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Review Article

Benefits of Ginger for Medical Welfare of Humanity

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Abstract

Ginger is an herbal medicinal product with a long history of use for treatment of rheumatic conditions because of its broad anti-inflammatory actions. Ginger extract has demonstrated the capacity in numerous cancer cell culture systems to suppress cell proliferation and induce cell death. Ginger exhibited mixed results as an inhibitor of tumor formation in models of colon, bladder, lung, and skin cancer. Ginger and some specific constituents have demonstrated antioxidant effects in several cell culture systems. Ginger extracts and individual ginger constituents such as [6]-gingerol can protect severaltissues and organs against damage due to a variety of oxidation-inducing stressors. Ginger extract also ameliorated acetic acid-induced ulcerative colitis, likely due to its antioxidant and anti-inflammatory actions. Interestingly, beverages produced by lactic fermentation of Zingiberaceae plants retained antioxidant activity. 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. Specific ginger constituents also have been linked to analgesic properties.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 dysmenorrheal.

Ginger extracts and individual constituents have been reported in in vitro studies to suppress the growth of a variety of common infectious bacteria including Staphylococcus aureus and Listeria monocytogenes. Commercial ginger paste demonstrated antimicrobial activity toward Escherichia coli O157:H7 in laboratory buffer and ground beef. Gingerol was also able to enhance the antimicrobial efficacy of drugs in the treatment of drug-resistant enterococci. Essential oil of ginger rhizome potentiated the antidepressant-like effect of magnolia bark extract by ameliorating abnormalities in serotoninergic and noradrenergic system functions. Herbal home remedies used in children consisting of teas made from ginger are considered benign, and ginger rhizome is considered relatively safe for treating common ear problems in pregnancy. Crude extract of ginger induced a dose-dependent (0.3–3 mg/kg) fall in the arterial blood pressure 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. In healthy volunteers, supplementation of a fatty meal with 5-g ginger powder prevented the postprandial fat-induced decline in fibrinolytic activity.

Ginger is beneficial in lowering problematic blood glucose and lipid concentrations. Specific extracts of ginger lowered blood glucose, cholesterol, and triglyceride levels and increased high-density lipoprotein cholesterol concentrations.

The ginger constituent zingiberone also produced lower blood glucose levels, body weight, and parametrial adipose tissue weight. Gingerol as having insulin-sensitizing and glucose uptake-enhancing actions. In addition, aldose reductase inhibitors, considered to have potential in the treatment of diabetes.Ginger exhibited mixed results as an inhibitor of tumor formation in models of colon, bladder, lung, and skin cancer.

Ginger extracts and individual ginger constituents such as [6]-gingerol can protect severaltissues and organs against damage due to a variety of oxidation-inducing stressors.

Key words: hypokalemia; periodic paralysis; emergency service

Introduction

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 (Young *et al*., 2006). In healthy volunteers, supplementation of a fatty meal with 5-g ginger powder prevented the postprandial fat-induced decline in fibrinolytic activity (Verma and Bordia, 2001). Yet, ginger at a dose of 3.6 g/d for 1 wk did not affect clotting status of health subjects taking warfarin (Jiang *et al*., 2005). Use of a cell culture assay detected several gingerol and shogaol constituents of ginger that bound to thrombocytes and elicited antiplatelet activity (Nurtjahja-Tjendraputra *et al*., 2003 and Nie *et al*., 2008). In rats, an aqueous extract of ginger was able to lower platelet thromboxane X2and prostaglandin E2production, responses that were highly dependent on the dose and route of administration (Thomson *et al*., 2002). Findings from several animal studies suggest that ginger may have beneficial effects on blood pressure (Ghayur and Gilani, 2005). Several animal studies indicate that ginger may be beneficial in lowering problematic blood glucose and lipid concentrations. In streptozotocin (STZ) Yinduced diabetic rats, specific extracts of ginger lowered blood glucose, cholesterol, and triglyceride levels and increased high-density lipoprotein cholesterol concentrations (Al-Amin *et al*., 2006; Bhandari *et al*., 2005 and Akhani *et al*., 2004). Furthermore, dietary intakes of dried ginger (0.5Y2.0% wt/wt) by STZ-treated diabetic rats were insulinotropic and superior to the antidiabetic actions of garlic (Islam and Choi, 2008). Similar results have been observed in other rodent models of hyperglycemia, hyperlipidemia, and hyperinsulinemia, effects that in part may be due to 6-gingerol (Kadnur and Goyal, 2005;2006; Chou *et al*., 2009 and Ojewole, (2006). The ginger constituent zingiberone also produced lower blood glucose levels, body weight, and parametrial adipose tissue weight in ovariectomized rats (Han *et al*., 2008). In vitro studies using adipocytes point to gingerol as having insulin-sensitizing and glucose uptake-enhancing actions (Sekiya *et al*., 2004). In addition, aldose reductase inhibitors, considered to have potential in the treatment of diabetes, have been detected in ginger using an in vitro assay (Kato *et al*., 2006). 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 withplacebo controls (Alizadeh-Navaei *et al*., 2006). Anticancer actions.Ginger extract has demonstrated the capacity in numerous cancer cell culture systems to\ suppress cell proliferation and induce cell death (Aggarwal and Shishodia, 2006; Aggarwal *et al*., 2008; Kim *et al*., 2008; Lee *et al*., 2008; Rhode *et al*., 2007; Chen et al., 2007; Lee *et al*., 2008; Kundu *et al*., 2009 and Park and Pezzuto, 2002).

In animals, ginger exhibited mixed results as an inhibitor of tumor formation in models of colon, bladder, lung, and skin cance r (Dias *et al*., 2006; Bidinotto *et al*., 2006; Mangu and Nalini, 2006; Ihlaseh *et al*., 2006; Kim *et al*., 2008; Sung *et al*., 2009 and Habib *et al*., 2008). Ginger and some specific constituents have demonstrated antioxidant effects in several cell culture systems (Asnani and Verma, 2007; Chohan *et al*., 2008 and Tao *et al*., 2008). Furthermore, there are animal studies showing that ginger extracts and individual ginger constituents such as [6]-gingerol can protect severaltissues and organs against damage due to a variety of oxidation-inducing stressors Kim *et al*., 2007; Mallikarjuna *et al*., 2008; Ahmed *et al*., 2008; Amin and Hamza, 2006; Haksar *et al*., 2006; Ansari *et al*., 2006; Ajith *et al*., 2007 and Ahmed *et al*., 2000). In rats, ginger extract also ameliorated acetic acid-induced ulcerative colitis, likely due to its antioxidant and anti-inflammatory actions (El-Abhar *et al*., 2008). Interestingly, beverages produced by lactic fermentation of Zingiberaceae plants retained antioxidant activity (Chen *et al*., 2008). Ginger is an herbal medicinal product with a long history of use for treatment of rheumatic conditions because of its broad anti-inflammatory actions (Gregory *et al*., 2006). In vitro experiments (Aktan *et al*., 2006; Lantz *et al*., 2007; Pan *et al*., 2008; Tripathi *et al*., 2007 and Frondoza *et al*., 2004) and several animal studies (Minghetti *et al*., 2007; Young *et al*., 2005; Ambire *et al*., 2007; Levy *et al*., 2006; Shen *et al*., 2003; Fouda and Berika, 2009 and Funk *et al*., 2009). 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 (Jung *et al*., 2009).

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 (Fajardo DiCesare, 2005; Chubrasik *et al*., 2007; Wigler *et al*., 2003 and Altman and Marcussen, 2001). Specific ginger constituents also have been linked to analgesic properties (Cady et al., 2005; Cortright *et al*., 2007 and Dedov *et al*., 2002). 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 (Black and O'Connor, 2008). 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 dysmenorrheal (Ozgoli *et al*., 2009). Ginger extracts and individual constituents have been reported in in vitro studies to suppress the growth of a variety of common infectious bacteria including Staphylococcus aureus and Listeria monocytogenes (Norajit and Laohakunjit, 2007) Commercial ginger paste demonstrated antimicrobial activity toward Escherichia coli O157:H7 in laboratory buffer and ground beef (Gupta and Ravishankar, 2005). [10]-Gingerol was also able to enhance the antimicrobial efficacy of drugs in the treatment of drug-resistant enterococci (Nagoshi *et al*., 2006). Of considerable interest is the reported capacity of gingerols and phenolic metabolites to inhibit growth of Helicobacter pylori and to enhance the effectiveness of drugs targeting this bacterium, suggesting a new potential use of ginger in combating H pylori- related gastrointestinal diseases (Mahady *et al*., 2003; Siddaraju and Dharmesh, 2007 and Nostro *et al*., 2006). In animal studies, ginger extracts exhibited the capacity to protect mice against infections caused by several microbes (Jageta *et al*., 2003 and Chen Nostro *et al*., 2007).

With regard to antifungal activity, ginger has been reported to be effective in some but not all studies (Ficker et al., 2003; Agarwal et al., 2008 and Pozzatti *et al*., 2008). Likewise, reports on the capacity of ginger to suppress virus growth are inconsistent (Imanishi *et al*., 2006 and Schnitzler *et al*., 2007). 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 (Iqbal et al., 2006). Several studies report the capacity of ginger to influence body temperature and metabolic rate, although the responses are inconsistent (Ueki et al., 2008 and Westerterp-Plantenga et al., 2006). Two in vitro studies point to potential benefits of ginger in alleviating neurological disorders such as Alzheimer disease (Kim *et al*., 2007 and Ghayur *et al*., 2008). 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 serotoninergic and noradrenergic system functions (Yi *et al*., 2009). Ginger also has been reported to decrease chemically induced liver toxicities in rodents (Yemitan and Izegbu, 2006 and Verma and Asnani, 2007).

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 (Moneret-Vautrin *et al*., 2002). Based on experimental data and findings from human studies, few adverse reactions have been reported (Kaul and Joshi, 2001). 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 (Rong *et al*., 2009). As mentioned previously, the safety of use of gingerfor pregnancy-induced nausea and vomiting warrants further study in large populations, although some consider potential risks to be minimal (Eberhard *et al*., 2005 and Fugh-Berman, 2003). 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 (Portnoi *et al*., 2003). In rodent studies, pregnant females administered high doses of ginger evidenced no maternal toxicity, although some evidence of fetal changes was reported (Wilkinson, 2000 and Weidner and Sigwart,

2001). Herbal home remedies used in children consisting of teas made from ginger are considered benign (Fugh-Berman, 2002), and ginger rhizome is considered relatively safe for treating common ear problems in pregnancy (Vlastarakos *et al*., 2008). 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 (Heck *et al*., 2000 and Ulbricht *et al*., 2008).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 (Spolarich and Andrews, 2007). One human case report described ginger-associated over anticoagulation by phenprocoumon (Kru¨th *et al*., 2004). In other studies, there appeared to be no indication of this effect at the ginger doses studied (Jiang *et al*., 2006). 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 (Chiang *et al*., 2006). More recently, Ghayur and Gilani et al. (2005) reported that the crude extract of ginger induced a dose-dependent (0.3–3 mg/kg) fall in the arterial blood pressure of anesthetized rats. In Guinea pig paired atria, the crude extract exhibited a cardio depressant activity on the rate and force of spontaneous contractions.

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