P<0.05 compared to the 5th week of L-NAME hypertensive rats. ANOVA followed by Tukey Kramer *post-hoc* test. Data are presented as mean±SEM. n=6-7. SEM: Standard error of the mean; *A. vulgaris: Alchemilla vulgaris*

DISCUSSION

In recent years a growing interest took place in the alternative therapies due to the increased evidence of drug related problems including ineffectiveness, low efficacy, developing resistance or serious adverse effects. In relation, many researchers paid more attention to investigate the effectiveness of medicinal plants especially rich in polyphenolic compounds and vasoactive flavonoids in disease conditions. Supportively, it was revealed that consumption of polyphenolic compounds and flavonoids

in the diet decrease the risk of cardiovascular diseases.[2] Besides, in several experimental studies favourable effects of polyphenolic compounds and flavonoids in terms of antioxidant, antiinflammatory, vasorelaxant and blood pressure lowering effects were demonstrated.[11,13,18] In studies investigating the pharmacological effects of medicinal plants generally liquid extracts that prepared by different extraction methods are used. As the vasoactive compound ingredient and their amounts determined in the plant extracts could vary in accordance to the extraction methods, evaluating the pharmacological effects of two differently processed extracts of the same herb is important for an accurate assessment. In this study, we investigated the effects of methanol and aqueous extracts of *A. vulgaris* paralelly in an *in vitro* and *in vivo* experimentation performed in rats, i.e. influences on isolated microvessels and systolic blood pressure. Herein, we originally found that (1) the methanol extract of *A. vulgaris,* induced a pronounced vasorelaxation response either in $PGF_{2\alpha}$ or K^+ precontracted rat mesenteric arteries whereas, the aqueous extract induced contrasting effects depending on the contractile agent used to increase vascular tone (2) in $PGF_{2\alpha}$ precontracted mesenteric arteries the relaxation responses obtained with methanol and aqueous extracts of *A. vulgaris* were independent from the endothelium and endothelial vasodilators (3) *in vitro* pretreatment effects of methanol and aqueous extracts on the contractile reactivity to spasmogens were reinforcing their direct influences on rat mesenteric arteries (4) oral administration of the methanol extract (10 mg/ml) for 2 weeks reduced the elevated blood pressure in L-NAME hypertensive rats whereas the aqueous extract (10 mg/ml) did not have a prominent effect.

$PGF_{2\alpha}$ and K^+ are spasmogens acting via different cellular mechanisms. $PGF_{2\alpha}$ constricts arteries mainly through the activation of receptor-operated calcium channels whereas K^+ induces contraction by depolarization of vascular smooth muscle cell membrane to provide Ca^{+2} influxes.[19] Our findings revealed that the methanol and aqueous extracts of *A. vulgaris* display similar relaxation responses against the receptor-operated spasmogen mediated contraction. Interestingly, contrasting effect, in terms of relaxation versus contraction, were obtained with these extracts when a receptor-independent spasmogen was used to induce contraction in isolated mesenteric arteries. Indeed, this diverse direct effectiveness of the extracts was supported with the findings obtained in pretreatment experiments. Thus, in parallel to acute vascular effects, pretreatment of rat mesenteric arteries with either methanol or aqueous extract (10 mg/ml, 20 min.) reduced significantly the maximal contractile response to $PGF_{2\alpha}$ whereas, opposite effects were observed against the vasoreactivity to K^+. Hence, our results demonstrated that methanol and aqueous extracts of *A. vulgaris* is effective in decreasing the vascular contractile tone induced by $PGF_{2\alpha}$ while, the aqueous extract evoked an increase in the contractility in particular, to a receptor independent spasmogen in rat mesenteric arteries.

Different responses obtained with the methanol and aqueous extracts of *A. vulgaris* in rat mesenteric arteries might be related with the differences in the phenolic composition of the extracts. The liquid extracts of *A. vulgaris* were previously shown to contain flavonoid glycosides composed of quercetin derivatives[3] and gallic acid.[4] Supportively, in our recent study, we also determined that the flavonoid amount of *A. vulgaris* is much higher in the methanol than the aqueous extract and as analysed by HPLC-DAD both extracts contained quercetin and gallic acid as the major vasoactive constituents.[10] Of these constituents, quercetin was demonstrated to induce relaxations[11] whereas; gallic acid was reported to produce contractions in isolated rat aorta.[20] Indeed, all these previous data are supporting our current findings in rat mesenteric arteries. Thus, much higher gallic acid content of the aqueous extract compared to the methanol extract might be one of the mechanisms that mediate its contractile responses in mesenteric arteries. Interestingly, opposite vascular effects of the extracts were apparent especially in K^+ precontracted arteries. Thus, it is possible that the vascular activity of flavonoids in the aqueous extract is diminished or abolished in the presence of high K^+. Besides, we also noticed that the maximal relaxation response to methanol extract was significantly diminished in K^+ precontracted mesenteric arteries compared to $PGF_{2\alpha}$ contracted arteries. Previously, weak or negligible vasorelaxant effects of several flavonoids, including quercetin, has been reported in K^+ contracted rat aortic rings in contrary to the pronounced relaxations against phenylephrine induced contractions.[21] Then, in concern with quercetin, it was suggested that the presence of -OH substitution at C-5 atom increases its selectivity towards a receptor operated spasmogen compared to a nonreceptor operated spasmogen, i.e. K^+.[21] This interpretation likely to support the differences in the relaxant responses of methanol extract, which contain quercetin as the major flavonoid, between $PGF_{2\alpha}$ and K^+ precontracted mesenteric arteries. Concerning the aqueous extract, high amount of gallic acid content in addition to the aforementioned low effectiveness of quercetin in the presence of high K^+ possibly explains its contractile influence in K^+ precontracted mesenteric arteries. Moreover, it is also known that relaxant properties of vasoactive substances acting via opening K^+ channels are remarkably diminished at high K^+ contractions.[22] Comparatively, the diminished or abolished relaxant influences of the methanol and aqueous extracts, respectively, in K^+ contracted arteries

may also suggest the involvement of K^+ channel activation in their mechanism of action which requires further investigation.

The vascular endothelium controls vascular tone via release of relaxant and contractile factors.[23] In the present study, we tested the probable role of endothelium in the vascular effects of the extracts. The relaxation responses to methanol and aqueous extracts were not changed in the presence of putative inhibitors of endothelium namely, L-NOARG, ODQ and indomethacin, in rat mesenteric arteries. The results obtained in endothelium denuded mesenteric arteries were also in parallel. These findings suggested that the endothelial vasodilators, namely, NO and prostacyclin probably do not mediate the acute relaxant effects of the methanol and aqueous extracts of *A. vulgaris* in mesenteric arteries. In literature, the relaxant effects of various flavonoids have been reported to be mediated either endothelium dependent[21] or independent[24] mechanisms. Quercetin, which is found in both extracts, was shown to induce endothelium-independent relaxations in isolated resistance mesenteric vascular bed.[13] In addition, vasorelaxing effects of several flavonoids including quercetin, were reported to be inhibited in the presence of K^+ channel blockers.[25] Hence, it is reasonable to suggest that K^+ channel activation may contribute to the endothelium-independent relaxant effects of *A. vulgaris* extracts in mesenteric arteries which is one of the goal of our further investigation.

The preventive role of long term *A. vulgaris* treatment on increased blood pressure was evaluated in L-NAME induced hypertensive rats. Oral administration of the methanol extracts but not the aqueous extract for 2 weeks significantly diminished the elevated blood pressure in accordance to its vasorelaxant effects in mesenteric arteries. We suggested that the prominent vascular relaxant and blood pressure lowering effects of the methanol extract of *A. vulgaris* is possibly due to its high flavonoid content, in particular quercetin. While, ineffectiveness in lowering blood pressure in L-NAME induced hypertensive rats as well as the augmentation of the contractile tone in the K^+ contracted arteries with the aqueous extract of *A. vulgaris* could be related to its low flavonoid content and high amount of gallic acid. Thus, the varying vascular effects of the aqueous and methanol extracts of *A. vulgaris* in rat mesenteric arteries either *in vitro* or *in vivo* experimentation is most likely to be related to distinct flavonoid composition resulted from different extraction process.

In conclusion, our results demonstrated that the methanol extract of *A. vulgaris* has more prominent and favourable vascular effects in normal and experimentally hypertensive conditions. The methanol extract instead of aqueous extract might have usage in cardiovascular disorders, especially in hypertension. These results most likely give rise to further studies to reveal its mechanism of action and clinical value of this herb.

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