



# Ginger

## An Overview of Health Benefits

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**Ginger (*Zingiber officinale* Roscoe) is a member of the Zingiberaceae family of plants. It has been a part of healing strategies in Asia, India, Europe, and the Middle East for centuries for treatment of such disorders as arthritis, stomach upset, asthma, diabetes, and menstrual irregularities, to name a few. There is scientific support that ginger may alleviate the symptoms of nausea and vomiting following pregnancy, surgery, cancer therapy, or motion sickness and suggestive evidence that ginger reduces inflammation and pain. Cell culture studies show that ginger has antioxidant properties. However, it is not known whether ginger antioxidant constituents are bioavailable in humans once ingested and whether they can affect markers of oxidative stress in human in vivo. There are preliminary data that ginger has antimicrobial potential, although there is little evidence supporting ginger's practical usefulness in combating infections in humans. Based on evidence primarily from animal and in vitro studies, ginger may have beneficial effects toward cardiovascular disease through its multiple actions counteracting inflammation, hyperlipidemia, platelet aggregation, and hypertension. Overall, based on the current body of scientific literature, more information is needed from clinical studies to confirm these promising multiple health benefits of ginger in human subjects and the doses that are most efficacious. *Nutr Today*. 2010;45(4):171–183**

**G**inger (*Zingiber officinale* Roscoe) is a member of the Zingiberaceae family of plants. The plant is native to Asia but is now cultivated in the West Indies, Africa, India, and other tropical regions. The underground stem (rhizome) is used for preparation of ginger and can be obtained in colors varying from white

to brown, depending on whether the exterior is scraped off and how it is initially treated. This rhizome can be processed into a powder, syrup, volatile oil, and oleoresin. Its use in culinary applications dates as far back as the 13th century.<sup>1</sup> Among all spices, it exhibits one of the greatest diversity of uses, such as in dietary supplements, beverages (such as ginger ales), and food products (such as in curry powder, confectionaries, soups, jams, and baked goods).<sup>1,2</sup> It has been a part of healing strategies in Asia, India, Europe, and the Middle East for centuries for treatment of such disorders as arthritis, stomach upset, asthma, diabetes, and menstrual irregularities, to name a few.<sup>1,3–5</sup>

The rhizome contains fats, carbohydrates, protein, fiber, water, and volatile oil. The quality and quantity of biologically active constituents of ginger depend on its cultivation practices and postharvest treatment. The chemical components of the ginger rhizome can vary considerably, depending on the location of cultivation and whether the product is fresh, dried, or processed.<sup>5</sup> The pungency of fresh ginger results from a group of phenols, the gingerols, of which [6]-gingerol is most abundant. Fresh ginger also may contain a 5-deoxy derivative of ginger called paradol. Dry ginger, on the other hand, exhibits a pungency due to the shogaols, which are dehydrated forms of gingerols resulting from thermal processing. Ginger also contains about 1% to 3% volatile oil that imparts a distinctive odor to ginger and which is composed mainly of monoterpenoids and sesquiterpenoids, including camphene, borneol, zingiberene, sesquiphellandrene, and bisabolene.<sup>1,5,6</sup> Monoterpenes are compounds that contain 10-carbon skeleton often arranged in a ring. Sesquiterpenoids have a 15-carbon skeleton. Besides the pungent phenolic compounds (gingerols and shogaols), there are also bioactive diarylheptanoids and zingerone that are believed to contribute to its purported health benefits.<sup>2,5–8</sup>

Despite the widespread use of ginger and the numerous studies into its actions, there is limited information on bioavailability of the ginger components



Ginger plant. Obtained from McCormick & Company, Inc.

particularly in humans. The biological activity of ginger once consumed will likely depend not only on the chemical profile of the specific ginger product but also on the metabolic fate of the ginger phytochemicals once ingested. When administered to rats (3mg/kg, intravenously), ginger constituents are rapidly eliminated from the blood ( $t_{1/2} = 7.2$  minutes) in part because of liver metabolism.<sup>5</sup> Oral administration of [6]-gingerol to rats results in substantial glucuronide conjugation and subsequent excretion in the bile with a smaller amount of polar metabolites appearing in the urine.<sup>9</sup> Similar results were obtained when rats were orally administered

ginger oleoresin.<sup>10</sup> Conjugation reaction is catalyzed by UDP-glucuronyl transferase enzymes located in the liver and the intestinal mucosa. Oral [6]-gingerol (240 mg/kg body weight) given to rats resulted in a maximum plasma concentration of 4.2  $\mu\text{g/mL}$  at 10 minutes after dosing. Furthermore, at 30 minutes after dosing, tissue levels were maximum and generally were greater than those levels in blood.<sup>11</sup> A recent report, in which healthy humans received oral doses of ginger ranging from 100 mg to 2g, showed that major gingerol and shogaol constituents were readily absorbed and appeared in the serum predominantly as glucuronide conjugates. Importantly, no free forms were detectable.<sup>12</sup> Maximum serum concentrations of ginger metabolites generally were reached following administration of 1.5- and 2.0-g doses. This lack of free gingerol constituents detected in the serum suggests that many in vitro experiments using nonconjugated ginger constituents may have limited clinical relevance.<sup>12</sup> In another study, the degradation kinetics and products of [6]-gingerol and [6]-shogaol under varying physiological conditions were characterized in a model of stomach and intestine environments.<sup>13</sup> In vitro experiments using microsomal preparations from both humans and rodents confirm that [6]-gingerol is metabolized to a complex mixture of glucuronidated polar metabolites.<sup>14,15</sup> There is also evidence that metabolism of [6]-gingerol, most notably by enzymes in rat liver but also by those of gut microorganisms, may affect the disposition of this ginger constituent.<sup>9</sup>

The scientific literature provides evidence that ginger has a number of potential health benefits.<sup>1,6,16</sup> This evidence suggests that ginger may help alleviate nausea, both during pregnancy and from other causes. Some research suggests positive benefits of ginger in alleviating inflammation, especially that contributing to osteoarthritis.<sup>17</sup> Preliminary evidence is also available on ginger and relief of hypertension<sup>18</sup> and that ginger intake may have a role in cancer prevention.<sup>19</sup> Finally, initial preclinical research demonstrates that ginger lowers blood cholesterol and blood glucose levels.<sup>20</sup> In general, the preclinical data and preliminary findings suggest a variety of potential health benefits of ginger, although clinical trials supporting these benefits are relatively few.

Examples of several uses for ginger are presented in the Table, and an effort is made to give an overview of the variety of scientific research on this topic. Points of view for rating of evidence in each category are based on consideration of the number and quality of cell culture experiments, animal studies, and human clinical data from the peer-reviewed scientific literature. A higher rating was given when there were both preclinical and clinical data. A higher rating also was given when there were in vivo data from relevant and well-controlled

**Table. Summary of Scientific Research**

Uses Based on Scientific Evidence	Rating <sup>a</sup>
<p><b>Nausea and vomiting (general).</b> Ginger is often promoted for treatment of nausea and vomiting. However, although ginger powder appears to ameliorate nausea of diverse causes, the strength of evidence depends on the context in which it is used for treatment, such as for symptoms following pregnancy, surgery, cancer therapy, or motion sickness. These are discussed separately.</p>	
<p><b>Nausea and vomiting of pregnancy (hyperemesis gravidarum).</b> Evidence for the benefit of ginger as an antiemetic in pregnancy is some of the strongest.<sup>6,21–25</sup> Preliminary studies suggest that ginger may be effective for mild to moderate nausea and vomiting of pregnancy when used at a recommended dose of 1-g dried ginger per day or its equivalent in the form of ginger syrup.<sup>6,22</sup> Unfortunately, the specific chemical profile for each of the extracts used in such studies is not known. Treatment effectiveness and lack of adverse effects have been reported for periods of ginger use ranging from 4 d to 3 wk.<sup>6,22</sup> Ginger has been reported to be as effective as vitamin B<sub>6</sub> in lessening symptoms of morning sickness.<sup>24</sup> Yet, using higher doses of ginger (&gt; 1 g/d) during pregnancy has been discouraged because of concerns about potential teratogenicity.<sup>26,27</sup> In general, clinical trials evaluating the use of ginger in pregnancy have provided little information on fetal outcomes. Concern also has been expressed about potential bleeding problems in light of ginger's purported ability to inhibit platelet function and blood coagulation.<sup>6</sup> Nonetheless, there is, as yet, no direct clinical evidence that consumption of ginger by pregnant women is harmful.<sup>28,29</sup> In this regard, no well-controlled study has been specifically designed to address maximum safe dose (of a chemically defined product), length of treatment, and evidence of adverse effects for women consuming ginger at different stages of pregnancy. Thus, additional research is needed to determine the safety and effectiveness of multiple doses of ginger during pregnancy before it can be recommended for extended periods. As with all health uses of ginger and especially for hyperemesis gravidarum, it will be important to better understand how the chemical profile of biologically active ginger phytochemicals impacts efficacy and reports of adverse effects. Comparative studies among a variety of anti-nausea agents including ginger could be helpful to medical practitioners in making recommendations to patients. Furthermore, the quality and integrity of ginger preparations manufactured for use by women during pregnancy need to be carefully established.<sup>2,8,30</sup></p>	E to S
<p><b>Motion sickness/seasickness.</b> There is a lack of consistent beneficial effect of ginger for use on motion sickness or kinetosis.<sup>31,32</sup> In 7 of 11 experimental and clinical motion sickness studies, ginger demonstrated an improvement in symptoms of motion discomfort, nausea, or vomiting, compared with controls or with antiemetic drugs, although statistical significance was not always reached.<sup>6,16</sup> Some of the disparities in findings may be a consequence of the ginger powder dosage administered. Doses of dried ginger ranged from 0.5 to 3.5 g/d. Doses of fresh, minced raw ginger ranged from 0.5 to 1.0 g/d. Also, the differences in the latency and length of the response period monitored could be additional causes of disparities in the results. The mechanisms of action of ginger in decreasing motion sickness have not been well characterized. It has been suggested that any antiemetic effect of ginger for motion sickness is likely to be restricted to actions on the gastrointestinal tract and not on the central nervous system.<sup>33</sup> Before a recommendation can be made, consistently effective doses of ginger need to be identified, and additional confirmatory studies are needed demonstrating ginger's effectiveness compared with other relevant drugs used to treat motion sickness.</p>	P
<p><b>Nausea due to chemotherapy.</b> There is limited evidence from animal models that ginger has antiemetic activity in reducing the adverse effects of agents used in chemotherapy.<sup>34–36</sup> Findings from human studies are mixed.<sup>6,16,37–39</sup> Doses of ginger powder used in these clinical investigations, where indicated, were typically 0.5–1.0 g/d. Some studies indicate that ginger may reduce the severity and length of time that a patient feels nausea after chemotherapy, whereas other studies show no significant effects. In this regard, a recent randomized, double-blind, placebo-controlled trial in 162 cancer patients found that ginger provided no additional benefit in reducing prevalence or severity of acute or delayed chemotherapy-induced nausea and vomiting when given with 5-HT<sub>3</sub> receptor antagonists and/or aprepitant.<sup>40</sup> Additional human trials evaluating ginger's efficacy (at multiple doses) for treating nausea associated with several chemotherapeutic agents are needed before recommendations can be made. Some prescription drugs are effective at controlling nausea in cancer patients undergoing chemotherapy. Therefore, in all cases, consultation with an oncologist about available options is recommended before any use of ginger in this context is attempted.</p>	P

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**Table. Summary of Scientific Research, continued**

Uses Based on Scientific Evidence	Rating <sup>a</sup>
<p><b>Postoperative nausea and vomiting.</b> The findings from human studies examining ginger for amelioration of nausea and vomiting after surgery (mostly gynecological and lower extremity surgeries) are not consistent.<sup>6,41–44</sup> Some of the disparities in study outcomes may be due to differences in dosages used. Typically 1 g/d of ginger powder was administered, although in some studies doses as low as 0.3 g/d and as high as 2.0 g/d were evaluated. Differences in timing of outcome measurements also could have contributed to disparities.<sup>42</sup> In those studies demonstrating efficacy, there were generally no adverse effects. Additional studies are needed before the preoperative use of ginger to help with postoperative nausea and vomiting can be recommended.</p>	P
<p><b>Mechanisms of antiemesis.</b> The possible mechanisms behind any antiemetic action of ginger are not well characterized. In rats and humans, ginger constituents appear to have differing effects on gastrointestinal motility and transit times, which in part may be due to differences in experimental conditions and dosages used.<sup>45–50</sup> In rodents, ginger extracts have been demonstrated to possess cholinergic agonist actions, muscarinic antagonist-like effects, and antiserotonin actions. Ginger also may act on the 5-HT<sub>3</sub> receptor ion-channel complex in the gastrointestinal tract.<sup>49,51–54</sup> In humans, ginger intake (1–2 g) may block production of gastric prostaglandins and decrease plasma vasopressin release induced by circularvection.<sup>55,56</sup></p>	
<p><b>Antiplatelet agent.</b> There are few investigations into ginger's capacity to alter blood clotting. One human study suggested that intake of 1-g ginger powder may have a synergistic effect on antiplatelet aggregation in hypertensive patients when used in combination with nifedipine.<sup>57</sup> In another investigation, a ginger powder dose of 10-g powder but not 4 g resulted in a significant reduction of platelet aggregation in patients with coronary artery disease.<sup>58</sup> In healthy volunteers, supplementation of a fatty meal with 5-g ginger powder prevented the postprandial fat-induced decline in fibrinolytic activity.<sup>59</sup> Yet, ginger at a dose of 3.6 g/d for 1 wk did not affect clotting status of health subjects taking warfarin.<sup>60</sup> Use of a cell culture assay detected several gingerol and shogaol constituents of ginger that bound to thrombocytes and elicited antiplatelet activity.<sup>61,62</sup> In rats, an aqueous extract of ginger was able to lower platelet thromboxane X<sub>2</sub> and prostaglandin E<sub>2</sub> production, responses that were highly dependent on the dose and route of administration.<sup>63</sup> In contrast, for humans given 15-g raw ginger root or 40-g cooked stem ginger daily for 2 wk, there was no effect on ex vivo platelet thromboxane production.<sup>64</sup> Clinical studies are needed in which the effects of a chemically defined ginger product on biomarkers of antiplatelet activity are determined. Such studies should evaluate a range of ginger doses as well as several duration periods. It would be helpful for any such action of ginger to be compared with other agents currently in use.</p>	P
<p><b>Hypotensive effects.</b> Findings from several animal studies suggest that ginger may have beneficial effects on blood pressure.<sup>5,18,20,65</sup> The mechanism for ginger's effect in lowering blood pressure may be mediated by inhibition of voltage-dependent calcium channels as well as by stimulating muscarinic receptors. However, individual gingerol and shogaol constituents of ginger appear to exhibit dissimilar actions with regard to blood vessel reactivity.<sup>5,20</sup> This action of ginger in alleviating hypertension needs to be better characterized.</p>	P
<p><b>Regulation of blood glucose and lipid levels.</b> Several animal studies indicate that ginger may be beneficial in lowering problematic blood glucose and lipid concentrations. In streptozotocin (STZ)-induced diabetic rats, specific extracts of ginger lowered blood glucose, cholesterol, and triglyceride levels and increased high-density lipoprotein cholesterol concentrations.<sup>66–68</sup> Furthermore, dietary intakes of dried ginger (0.5–2.0% wt/wt) by STZ-treated diabetic rats was insulinotropic and superior to the antidiabetic actions of garlic.<sup>69</sup> Similar results have been observed in other rodent models of hyperglycemia, hyperlipidemia, and hyperinsulinemia, effects that in part may be due to 6-gingerol.<sup>70–73</sup> The ginger constituent zingiberone also produced lower blood glucose levels, body weight, and parametrial adipose tissue weight in ovariectomized rats.<sup>74</sup> In vitro studies using adipocytes point to gingerol as having insulin-sensitizing and glucose uptake-enhancing actions.<sup>75</sup> In addition, aldose reductase inhibitors, considered to have potential in the treatment of diabetes, have been detected in ginger using an in vitro assay.<sup>76</sup> In contrast to these preclinical experiments, one human study, in which ginger powder was administered in 4-g daily doses for 3 months to patients with coronary artery disease, did not demonstrate any changes in either blood glucose or blood lipid levels.<sup>58</sup> Yet, a recent double-blind controlled clinical trial with hyperlipidemic patients showed that 3-g ginger powder per day for 45 d had a significant serum lipid-lowering effect compared with</p>	P

**Table. Summary of Scientific Research, continued**

Uses Based on Scientific Evidence	Rating <sup>a</sup>
<p>placebo controls.<sup>77</sup> Clearly, in light of these mixed findings, more attention needs to be focused on completing well-controlled human studies that determine the chronic effect of multiple doses of ginger on these end points.</p>	
<p><b>Anticancer actions.</b> Ginger extract has demonstrated the capacity in numerous cancer cell culture systems to suppress cell proliferation and induce cell death.<sup>19,78–86</sup> In animals, ginger exhibited mixed results as an inhibitor of tumor formation in models of colon, bladder, lung, and skin cancer.<sup>87–94</sup> Its benefit for treating or preventing cancer in humans is not known.</p>	P
<p><b>Antioxidant actions.</b> Ginger and some specific constituents have demonstrated antioxidant effects in several cell culture systems.<sup>95–99</sup> Furthermore, there are animal studies showing that ginger extracts and individual ginger constituents such as [6]-gingerol can protect several tissues and organs against damage due to a variety of oxidation-inducing stressors.<sup>99–107</sup> In rats, ginger extract also ameliorated acetic acid–induced ulcerative colitis, likely due to its antioxidant and anti-inflammatory actions.<sup>108</sup> Interestingly, beverages produced by lactic fermentation of Zingiberaceae plants retained antioxidant activity.<sup>109</sup> There has been, however, no demonstration of antioxidant efficacy toward in vivo markers of oxidative stress following consumption by humans.</p>	P
<p><b>Alleviation of rheumatoid arthritis/osteoarthritis/joint and muscle pain.</b> Ginger is a herbal medicinal product with a long history of use for treatment of rheumatic conditions because of its broad anti-inflammatory actions.<sup>17,110</sup> In vitro experiments<sup>111–115</sup> and several animal studies<sup>73,116–126</sup> provide suggestive evidence that ginger and its active ingredients have the capacity to decrease symptoms of inflammation-associated conditions such as arthritis. Ginger's anti-inflammatory effects may be due in part to its inhibition of cyclooxygenase, inducible nitric oxide synthase, and lipoxygenase activities, as well as suppression of inflammatory prostaglandin synthesis and interference in cytokine signaling.<sup>5,6,17,127</sup> A number of ginger constituents including gingerols, shogaols, and diarylheptanoids may contribute to these actions.<sup>5,17</sup> Human studies evaluating the efficacy of ginger (using doses ranging from 0.5–50 g/d) in alleviating symptoms of arthritis and of joint and knee pain have provided mixed results.<sup>6,31,110,128–133</sup> Five clinical studies did show some evidence of short-term pain-relieving effects of ginger. In some cases, it was noticed that oral intake of ginger extract may cause mild gastrointestinal discomfort associated with nausea, dyspepsia, and eructation, although any adverse effects of ginger appeared to be less severe than those produced by conventional nonsteroidal anti-inflammatory drugs.<sup>5,128,131,132</sup> In general, it is unclear from these investigations what form and dose of ginger are most advantageous for treatment.<sup>6</sup> Specific ginger constituents also have been linked to analgesic properties.<sup>17,134–137</sup> In a human exercise study in which a 2-g dose of ginger or placebo was administered in a double-blind crossover design, no clinically meaningful or statistically significant effect was noted for perception of muscle pain, rating of perceived exertion, work rate, heart rate, or oxygen uptake.<sup>138</sup> A recent double-blind comparative clinical trial in women demonstrated that 1-g ginger powder per day for 3 d from the start of their menstrual period was as effective as mefenamic acid and ibuprofen in relieving the pain of primary dysmenorrhea.<sup>139</sup> No severe adverse effects were reported, and no differences in satisfaction with treatments were observed among groups. Additional well-controlled human trials are needed that examine longer duration of treatment and multiple dosage levels (administered per kg body weight) using well-characterized plant extracts before recommendations can be made supporting ginger for routine treatment of rheumatic conditions.<sup>128</sup></p>	P
<p><b>Antimicrobial activity.</b> Ginger extracts and individual constituents have been reported in in vitro studies to suppress the growth of a variety of common infectious bacteria including <i>Staphylococcus aureus</i> and <i>Listeria monocytogenes</i>.<sup>140</sup> Commercial ginger paste demonstrated antimicrobial activity toward <i>Escherichia coli</i> O157:H7 in laboratory buffer and ground beef.<sup>141</sup> [10]-Gingerol was also able to enhance the antimicrobial efficacy of drugs in the treatment of drug-resistant enterococci.<sup>142</sup> Of considerable interest is the reported capacity of gingerols and phenolic metabolites to inhibit growth of <i>Helicobacter pylori</i> and to enhance the effectiveness of drugs targeting this bacterium, suggesting a new potential use of ginger in combating <i>H pylori</i>-related gastrointestinal diseases.<sup>143–145</sup> In animal studies, ginger extracts exhibited the capacity to protect mice against infections caused by several microbes.<sup>146,147</sup> With regard to antifungal activity, ginger has been reported to be effective in some but not all studies.<sup>148–151</sup> Likewise, reports on the capacity of ginger to suppress virus growth are inconsistent.<sup>152,153</sup> Lastly, a study showed that ginger possessed in vivo antiparasitic activity in sheep given at a dose of 1 to 3 g of ginger powder/kg body weight.<sup>154</sup></p>	P

(continues)

**Table. Summary of Scientific Research, continued**

Uses Based on Scientific Evidence	Rating <sup>a</sup>
<p><b>Miscellaneous effects.</b> Several studies report the capacity of ginger to influence body temperature and metabolic rate, although the responses are inconsistent.<sup>155–159</sup> Two in vitro studies point to potential benefits of ginger in alleviating neurological disorders such as Alzheimer disease.<sup>160,161</sup> Doses used in these cell culture studies were about 18 to 34-<math>\mu</math>g dried residue per milliliter obtained from organic solvent extractions of ginger. Another cell culture study demonstrated anti-inflammatory actions of ginger extract in mouse microglial cells.<sup>127</sup> A recent study in mice reported that the essential oil of ginger rhizome potentiated the antidepressant-like effect of magnolia bark extract by ameliorating abnormalities in serotonergic and noradrenergic system functions.<sup>162</sup> Ginger also has been reported to decrease chemically induced liver toxicities in rodents.<sup>163,164</sup></p>	P

<sup>a</sup>Ratings: S = strong, convincing; E = emerging, suggestive; P = preliminary, inconclusive.

animal models, and there was consistency of findings among well-controlled human studies. Although some references listed in Table are reviews, the quality of the data from the original studies therein was considered in assigning ratings.

### Safety

The Food and Drug Administration has given ginger GRAS (generally recognized as safe) status for use as a food supplement. Food allergy to spices is infrequent.<sup>165</sup> Based on experimental data and findings from human studies, few adverse reactions have been reported.<sup>16,166,167</sup> Uncommon adverse reactions reported in these trials include mild gastrointestinal distress, heart burn, diarrhea, and oral irritation.<sup>6</sup> A comprehensive review of human trials concluded that ginger at doses up to 2 g/d resulted in minimum toxicity for humans.<sup>21</sup> Likewise, a recent systemic safety assessment of ginger in female and male rats reported that doses of ginger powder of 500, 1000, and 2000 mg/kg body weight given by gavage for 35 days were not associated with any mortalities and abnormalities in general conditions, behavior, growth or food intake, or hematologic and blood biochemical parameters.<sup>168</sup> Only at the highest dose in males a slightly reduced weight of testes was observed. Ginger constituents can be cytotoxic and mutagenic,<sup>6,80</sup> although it is unclear whether this effect is relevant at blood levels of ginger constituents encountered after oral ingestion of ginger.

As mentioned previously, the safety of use of ginger for pregnancy-induced nausea and vomiting warrants further study in large populations, although some consider potential risks to be minimal.<sup>6,21,169,170</sup> In a human study, the risk for major malformations was similar between 2 groups of women, one using ginger for treatment of emesis during the first trimester of pregnancy and the other not receiving this therapy

during the same period.<sup>171</sup> In rodent studies, pregnant females administered high doses of ginger evidenced no maternal toxicity, although some evidence of fetal changes was reported.<sup>172,173</sup> Ginger has been reported to bind testosterone, raising concerns about possible consequences for the developing embryo.<sup>27</sup> In the German Commission E monographs, ginger is not recommended for use to treat morning sickness.<sup>174</sup> Therefore, in light of these varying perspectives, if ginger is considered for use by pregnant women, the recommendations to use proprietary preparations that have been tested for safety and efficacy and to consult a physician seem prudent.<sup>21</sup> Herbal home remedies used in children consisting of teas made from ginger are considered benign,<sup>175</sup> and ginger rhizome is considered relatively safe for treating common ear problems in pregnancy.<sup>176</sup>

As with any alternative therapeutic agent, there is a safety concern regarding potential interactions with prescription medications, particularly those with narrow therapeutic indexes, such as the blood-thinning agent warfarin.<sup>177,178</sup> In light of ginger's capacity to inhibit platelet function and blood coagulation, the potential exists that ginger could increase the risk of bleeding or potentiate the effects of warfarin therapy or, generally, of anticoagulants, platelet inhibitors, and thrombolytic agents.<sup>177–180</sup> One human case report described ginger-associated overanticoagulation by phenprocoumon.<sup>181</sup> In other studies, there appeared to be no indication of this effect at the ginger doses studied.<sup>60,182</sup> A recent animal study documented that ginger significantly decreased the oral bioavailability of the immunosuppressant cyclosporine, with the authors recommending that patients treated with cyclosporine discontinue use of ginger products.<sup>183</sup>

It should be reiterated that just as in judging efficacy of ginger, the safety of ginger cannot be adequately addressed until clinical studies provide more complete

information on possible adverse events following administration of multiple doses of ginger for periods of short and long duration and using ginger products of defined composition.

## Summary of Research

It is apparent from preclinical data that ginger and its bioactive constituents possess multiple biological activities that suggest potential benefit for alleviating a variety of health problems.

For example, cell culture studies show that ginger has antioxidant properties, which probably arise from several active constituents. However, it is not known whether these constituents are bioavailable in humans once ingested and whether they can affect markers of oxidative stress in human *in vivo*. There are preliminary data from *in vitro* experiments pointing to ginger's antimicrobial potential, although there is little evidence supporting ginger's practical usefulness in combating infections in humans.

Likewise, animal studies suggest that ginger may also help alleviate problematic blood lipid and glucose levels associated with heart disease and/or diabetes. Similarly, based on evidence primarily from animal and *in vitro* studies, ginger may have beneficial effects toward cardiovascular disease through its multiple actions counteracting inflammation, hyperlipidemia, platelet aggregation, and hypertension. There also is suggestive evidence that ginger reduces inflammation and pain, although additional controlled human studies are needed before definitive conclusions can be made about these varied actions.

Of all the purported health benefits of ginger, the clinical evidence is increasingly convincing that ginger may alleviate pregnancy-associated nausea at doses typically consumed (1-g ginger powder per day). However, consistent information on ginger product composition from published studies is lacking, especially at doses greater than 1 g/d for extended duration of use. Although no significant adverse effects of ginger use at 1 g/d on mother and developing fetus have been documented, concerns about safety dampen enthusiasm for recommending ginger as a natural product alternative for minimizing nausea during pregnancy. The strength of evidence for ginger's benefit is less convincing for nausea and vomiting due to surgery, cancer therapy, or motion sickness. Future studies should address several issues. A better understanding of ginger's *in vivo* mechanisms of action from preclinical studies can better assist in the selection of relevant biomarkers for and the design of additional larger clinical trials. Clinical studies comparing ginger and other conventional therapies could

provide insights into ginger's relative efficacy and cost-effectiveness to alleviate various conditions.<sup>184</sup> In general, clinical studies need to determine the effects of multiple doses and of different dosing schedules of chemically defined ginger products on efficacy and safety. Variation in ginger product composition among clinical trials is a barrier to meaningful interstudy comparisons that needs to be resolved.

Overall, based on the current body of scientific literature, ginger demonstrates some promising health benefits, and more information gleaned from additional clinical studies will help confirm whether ginger's multiple health benefits can be realized in humans. At the moment, it is unclear whether the culinary use of ginger can be expected to significantly produce these health benefits highlighted in this overview. Future trials examining both chronic intake of lower doses of ginger (<500 mg/d) and the most effective dosing schedule could provide helpful insights into this issue.

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