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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.

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