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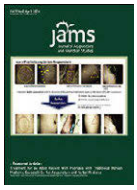

RESEARCH ARTICLE

Effect of Two Ginger Varieties on Arginase Activity in Hypercholesterolemic Rats

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Abstract
Recently, ginger has been used in traditional Chinese medicine as an herbal therapy for treating several cardiovascular diseases, however, information on its mechanism of action is limited. The present study assessed the effect of two ginger varieties (*Zingiber officinale* and *Curcuma longa*) on the arginase activity, atherogenic index, levels of liver thiobarbituric acid reactive substances (TBARSs), and plasma lipids in rats fed with a high-cholesterol (2%) diet for 14 days. Following the treatment period, it was found that feeding a high-cholesterol diet to rats caused significant ($p < 0.05$) increases in arginase activity, atherogenic index, levels of TBARS, total cholesterol (TC), triglycerides (TGs), and low-density lipoprotein cholesterol (LDL-C) with a concomitant decrease in high-density lipoprotein cholesterol (HDL-C). However, both ginger and turmeric (2% and 4%) caused significant ($p < 0.05$) decreases in arginase activity and the atherogenic index, and prevented hypercholesterolemia by decreasing the TC, TGs, and LDL-C while increasing the HDL-C when compared with the controls. In conclusion, dietary supplementation with both types of rhizomes (ginger and turmeric) inhibited arginase activity

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and prevented hypercholesterolemia in rats that received a high-cholesterol diet. Therefore, these activities of ginger and turmeric represent possible mechanisms underlying its use in herbal medicine to treat several cardiovascular diseases.

1. Introduction

Hypercholesterolemia is well-known as one of the most important risk factors of atherosclerosis; atherosclerosis in turn is the leading cause of death in developed countries and has been linked to causing hypertension [1]. It has been shown that hypercholesterolemia increases oxidative stress and leads to lipid peroxidation [1]. Recently, it has been reported that arginase plays a major role in the regulation of vascular function in various cardiovascular disorders such as hypertension [2] and atherosclerosis [3], by impairing nitric oxide (NO) production. As a biological messenger, NO plays a role in the pathogenesis of many metabolic disorders such as cardiovascular diseases, atherosclerosis, and hypertension [4,5] by regulating various physiological processes, including vasodilation, inflammation, and metabolism [6]. In addition, the reduced bioavailability of endothelium-derived NO has been reported to be closely associated with hypercholesterolemia [7]. NO is synthesized by endothelial NO synthase (eNOS) using L-arginine as substrate, and arginase reciprocally regulates eNOS and NO production by competing for L-arginine [8]. In various cardiovascular disorders, arginase has been shown to regulate vascular cell functions primarily through impairment of NO production [8]. Furthermore, it has been reported that there is a significant upregulation of arginase 1 in the peripheral blood mononuclear cells of overweight/obese individuals [9], which suggests an association between arginase activity in the endothelium, eNOS-dependent NO production, and the endothelial dysfunction evident in hypercholesterolemia.

Very recently, it was discovered that inhibition of arginase activity ameliorates obesity-induced abnormalities in hepatic lipids and whole-body adiposity through the mechanism that activates pathways involved in hepatic triglyceride (TG) metabolism and mitochondrial function [7]. Hypercholesterolemia has been closely associated with endothelial dysfunction through oxidative stress mechanisms that will in turn lead to an impaired production of NO. Therefore, it is necessary to assess whether inhibition of arginase could offer protection against hypercholesterolemia because both arginase and eNOS share the same substrate (i.e., arginine), which is needed for NO production.

Traditionally, Chinese medicine includes herbal medicine and acupuncture. Recently, spices such as ginger have been reported to be used in traditional Chinese medicine as herbal therapy against several cardiovascular diseases [10]. Studies have shown that ginger (*Zingiber officinale*) rhizome possesses anti-inflammatory, hypoglycemic, and hypolipidemic properties [11,12]. Furthermore, turmeric (*Curcuma longa*), which is commonly known as "red ginger," is another rhizomatous plant belonging to the ginger family (Zingiberaceae) that has been used as a food flavoring agent. Curcuminoids are the main phytochemicals in turmeric, which are responsible for the characteristic yellow color [11]. Curcumin, one of the predominant curcuminoids and a flavonoid, has been investigated for anti-inflammatory and antioxidant properties [13]. Curcumin has also been underlined to "mop-up" superoxide anions, peroxynitrite radicals, and singlet oxygen [13]. Ginger has been listed in the "Generally Recognized as Safe" documentation of the U.S. Food and Drug Administration. A dose of 1—5 g of ginger and turmeric powder ingested for periods ranging from 3 months to 2.5 years did not cause any adverse effects [14]. Recently, it has been reported that these two spices (ginger and turmeric) inhibit the activity of angiotensin-converting enzyme under *in vivo* and *in vitro* conditions [15,16]. In addition, extract from these rhizomes inhibit arginase activity *in vitro* (data not shown). This activity was due to the presence of some polyphenolic compounds that have been reported to be a potent inhibitor of arginase activity. Although ginger has been reportedly used in folklore as a pharmocopuncture therapy for the management/prevention of hypertension and other cardiovascular diseases, there is a dearth of information on the possible mechanism of action by which it exerts this therapeutic effect. Hence, this study investigated the effect of both spices on arginase activity, atherogenic index, and plasma lipids in high-cholesterol-diet-fed rats for 14 days to explain the possible mechanism of action underlying their medicinal properties and traditional use.

2. Materials and methods

2.1. Sample collection

Fresh samples of ginger (*Z. officinale*) and turmeric (*C. longa*) rhizomes were obtained from a farmland at Akure metropolis, Nigeria. Authentication of the plants was carried out at the Department of Biology, Federal University of Technology, Akure, Nigeria. The voucher specimens were deposited at the Herbarium of the Plants (Department of Biology, Federal University of Technology).

2.2. Chemicals and reagents

Chemicals and reagents used such as thiobarbituric acid, arginine, and methanol were procured from Sigma-Aldrich Chemie GmbH (Steinheim, Germany). Acetic acid was obtained from BDH Chemicals Ltd. (Poole, UK). Tris—HCl buffer, manganese chloride ($MnCl_2$), and sodium dodecyl sulfate were of analytical grade. Unless stated otherwise, all other chemicals and reagents used were of analytical grades and the water was glass distilled.

2.3. Diet formulation for hypercholesterolemia

The diets were freshly formulated according to the modified method of Akinyemi et al [15] and in consultation with the Department of Animal Production and Health, Federal University of Technology (Table 1).

2.4. Bioassay

The bioassay was carried out according to the modified method described by Hor et al [17]. Wistar strain albino rats (weight, 110–200 g) were obtained from the Department of Animal Production and Health, Federal University of Technology, Akure, Nigeria. The animals were acclimatized for 2 weeks and allowed *ad libitum* access to a commercial diet. The handling of animals was in accordance with the recommended international standard. The rats were subsequently divided into six groups (6 animals in each group) as follows: Group 1, normal control, placed on a basal diet as presented in Table 1; Group 2, hypercholesterolemic rats, placed on a basal diet plus 2% cholesterol; Group 3, rats fed with a diet supplemented with 2% red ginger plus 2% cholesterol; Group 4, rats fed with a diet supplemented with 4% red ginger plus 2% cholesterol; Group 5, rats fed with a diet supplemented with 2% white ginger plus 2% cholesterol; and Group 6, rats fed with a diet supplemented with 4% white ginger plus 2% cholesterol. Animals were fed with the high-cholesterol diet for the entirety of the 14-day treatment.

The experiment lasted for 14 days after which the rats were killed by cervical dislocation. Their blood was collected into EDTA bottles, and the plasma was subsequently prepared. Thereafter, the contents of plasma total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and TGs were determined using commercial colorimetric enzymatic diagnostic kits (Randox Laboratories Ltd., Crumlin, UK). Furthermore, liver malondialdehyde content was determined as reported by Ohkawa et al [18]. Arginase activity was also assessed according to the spectrophotometric method of White et al [19].

2.5. Quantification of compounds by high-performance liquid chromatography-diode array detector

Reverse-phase chromatographic analyses were carried out under gradient conditions using a C_{18} column (4.6 mm $\times$ 150 mm) packed with 5-μm diameter particles; the mobile phase comprised water containing 2% acetic acid (A) and methanol (B), and the composition gradient was as follows: 5% of B for 2 minutes and then changed to 25%, 40%, 50%, 60%, 70%, and 100% at 10, 20, 30, 40, 50, and 80 minutes, respectively, in accordance with the method described by Barbosa Filho et al [20] with slight modifications. Ginger aqueous extracts were analyzed at a concentration of 15 mg/mL. The presence of some antioxidants compounds was investigated, namely, gallic acid, caffeic acid, catechin, epicatechin, quercetin, quercitrin, rutin, kaempferol, luteolin, and curcumin. Identification of these compounds was performed by comparing their retention time and UV absorption spectrum with those of the commercial standards. The flow rate was 0.6 mL/min and the injection volume 50 μL. The samples and mobile phase were filtered through a 0.45-μm membrane filter (Millipore, Sigma–Aldrich, Steinheim, Germany) and then degassed by ultrasonic bath before use. Stock solutions of standards (references) were prepared in the high-performance liquid chromatography (HPLC) mobile phase at concentrations of 0.030–0.250 mg/mL. Chromatography peaks were confirmed by comparing their retention time with those of reference standards and by diode array detector spectra (200–500 nm). All chromatography operations were carried out at ambient temperature and in triplicate. The limit of detection and limit of quantification were calculated based on the standard deviation of the responses and the slope using three independent analytical curves, as defined by Barbosa Filho et al [20].

2.6. Protein determination

The protein content was determined according to the principle based on the biuret reaction, as described by Gornall et al [21] using bovine serum albumin as the standard.

Table 1 Diet formulation for basal and supplemented diets for the control and test groups.

Treatment (WG)	Group 1 (Basal)*	Group 2 (Control)†	Group 3 (2% RG)	Group 4 (4% RG)	Group 5 (2% WG)	Group 6 (4% WG)
Skimmed milk‡	28	28	28	28	28	28
Oil	10	10	10	10	10	10
Premix§	4	4	4	4	4	4
Corn starch	58	56	54	52	54	52
Cholesterol	—	2	2	2	2	2
Spice	—	—	2	4	2	4
Total (g)	100	100	100	100	100	100

* Basal = without cholesterol and test samples.
† Control = 2% cholesterol without test samples.
‡ Skimmed milk = 32% protein.
§ One gram of mineral and vitamin premix = 3,200 IU vitamin A, 600 IU. vitamin D_3, 2.8 mg vitamin E, 0.6 mg vitamin K_3, 0.8 mg vitamin B_1, 1 mg vitamin B_2, 6 mg niacin, 2.2 mg pantothenic acid, 0.8 mg vitamin B_6, 0.004 mg vitamin B_{12}, 0.2 mg folic acid, 0.1 mg biotin H2, 70 mg choline chloride, 0.08 mg cobalt, 1.2 mg copper, 0.4 mg iodine, 8.4 mg iron, 16 mg manganese, 0.08 mg selenium, 12.4 mg zinc, and 0.5 mg antioxidant.
RG = red ginger; WG = white ginger.

2.7. Statistical analysis

Statistical analysis was performed using Statistical Program for Social Science (version 16.0; SPSS, Inc., Chicago, IL, USA). Results were represented as mean ± standard error of the mean, and the differences among the experimental groups were analyzed using one-way analysis of variance with Duncan multiple range analysis ($p < 0.05$).

3. Results

3.1. Effect of ginger rhizomes on arginase activity

Feeding a high-cholesterol diet to rats caused a significant ($p < 0.05$) increase in both plasma and liver arginase activity as presented in Fig. 1A and B. However, both rhizomes (2% and 4%) caused a significant ($p < 0.05$) decrease in plasma and liver arginase activity when compared with the control.

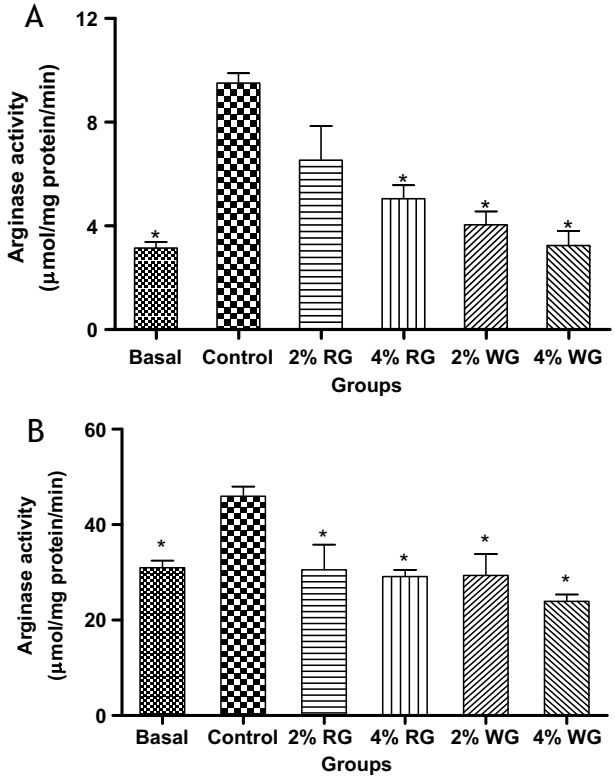

Figure 1 Effect of dietary supplementation with red ginger (turmeric) and white ginger (2% and 4%) on (A) plasma and (B) liver arginase activity in high-cholesterol-diet-fed rats. Values represent mean ± standard error of the mean ($n = 6$). * Significantly different from the control group at $p < 0.05$. 2% RG = rats fed with diet supplemented with 2% red ginger plus 2% cholesterol; 2% WG = rats fed with diet supplemented with 2% white ginger plus 2% cholesterol; 4% RG = rats fed with diet supplemented with 4% red ginger plus 2% cholesterol; 4% WG = rats fed with diet supplemented with 4% white ginger plus 2% cholesterol; basal = normal control rats, fed with basal diet; control = rats fed with basal diet plus 2% cholesterol (hypercholesterolemic rats).

3.2. Effect of ginger rhizomes on plasma lipid profiles and atherogenic index

Feeding a high-cholesterol diet to rats caused a significant ($p < 0.05$) increase in the atherogenic index (Fig. 2) and TC, TGs, and low-density lipoprotein-cholesterol (LDL-C) levels, and a decrease in the HDL-C level (Table 2). However, both rhizomes (2% and 4%) caused a significant ($p < 0.05$) decrease in the atherogenic index, and TC, TGs, and LDL-C levels with a concomitant increase in HDL-C level compared with the control.

3.3. Effect of ginger on the thiobarbituric acid reactive substances level

Fig. 3 shows the values of thiobarbituric acid reactive substances (TBARSs) from the liver of rats. These values indicate an increase in lipid oxidation in hypercholesterolemic rats. However, both rhizomes (2% and 4%) caused a significant ($p < 0.05$) reduction in the TBARS levels when compared with the control.

3.4. HPLC screening

HPLC fingerprinting of ginger aqueous extracts revealed the presence of gallic acid ($t_R = 9.97$ minutes; Peak 1), catechin ($t_R = 16.81$ minutes; Peak 2), caffeic acid ($t_R = 24.79$ minutes; Peak 3), epicatechin ($t_R = 32.56$ minutes; Peak 4), rutin ($t_R = 38.07$ minutes; Peak 5), quercitrin ($t_R = 46.51$ minutes; Peak 6), quercetin ($t_R = 50.43$ minutes; Peak 7), kaempferol ($t_R = 53.97$ minutes; Peak 8),

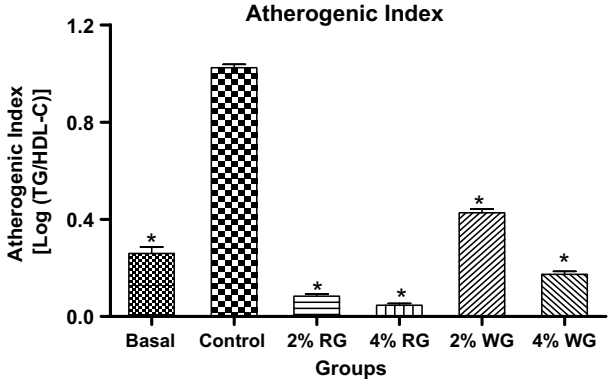

Figure 2 Effect of dietary supplementation with red ginger (turmeric) and white ginger (2% and 4%) on atherogenic index in high-cholesterol-diet-fed rats. Values represent mean ± standard error of the mean ($n = 6$). * Significantly different from the control group at $p < 0.05$. 2% RG = rats fed with diet supplemented with 2% red ginger plus 2% cholesterol; 2% WG = rats fed with diet supplemented with 2% white ginger plus 2% cholesterol; 4% RG = rats fed with diet supplemented with 4% red ginger plus 2% cholesterol; 2% WG = rats fed with diet supplemented with 4% white ginger plus 2% cholesterol; basal = normal control rats, fed with basal diet; control = rats fed with basal diet plus 2% cholesterol (hypercholesterolemic rats); HDL-C = high-density lipoprotein-cholesterol; TG = triglyceride.

Table 2 Effect of dietary supplementation of red ginger (turmeric) and white ginger (2% and 4%) on plasma lipid profiles in high-cholesterol-diet-fed rats.

Groups (mg/mL)	TC (mg/mL)	TG (mg/mL)	HDL-C (mg/mL)	LDL-C (mg/mL)
Basal[†]	28.1 ± 1.3*	31.5 ± 1.3*	16.3 ± 1.3*	5.5 ± 0.13*
Control[‡]	52.8 ± 3.6	63.1 ± 3.6	6.0 ± 0.94	26.7 ± 0.64
2% RG	37.5 ± 1.1*	29.4 ± 1.1*	24.3 ± 2.1*	7.2 ± 0.21*
4% RG	33.3 ± 2.1*	26.0 ± 1.1*	25.3 ± 2.1*	2.8 ± 0.24*
2% WG	33.3 ± 1.1*	44.1 ± 2.1*	16.3 ± 1.1*	8.2 ± 0.19*
4% WG	29.1 ± 1.0*	27.3 ± 1.0*	19.5 ± 1.0*	4.1 ± 0.10*

Values represent mean ± standard error of the mean ($n = 6$).
2% RG = rats fed with a diet supplemented with 2% red ginger plus 2% cholesterol; 2% WG = rats fed with a diet supplemented with 2% white ginger plus 2% cholesterol; 4% RG = rats fed with a diet supplemented with 4% red ginger plus 2% cholesterol; 4% WG = rats fed with a diet supplemented with 4% white ginger plus 2% cholesterol; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; TG = triglyceride.
* Significantly different from the control group at $p < 0.05$.
[†] Basal = normal control rats fed with basal diet.
[‡] Control = rats fed with basal diet plus 2% cholesterol (hypercholesterolemic rats).

luteolin (t_R = 58.62 minutes; Peak 9), and curcumin (t_R = 65.19 minutes; Peak 10) (Fig. 4A and B; Table 3).

4. Discussion

Hypercholesterolemia is well-known as one of the most important risk factors of atherosclerosis [1]. It has been closely linked to endothelial dysfunction, and high fat/cholesterol-induced endothelial dysfunction is associated with decreased NO production due to impaired eNOS activity and expression [7]. Decreased bioavailability of the vasoprotective endothelial NO is known to indicate a dysfunctional endothelium or endothelial dysfunction under pathological conditions and in the presence of risk factors [7]. Arginase has emerged as an important regulator of NO bioavailability; it regulates eNOS production by competing for L-arginine, the common substrate for the two enzymes. Increased arginase activity has been reported in a variety of disease conditions characterized by cardiovascular dysfunction [9]. This finding suggests that arginase expression and/or its activity may be responsible for many

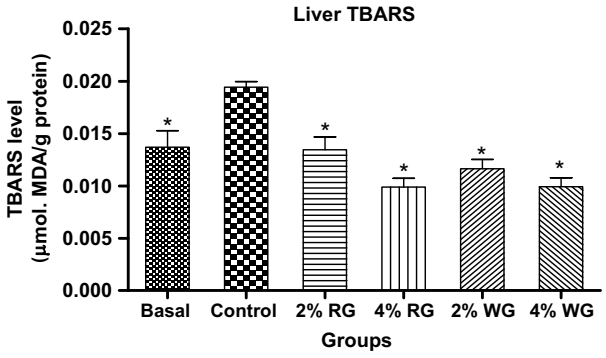

Figure 3 Effect of dietary supplementation with red ginger (turmeric) and white ginger (2% and 4%) on the level of liver thiobarbituric acid reactive substances (TBARSs) in high-cholesterol-diet-fed rats. Values represent mean ± standard error of the mean ($n = 6$). * Significantly different from the control group at $p < 0.05$. 2% RG = rats fed with diet supplemented with 2% red ginger plus 2% cholesterol; 2% WG = rats fed with diet supplemented with 2% white ginger plus 2% cholesterol; 4% RG = rats fed with diet supplemented with 4% red ginger plus 2% cholesterol; 4% WG = rats fed with diet supplemented with 4% white ginger plus 2% cholesterol basal = normal control rats, fed with basal diet; control = rats fed with basal diet plus 2% cholesterol (hypercholesterolemic rats); MDA = malondialdehyde.

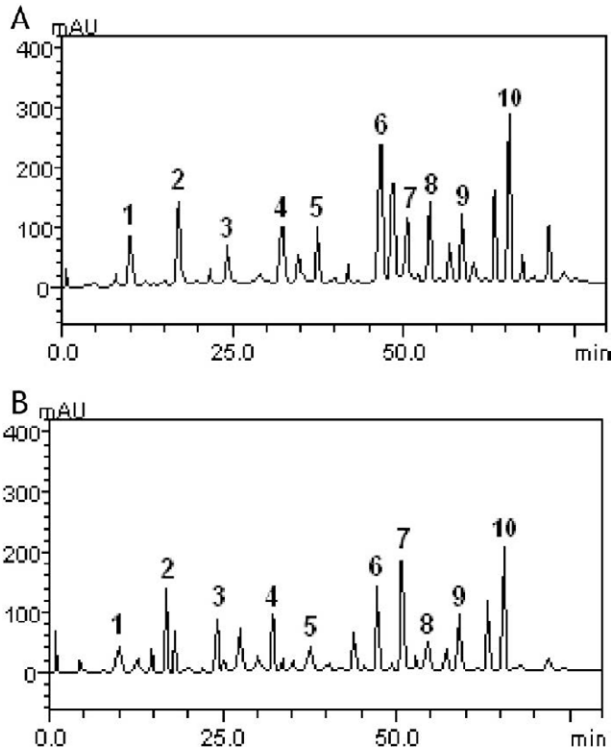

Figure 4 Representative high-performance liquid chromatography profile of (A) red ginger (turmeric) and (B) white ginger aqueous extract. Peak 1 = gallic acid; Peak 2 = catechin; Peak 3 = caffeic acid; Peak 4 = epicatechin; Peak 5 = rutin; Peak 6 = quercitrin; Peak 7 = quercetin; Peak 8 = kaempferol; Peak 9 = luteolin; and Peak 10 = curcumin. The chromatographic conditions are described in the "Materials and methods" section.

Table 3 Composition of red ginger (*Curcuma longa*) and white ginger (*Zingiber officinale*) aqueous extracts.

Ginger compounds	Red ginger (mg/g)	White ginger (mg/g)	LOD (μg/mL)	LOQ (μg/mL)
Gallic acid	3.27 ± 0.02*	1.83 ± 0.03*	0.024	0.079
Catechin	5.08 ± 0.01*	4.95 ± 0.02*	0.009	0.034
Caffeic acid	2.15 ± 0.03*	2.93 ± 0.01*	0.015	0.050
Epicatechin	3.31 ± 0.02*	3.05 ± 0.03*	0.037	0.123
Rutin	3.19 ± 0.01*	1.87 ± 0.01*	0.018	0.062
Quercitrin	10.52 ± 0.03*	5.01 ± 0.02*	0.011	0.037
Quercetin	3.28 ± 0.02*	6.78 ± 0.03*	0.029	0.096
Kaempferol	5.11 ± 0.01*	1.80 ± 0.02*	0.023	0.075
Luteolin	4.06 ± 0.02*	3.09 ± 0.01*	0.014	0.046
Curcumin	12.75 ± 0.01*	6.93 ± 0.01*	0.008	0.027

Results are expressed as mean ± standard error of the mean of three determinations.
*Differ by Tukey test at $p < 0.05$.
LOD = limit of detection; LOQ = limit of quantitation.

of the pathological changes associated with vascular dysfunction possibly through interference with NO bioavailability by limiting L-arginine sources. Arginase 1, encoded by *Arg1*, is a cytosolic enzyme that is abundantly expressed in the liver [22].

In this present study, feeding a high-cholesterol diet to rats caused a significant ($p < 0.05$) increase in both plasma and liver arginase activity (Fig. 1A and B). The result agrees with a recent study where an increase in arginase activity was observed in hypercholesterolemic (ApoE$^{-/-}$) mice [23]. In addition, our finding is in agreement with Chung et al [24], who reported increased arginase activity in high-fat-diet-fed mice. However, both rhizomes (ginger and turmeric) caused a decrease in plasma and liver arginase activity when compared with the control. This is an indication that inhibition of arginase activity plays a major role in vascular dysfunction by restoring endothelial vasorelaxant function, reducing vascular stiffness, and markedly reducing atherosclerotic plaque burden as previously reported by Ryoo et al [23].

The inhibition of arginase activity will result in the increase in NO bioavailability through activation of eNOS. This finding that arginase knockdown led to upregulation of eNOS expression has been confirmed by the results of *in vitro* analysis in human umbilical vein endothelial cells. In addition, it has been reported that arginase inhibition restores endothelial function in the vasculature of experimental models of atherosclerosis, myocardial ischemia, hypertension, and aging [25,26]. However, our finding in this high-cholesterol-diet model of hypercholesterolemia clearly supports the important role of arginase in vascular endothelial dysfunction and regulation of NO bioavailability. Nevertheless, the inhibitory effect of the dietary supplementation of the two rhizomes could be a result of phenolic compounds (Fig. 4; Table 3), which have been shown to be potent inhibitors of arginase activity [25,26].

Atherogenic index is a predictor of the development of atherosclerosis and underscores the progression of cardiovascular disease. The present study revealed an agreement between the atherogenic index and the *in vivo* arginase activity in the experimental animals, and invites a new understanding of potential therapeutic approaches in atherogenesis and other cardiovascular diseases. The possible mechanism of action by which arginase activity has been linked to cause atherogenesis is through induction by oxidized LDL (OxLDL). Recently, OxLDL, the primary pathogenic lipid in atherogenesis, has been shown to activate endothelial cell arginase [27]. This consequently leads to a decrease in endothelial NO production. However, both ginger and turmeric rhizomes caused a significant ($p < 0.05$) decrease in the atherogenic index (Fig. 2). Hence, the lower atherogenic index in rats fed with a supplemented diet of the rhizomes might be due, in part, to their inhibitory effect on arginase activity. Ryoo et al [26] revealed that treating atherogenic-prone apolipoprotein E-null (ApoE$^{-/-}$) mice with arginase inhibitor restored NO bioavailability, reactive oxygen species production, endothelial function, and arterial stiffness compared with the wild-type phenotype. This clearly supports the claim that arginase inhibition actively augments NO production, and has had reportedly beneficial effects on cardiac and vascular wall functions in atherogenesis and aging [25,27].

Furthermore, it has been documented that lowering circulating cholesterol levels can reduce the risk of cardiovascular diseases [28]. This study also revealed that a high-cholesterol diet caused a significant ($p < 0.05$) increase in the rats' plasma TC, TGs, and LDL-C levels. This is in agreement with earlier findings that a high-cholesterol diet caused markedly elevated plasma TC and TG levels in rats [29]. However, both ginger and turmeric rhizomes caused a significant ($p < 0.05$) decrease in TC, TG, and LDL-C with a concomitant increase in the HDL-C level when compared with the control. The hypocholesterolemic effect of the gingers is in agreement with our earlier reports in which they were shown to possess some cholesterol-lowering agents [15]. However, the mechanism by which these gingers lower plasma cholesterol could be due to high polyphenols (Table 3; Fig. 4). It is well-known that plasma cholesterol concentration can be regulated by cholesterol biosynthesis, cholesterol removal from the circulatory system, the absorption of dietary cholesterol, and its excretion via bile and feces [30].

Hypercholesterolemia has been reported to be related to enhanced oxidative stress and increased lipid peroxidation, and an increase in OxLDL generation was identified as a major contributor to the vascular damage induced by high cholesterol levels. Therefore, inhibiting oxidative stress in the hypercholesterolemic state is considered an important therapeutic approach. Polyphenols are plant phytochemicals that are reported to possess strong antioxidant properties, and therefore, an increase in the consumption of polyphenol-rich food has been inversely linked to the occurrence of cardiovascular diseases. Polyphenols are capable of scavenging free radicals, chelating transition metals, preventing the oxidation of LDL-C, and inhibiting lipid peroxidation [1]. A report has shown an inverse correlation between polyphenol (flavonoid) intake and total plasma cholesterol concentrations [31]. In the present study, rats fed with a high-cholesterol diet showed a significant ($p < 0.05$) increase in the liver TBARS level. However, both ginger rhizomes caused a significant ($p < 0.05$) reduction in the TBARS levels when compared with the control. This clearly indicates a marked improvement in the *in vivo* antioxidant status following supplementation of the diets with spices that are rich in antioxidant phytochemicals such as polyphenolic compounds.

In conclusion, dietary supplementation with both ginger rhizomes inhibited arginase activity and prevented hypercholesterolemia in high-cholesterol-diet-fed rats. Therefore, this present activity of ginger and turmeric could be part of the possible mechanism underlying its antihypertensive property, which could lay credence to its use in folk medicine.

Disclosure statement

The authors declare that they have no conflicts of interest and no financial interests related to the material of this manuscript.

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