

# Recent perspectives on the medicinal potential of ginger

KDPP Gunathilake<sup>1</sup>  
HP Vasantha Rupasinghe<sup>2</sup>

<sup>1</sup>Department of Food Science and Technology, Faculty of Livestock, Fisheries and Nutrition, Wayamba University of Sri Lanka, Makandura, Gonawila, Sri Lanka; <sup>2</sup>Department of Environmental Sciences, Faculty of Agriculture, Dalhousie University, Truro, NS, Canada

**Abstract:** Ginger (*Zingiber officinale*) is a globally known food and flavoring ingredient which is also reputed for its wide range of medicinal properties. The rhizome of ginger consists of a unique homologous series of compounds, gingerols, which are the major phenolic plant secondary metabolites responsible for its unique flavor and health benefits. Over the last 2 decades, extensive research has been conducted to identify bioactive constituents and medicinal potential of ginger. This review deliberates chemical composition as well as the most recent research findings on potential health benefits of ginger, including its antimicrobial, anti-inflammatory, blood pressure-lowering, cholesterol-lowering, antiplatelet aggregation, chemopreventive, antioxidant, and hypoglycemic properties.

**Keywords:** ginger, gingerols, medicinal properties, *Zingiber officinale*, health

## Introduction

Ginger (*Zingiber officinale* Roscoe) is a well-known and widely used spice and condiment, especially in Asia. The rhizome of ginger contains several interesting bioactive constituents and possesses health-promoting properties. Interestingly, in recent years, the demand for ginger has been growing in North America, not only for the use as a food ingredient, but also for its health benefits.<sup>1</sup> Ginger has been widely used in Chinese, Ayurvedic, and Unani-Tibb medicines.<sup>2</sup> Based on the scientific findings through in vitro, in vivo, and human clinical trials, ginger has the potential to treat many aspects of cardiovascular diseases such as hyperlipidemia,<sup>3</sup> platelet aggregation,<sup>4</sup> and hypertension.<sup>5</sup> The antiatherogenic effect of ginger is associated with reductions in plasma and hepatic low-density lipoprotein cholesterol (LDL-C) levels, as well as their susceptibility to oxidation and aggregation.<sup>3,6</sup> The pungency of fresh ginger is primarily due to the gingerols which are a homologous series of phenolic compounds, whereas the pungency of dried ginger is mainly due to the presence of shogaols, mainly (6)-shogaol, which are dehydrated forms of gingerols.<sup>2</sup> In the cardiovascular system, both (6)-shogaol and (6)-gingerol are the two active components of ginger which produce a depressor response on blood pressure at lower doses.<sup>7</sup> Because of these health-promoting properties, ginger can be considered as an active ingredient for designing functional foods targeted for reducing the risk of cardiovascular disease.<sup>8,9</sup> This review discusses the potential health benefits of ginger with special reference to phytochemical composition and physiological benefits such as anticancer, anti-inflammatory, antioxidant, and cardioprotective properties.

Correspondence: HP Vasantha Rupasinghe  
Department of Environmental Sciences,  
Faculty of Agriculture, Dalhousie  
University, Truro, NS B2N 5E3, Canada  
Tel +1 902 893 6623  
Fax +1 902 893 1404  
Email vrupasinghe@dal.ca

## Phytochemical composition

The main pungent compounds in fresh ginger are gingerols, whereas the pungency of dry ginger is mainly due to shogaols, for example [6]-shogaol, which are dehydrated forms of [6]-gingerols. Most abundant gingerol found in ginger is [6]-gingerol.<sup>10</sup> Other gingerols with different chain lengths are also present in comparatively small quantities.<sup>2</sup> Jolad et al<sup>11</sup> reported that they have identified 51 compounds on organically grown fresh ginger, 31 compounds were previously reported as constituents of ginger and additional 20 are yet to be characterized. The identified compounds included gingerols, shogaols, paradols, dihydroparadols, [3]-dihydroshogaols, acetyl derivatives of gingerols, gingerdiols, mono- and di-acetyl derivatives of gingerdiols, 1-dehydrogingerdiol, diarylheptanoids, zingiberene, phellandrene and methyl ether derivatives of some of these compounds. In addition to [6]-gingerol, [4]-, [7]-, [8]-, and [10]-gingerol were identified. Figure 1 shows the chemical structures of the major gingerols and shogaol present in ginger. Masuda et al<sup>12</sup> suggested that the substituents on the alkyl chain of gingerol and related compounds might contribute to antioxidant properties. Over 50 components in ginger oil have been characterized and these are mainly monoterpenoids and sesquiterpenoids.<sup>2</sup>

## Antibiotic/antimicrobial properties

Ginger and its products have been used widely as a food spice as well as in herbal medicine. In particular, gingerol-related components have been reported to possess antimicrobial and antifungal properties, as well as several

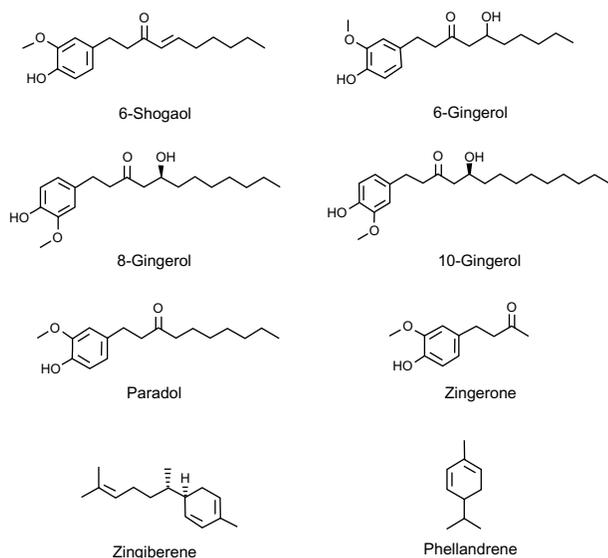
anti-infective properties.<sup>13</sup> Most of the reported findings are through in vitro studies, however, a few preclinical investigations are published. The antibacterial activity of different solvent extracts of ginger was studied by Malu et al,<sup>14</sup> and it was found that *n*-hexane, ethyl acetate, and ethanol extracts of ginger showed a bacterial growth inhibition activity in a dose-dependent manner. Ekwenye and Elegalam<sup>13</sup> have reported an inhibitory effect of ethanol extract of ginger on *Escherichia coli* and *Salmonella typhimurium* with a minimum inhibitory concentration (MIC) between 75 and 250 mg/mL.

Ethanol and *n*-hexane extracts of ginger exhibit antibacterial activities against three anaerobic gram-negative periodontal disease-causing bacteria such as *Porphyromonas gingivalis* ATCC 53978, *Porphyromonas endodontalis* ATCC 35406, and *Prevotella intermedia* ATCC 25611. Two highly alkylated gingerols, [10]-gingerol and [12]-gingerol, seem to be effective in inhibiting the growth of these oral pathogens at a MIC range of 6–30 µg/mL and killing these oral pathogens at a minimum bactericidal concentration range of 4–20 µg/mL.<sup>15</sup> Four ginger components namely, [6]-dehydrogingerdiol, [10]-gingerol, [6]-shogaol, and [6]-gingerol have shown antibacterial effects against extensively drug-resistant *Acinetobacter baumannii*.<sup>16</sup>

Ethanol extracts of ginger on *Staphylococcus aureus* and *Streptococcus pyogenes* have shown the similar effect like that of conventional antibiotics such as chloramphenicol, ampicillin, and tetracycline,<sup>17</sup> and the MIC of the extracts ranged from 0.3 ng/mL to 0.7 µg/mL.<sup>18</sup> Limited synergism capacity between 13 antimicrobial drugs and 8 plant extracts, including ginger, against *S. aureus* strains was verified by Betoni et al<sup>19</sup> Further, ginger root has been used traditionally for the treatment of gastrointestinal ailments such as motion sickness, dyspepsia, and peptic ulcer disease. *Helicobacter pylori* is the primary etiological agent associated with these diseases, and the methanol extract of the dried powdered ginger rhizome, fractions of the extract, and the isolated constituents, 6-, 8-, 10-gingerol and 6-shogaol showed inhibitory effect on 19 strains of *H. pylori* with a MIC range of 6.25–50 µg/mL.<sup>20</sup>

## Antioxidant properties

Ginger has been used as a spice for over thousands of years and its rhizomes and extracts contain phenolic compounds such as 6-gingerol and its derivatives, which have a high antioxidant activity.<sup>21–23</sup> It has also been revealed by many authors that the ginger has antioxidant properties. The substituent on the alkyl chain of these compounds might



**Figure 1** Chemical structures of selected major bioactive constituents of ginger.

contribute to both radical scavenging effect and inhibitory effects against the peroxy radical-induced peroxidation of liposome. The antioxidant activity might be due to radical scavenging activity.<sup>12</sup> It has been shown that [6]-gingerol possesses strong antioxidant activity both in vivo and in vitro.<sup>24</sup> Similarly, Gunathilake and Rupasinghe<sup>25</sup> have reported that pure phenolic bioactives of ginger, such as [6]-gingerol, were strong inhibitors of copper-induced low LDL-C oxidation in vitro. Ginger has been shown to be effective in prevention of ultraviolet B (UVB)-induced reactive oxygen species production and cyclooxygenase-2 (COX-2) expression, and a possible therapeutic agent against UVB-induced skin disorders.<sup>24</sup> In another study, it was reported that ginger causes a decrease in lipid peroxidation, an increase of plasma antioxidant capacity, and a reduction in renal nephropathy in rats.<sup>26</sup> Aeschbach et al<sup>27</sup> found that gingerol is a good scavenger of peroxy radicals generated by pulse radiolysis suggesting that [6]-gingerol could be used as a “natural” replacement for “synthetic” antioxidant food additives. Gunathilake et al<sup>9</sup> reported that a functional beverage consists of [6]-gingerol-rich extract that exhibits hypocholesterolemic effect in spontaneously hypertensive rats. Furthermore, water extracts of ginger can be incorporated into fruit-based functional beverages designed for cardioprotection. Oxidation of LDL-C has been suggested to play a significant role in the process of development of atherosclerosis.<sup>28</sup> It has been suggested that among all in vitro antioxidant capacity assays, measuring LDL-C antioxidant activity is more pathophysiologically important and more informative for screening antioxidant activity of foods for preventing atherosclerosis.<sup>29</sup> Copper-induced LDL-C oxidation inhibition by water, ethanol, methanol, ethyl acetate, and hexane extracts of ginger were 43%, 71%, 76%, 67%, and 67%, respectively, at their optimum extraction conditions.<sup>25,30</sup> In a rat study, ginger at 1% (w/w) lowers the lipid peroxidation by maintaining the activities of the antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase and indicated that the ginger is comparatively as effective as ascorbic acid as an antioxidant.<sup>31</sup> The 2,2-diphenyl-1-picrylhydrazyl radical scavenging activity of ginger is comparable to that of butylated hydroxytoluene and it was shown that the ginger extract chelates Fe<sup>3+</sup> in the solution.<sup>32</sup> Leaves of ginger have also shown higher antioxidant activity and phenolic contents compared with the rhizomes and stems of ginger.<sup>33</sup> However, it has been shown that ferric-reducing antioxidant power activity of the rhizomes is higher than that of leaves.<sup>33</sup> Gunathilake and Rupasinghe<sup>30</sup> have also reported an ultrasonication-based extraction method to prepare

[6]-gingerol-rich water-based ginger extract for functional food formulations.

## Hypoglycemic properties

Diabetes mellitus is one of the major metabolic disorders, and it is a global epidemic. Many traditional plant treatments exist as a hidden wealth of potentially useful natural products for diabetes treatment and management.<sup>34</sup> Ginger has been traditionally used in the treatment of diabetes mellitus, and studies have reported the hypoglycemic properties of ginger in in vitro and in vivo. Oral administration of aqueous ginger extract to streptozotocin (STZ)-induced diabetic rats for a period of 30 days showed a dose-dependent antihyperglycemic effect, and the plasma glucose level decreased by 68% at the dose of 500 mg/kg body weight daily, indicating that ginger is a potential phytotherapy for the treatment of diabetes.<sup>35</sup> Similarly, other studies have also confirmed that both ginger extracts<sup>36</sup> as well as 6-gingerol<sup>37</sup> have shown hypoglycemic effect on diabetic rats. Aqueous extracts of ginger rhizomes have been studied to evaluate their antidiabetic effects on protein glycation and on the diffusion of glucose in vitro in a dose-dependent manner. This antidiabetic potential of ginger is mainly through the inhibition of the glucose diffusion and, to a limited extent, by reducing the glycation of proteins.<sup>38</sup> In a study assessing the effect of several plant foods on glucose uptake activity in L6 myotubes, it has been reported that onion and ginger are potent regulators of glucose transport.<sup>39</sup>

The modulatory effects of spices (including ginger) on the metabolic syndrome and oxidative stress in STZ-nicotinamide diabetic rats have shown that ginger alleviates (80%–97%) the signs of the metabolic syndrome (hyperglycemia and dyslipidemia) by increasing the production of insulin (26%–37%), enhancing the antioxidant defense system (31%–52%), especially glutathione, and decreasing lipid peroxidation (60%–97%).<sup>40</sup> Advanced glycation end products (AGE) are associated in the development of several pathophysiological conditions, including diabetic cataract, and ginger is a prominent agent to inhibit the AGE formation in vitro as well as in vivo.<sup>41</sup> Ginger has a potential to prevent diabetic cataract in rats mainly through its antiglycation potential and to a lesser extent by inhibition of the polyol pathway, indicating that the ginger may be explored for the prevention or delay of diabetic complications.<sup>41</sup>

Ethyl acetate extract of ginger at 5 µg/mL concentration has been shown to enhance glucose uptake in cell lines. Further, in an antibody-based study in treated cells the effect of ethyl acetate extract of ginger in expressing GLUT4 on

the cell surface membrane was revealed. These findings experimentally proved that the antidiabetic effect of ginger is initiated by its antioxidant and antiglycation properties and the potential to express or transport GLUT4 receptors from internal vesicles.<sup>42</sup> In a study evaluating the effects of ginger on some biochemical parameters in type 2 diabetic patients in a randomized double-blind placebo-controlled trial, it was found that the ginger supplementation significantly lowered the levels of glucose and increased the quantitative insulin-sensitivity check index. Thus, ginger supplementation improved the insulin sensitivity and some fractions of lipid profile in type 2 diabetic patients.<sup>43</sup> In another human clinical trial with diabetic and hypercholesterolemia subjects, it was reported that a dose of 3 g/d for a period of 30 days resulted in a significant reduction in blood glucose, total cholesterol, triglycerides, LDL-C, and very low-density lipoprotein-cholesterol (VLDL-C) levels.<sup>44</sup>

Gingerols, the major pungent components of ginger, are known to improve diabetes, including the effect of enhancement against insulin sensitivity. Extracts of ginger prepared using hexane, ethyl acetate, methanol, 70% methanol-water, and water were studied to determine the potential of these extracts to inhibit key enzymes relevant to type 2 diabetes, and the results indicated that ginger has a very good potential for inhibition of  $\alpha$ -glucosidase and  $\alpha$ -amylase activities, which is important for the management of type 2 diabetes.<sup>45</sup>

## Anti-inflammatory properties

Since ancient times, in various populations worldwide, inflammatory disorders and related diseases like rheumatic conditions have been treated with ginger or ginger-derived formulations because of its broad anti-inflammatory actions.<sup>46</sup> Recent research findings provide scientific support for the long-held belief that ginger contains phytochemicals with anti-inflammatory properties. Some phytochemical constituents of ginger share pharmacological properties of nonsteroidal anti-inflammatory drugs (NSAIDs).<sup>47</sup> In vitro studies and several animal trials provide evidence that ginger has the capacity to ameliorate symptoms of inflammation-associated conditions such as arthritis.<sup>48</sup> Based on an animal study, ethanol extract of ginger possesses analgesic and anti-inflammatory properties, and thus this gives pharmacological support to folkloric, ethnomedical uses of ginger in the treatment and management of painful, arthritic inflammatory conditions.<sup>49</sup> Hexane, ethyl acetate, and methanol extracts of ginger have the potential to inhibit key enzymes associated with inflammation such as cyclooxygenase (COX).<sup>45</sup>

Ginger also suppresses prostaglandin synthesis through inhibition of COX-1 and COX-2 and leukotriene biosynthesis by inhibiting 5-lipoxygenase. It is interesting to note that ginger has no or fewer side effects when compared with NSAIDs.<sup>47</sup> Ginger extract also inhibits the induction of several genes involved in encoding the inflammatory response proteins such as cytokines and chemokines, indicating that ginger modulates biochemical pathways which are activated due to chronic inflammation.<sup>47</sup>

Gingerols inhibit the production of inflammatory mediators such as nitric oxide and Prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) in a dose-dependent manner.<sup>50</sup> The expressions of nuclear factor  $\kappa$ -B and the proinflammatory tumor necrosis factor alpha is reduced in rats with liver cancer when given a diet supplemented with ginger, indicating that ginger may act as an anticancer and anti-inflammatory agent.<sup>51</sup> Acetone extract of ginger exerted a dose-dependent topical anti-inflammatory activity in mice irrespective of the gingerol concentration in the extract.<sup>52</sup> Ginger at the dose of 200 mg/kg body weight per day significantly suppressed the incidence and severity of adjuvant-induced arthritis in rats by modulating the production of anti-inflammatory/proinflammatory cytokines and activating the antioxidant defense system. These effects are comparable with indomethacin, an NSAID.<sup>53</sup> Inhibition of acetic-acid-induced writhing response and formalin-induced licking time in the late phase was shown with intraperitoneal administration of [6]-gingerol in the range of 25–50 mg/kg. Further, [6]-gingerol at a range of 50–100 mg/kg has also produced an inhibition of paw edema induced by carrageenin, suggesting that [6]-gingerol possesses analgesic and anti-inflammatory activities.<sup>54</sup>

## Cholesterol-lowering properties

In a study of experimental rats, a low dose of ginger (50 mg/kg/d) showed no effect on reduction in the serum thromboxane-B<sub>2</sub> levels and cholesterol levels although oral administration caused significant changes in the serum PGE<sub>2</sub>. However, high doses of ginger (500 mg/kg/d) lower the serum PGE<sub>2</sub> and cholesterol level.<sup>55</sup> The results suggest that ginger could be used as a cholesterol-lowering agent. Oxidative modification of LDL-C is thought to play a key role in the pathogenesis of atherosclerosis. An ex vivo study on the effect of standardized ginger extract on the development of atherosclerosis in apolipoprotein E-deficient (E<sup>0</sup>) mice showed a 44% reduction in aortic atherosclerotic lesion areas, 27% reduction in plasma triglycerides, and 29% reduction in cholesterol, as well as a reduction of VLDL-C and LDL-C by 58% and 33%, respectively, in mice fed with

250 µg of ginger extract/day. Furthermore, consumption of 25 or 250 µg of ginger extract/day had shown lower capacity to oxidize LDL-C and to take up and degrade oxidized LDL-C. Dietary consumption of ginger extract by E<sup>0</sup> mice significantly attenuates the development of atherosclerotic lesions and reduces plasma LDL-C levels and their susceptibility to oxidation and aggregation.<sup>3</sup>

The modulatory effects of ginger on the metabolic syndrome and oxidative stress in STZ–nicotinamide diabetic rats have shown that the ginger may have a role in alleviating the risks of the metabolic syndrome and cardiovascular complications.<sup>40</sup> Ethanol extract of ginger (200 mg/kg) reduces the serum and tissue cholesterol, serum triacylglycerol, serum lipoprotein, and phospholipid levels in cholesterol-fed rabbits, and the effect is comparable with gemfibrozil, a standard orally effective hypolipidemic drug.<sup>56</sup> Oral administration of [6]-gingerol in type 2 diabetic db/db mice decreases the plasma triglycerides, total cholesterol, free fatty acid, and LDL-C, suggesting that [6]-gingerol exhibits a significant potential as a lipid-lowering agent.<sup>57</sup>

The effects of air-dried ginger powder on experimentally induced atherosclerosis in rabbits showed reduction in the development of atheroma in aorta and coronary arteries by approximately 50%, a decrease in lipid peroxidation, and an enhancement of fibrinolytic activity following ginger administration. However, it has been reported that ginger has no effect on blood lipids. This distinct antiatherogenic potential of ginger may be due to its free-radical-scavenging, prostaglandin-inhibitory, and fibrinolysis-enhancing properties.<sup>58</sup> The protective effects of an ethanol extract of ginger at doses of 100, 200, and 400 mg/kg body weight on development of metabolic syndrome in a high-fat diet-fed rats showed significant reduction of body weight and a reduction in total cholesterol, LDL-C, triglycerides, free fatty acids, and phospholipids in serum of the rats, but no effect on serum high-density lipoprotein cholesterol.<sup>59</sup> On the other hand, Bordia et al<sup>60</sup> reported that ginger has no effect on the blood lipids and blood sugar. In contrast, another study has shown that the ethanol extract of ginger can protect the tissues from lipid peroxidation and exhibit lipid-lowering activity in diabetic rats.<sup>61</sup>

Administration of 80 mg/kg atorvastatin for 4 weeks showed a major hepatotoxic effect, whereas the lower dose (20 mg/kg) seems to cause mild liver injury. Besides lowering serum total cholesterol and hepatic SOD and catalase, atorvastatin significantly increased serum aminotransferases, hepatic malondialdehyde, and nitric oxide. Concurrent administration of ginger extract and atorvastatin had the

opposite effect. A histopathological study revealed that ginger extract reduced liver lesions induced by atorvastatin. The results revealed that combination regimens containing ginger extract and low dose of statins could be advantageous in treating hypercholesterolemia patients who are susceptible to liver function abnormalities.<sup>62</sup> In a double-blind controlled clinical trial with patients showed a reduction in triglyceride, cholesterol, LDL-C, and VLDL-C levels.<sup>63</sup>

## Blood pressure-lowering effect

Ginger has been used traditionally in a wide variety of ailments, including hypertension. The crude extract of ginger induced a dose-dependent (0.3–3 mg/kg) fall in the arterial blood pressure of anesthetized rats and a cardiodepressant activity in guinea pigs. The blood-pressure-lowering effect of ginger is mediated through blockade of voltage-dependent calcium channels.<sup>5</sup> In another study, it was reported that the aqueous ginger extract lowers blood pressure through a dual inhibitory effect mediated via stimulation of muscarinic receptors and blockade of Ca<sup>++</sup> channels, and this study provides sound mechanistic basis for the use of ginger in hypertension and palpitations.<sup>64</sup> The effect of ginger tea on blood pressure of hypertensive individuals has been studied to determine and compare the mean arterial pressure, median number of hypertensive episodes of the respondents with and without intake of ginger tea. When the respondents started to drink 10 g of ginger tea twice a day from the 5th to 8th week, it has been shown that the average mean arterial pressure lowered to 94.804 mmHg.<sup>65</sup>

## Effect on platelet aggregation

Based on recent studies, pungent constituents of ginger and its related substances represent a potential new class of antiplatelet agents. [6]-Gingerol, [6]-shogaol, [8]-gingerol, [8]-shogaol, [8]-paradol, and gingerol analogs exhibit antiplatelet activities.<sup>66,67</sup> It has been reported that the half-maximal inhibitory concentration (IC<sub>50</sub>) values of ginger range from 3 to 7 µM, while aspirin showed an IC<sub>50</sub> value of 20±11 µM.<sup>66</sup> Most importantly, the COX-1 inhibitory activity of [8]-paradol is more potent than the gingerol analogs. The earlier findings reveal that gingerol compounds and their derivatives are more effective antiplatelet agents than aspirin under similar conditions and that [8]-paradol is found to be the most potent COX-1 inhibitor and antiplatelet aggregation agent of ginger. The mechanism underlying the arachidonic acid-induced platelet aggregation inhibition may be related to attenuation of COX-1/thromboxane synthase activity.<sup>66</sup> In a similar study, gingerols and related analogs inhibited the

arachidonic acid-induced platelet release reaction in a similar dose range as aspirin and also inhibited the human platelet aggregation. The mechanism underlying the inhibition of this platelet release reaction and aggregation by gingerol and its related analogs may be through regulation of COX activity in platelets, because gingerols potently inhibited COX activity in rat basophilic leukemia cells.<sup>68</sup>

Administration of powdered ginger at 4 g/d for 3 months has no effect on platelet aggregation, fibrinolytic activity, and fibrinogen level in a placebo-controlled study with healthy individuals and patients with coronary artery disease and in diabetics. However, a single dose of 10 g powdered ginger administered to coronary artery disease patients produced a significant reduction in platelet aggregation induced by the two agonists. Similarly, it has been reported that the dosages of 5 g or more had antiplatelet activity.<sup>69</sup> In a study with human subjects, it was reported that the ginger and nifedipine possessed synergistic effect on antiplatelet aggregation, and a combination of 1 g ginger with 10 mg nifedipine per day could be valuable for cardiovascular and cerebrovascular complication due to platelet aggregation.<sup>4</sup> However, more human trials are needed to find the effective minimum dosage of a standardized ginger extract.

## Chemoprevention and anticancer properties

The cancer preventive properties of ginger are supposed to be mainly due to free radical scavenging, alteration of gene expressions, and induction of apoptosis, all of which contribute to inhibit or retard the tumor initiation, promotion, and progression.<sup>70</sup> There are a number of mechanisms that contribute to the chemopreventive effects of ginger based on in vitro and in vivo studies.<sup>70</sup> Purified ginger constituents such as [6]-, [8]-, and [10]-shogaols showed much stronger growth inhibitory effects than gingerols on H-1299 human lung cancer cells and HCT-116 human colon cancer cells.<sup>71</sup> Some pungent constituents present in ginger, such as [6]-gingerol, [6]-paradol, shogaols, and zingerone, exhibit cancer preventive activity in experimental carcinogenesis.<sup>72</sup> Ginger has been reported to possess chemopreventive activity in colon cancer.<sup>73</sup> Gingerol also inhibits the growth of human colorectal cancer cells<sup>74</sup> and induces apoptosis and autophagocytosis in ovarian cancer cells.<sup>75</sup> Development of mammary tumors was significantly inhibited in mice with the supplement of hot water extract of ginger rhizome.<sup>76</sup> Dietary phytochemicals offer nontoxic therapeutic management as well as chemopreventive intervention for slow-growing prostate cancers. Brahmabhatt et al<sup>77</sup> recently reported growth-inhibiting and

apoptosis-inducing properties of ginger extract in in vitro and in vivo prostate cancer models. These findings demonstrate that binary combinations of ginger phytochemicals synergistically inhibit proliferation of PC-3 cells with Chou–Talalay combination-index values ranging from 0.03 to 0.88. Furthermore, [6]-gingerol inhibits cell adhesion, invasion, motility, and activities of extracellular matrix-degrading enzymes (matrix metalloproteinases) of human breast cancer MDA-MB-231 cells.<sup>78</sup> Therefore, [6]-gingerol may also contribute to the suppression of metastasis, and thus could also be explored for treating some cancer. The aforementioned mechanisms of ginger seem to be promising for cancer prevention and treatment; therefore, additional clinical studies are needed to assess the efficacy and safety of ginger.

## Other medicinal and toxicological properties

Ginger is also an important commodity of many traditional medicines and has been extensively used in Chinese, Ayurvedic, Tibb-Unani, Sri Lankan, Arabic, and African traditional medicines to treat many unrelated human ailments including fever, sore throats, cold, vomiting, motion sickness, gastrointestinal diseases, indigestion, constipation, arthritis, rheumatism, sprains, muscular aches, pains, cramps, hypertension, dementia, fever, infectious diseases, and helminthiasis. Ginger has been traditionally used from time immemorial for varied human ailments in different parts of the world, to aid digestion and treat stomach upset, diarrhea, nausea, and migraine. Significantly fewer recorded incidences of nausea were reported in the group that received ginger root and was comparable with the placebo in a double-blind, randomized study with 60 women who had major gynecological surgery.<sup>79</sup> Maghbooli et al<sup>80</sup> undertook a comparative-effectiveness trial of ginger (250 mg of ginger rhizome powder) versus sumatriptan (50 mg, a synthetic drug used to treat migraine headache) in 100 adults with common migraine (no aura). Both medications demonstrated a 44% reduction in pain score 2 hours following the treatments, though it is unknown how much of this effect was due to natural history and/or a placebo response.

Systemic in vivo studies of the overall safety and toxicological effects of ginger are relatively rare. In a rat study, it has been reported that the administration of lower dosage of ginger (50 mg/kg/d) showed no toxicity or histological changes in liver and lungs.<sup>81</sup> When a patented ginger extract (EV.EXT33) was administered orally up to 1 g/kg body weight to pregnant rats during the period of organogenesis,

neither maternal nor developmental toxicity was observed.<sup>82</sup> However, if ginger is consumed exceeding 6 g/d, then gastric irritation could occur in humans.<sup>1</sup>

## Conclusion

Ginger is an important herb which exhibits many medicinal and ethnomedicinal properties. There are a number of bioactive compounds which are responsible for providing various medicinal properties of ginger. The major bioactive constituents in ginger are the gingerols, of which 6-gingerol is the most abundant. As reviewed in this study, recently conducted in vivo and in vitro studies revealed that ginger exhibits a significant potential due to its antibiotic, antioxidant, hypoglycemic, hypotensive, anti-inflammatory, lipid lowering, antiplatelet aggregation, and chemopreventive properties. However, most of these pharmacological effects of ginger need to be validated using proper clinical studies which could endorse the pharmacological value of ginger and its constituents.

## Disclosure

The authors report no conflicts of interest in this work.

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