Journal of Herbal Medicine xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Journal of Herbal Medicine

journal homepage: www.elsevier.com/locate/hermed

Review article

The effect of ginger (Zingiber Officinale) as an ancient medicinal plant on improving blood lipids

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ARTICLE INFO

Keywords:
Ginger
Zingiber Officinale
Blood lipids
Cholesterol
Triglyceride
Diabetes

ABSTRACT

Ginger (Zingiber Officinale Roscoe) is a plant that is used as a popular spice in foods, desserts and drinks all around the world. This plant is native to Asia and has been used since ancient times in the prevention and treatment of many diseases. To date, several properties of ginger such as antioxidant, anti-inflammatory and anticoagulation activities have been studied and the effect of the plant to reduce pain and improve nausea and vomiting has been established. Among human and animal studies that have been carried out in recent years on the properties of ginger, some literature aimed to investigate the effect of this plant on blood lipids. In this review, we consider those studies and their possible enzymatic and molecular mechanisms regarding the effect of ginger on lipid profiles.

1. Introduction

Ginger, the rhizome of Zingiber officinale, is used as a spice all over the world (Lantz et al., 2007). It is a member of the zingiberaceae plant family and is native to Asia, although now grown in Africa, India and other tropical regions (Singletary, 2010).

Ginger is a plant with thick roots and vertical, upright stems. This perennial plant has nodal rhizomes with many divided swells. The rhizome of ginger grows horizontally and its outer membrane can be seen to be yellow or brown. The internal membrane of the rhizome is yellowish brown and has numerous vessel elements and cells, containing oleoresin. Ginger has an appealing odor and spicy taste, with the dried powder, appearing a yellowish white to yellowish brown (Arablou and Aryaeian, 2014).

To date, more than 400 different compounds have been identified in ginger (Singh et al., 2010). The amount and quality of active components of ginger depend on the region of cultivation, the cultivation and processing method used, and whether used in fresh or dried form. The odor of ginger depends on the amount of ginger oil present, the levels usually varying between 1% and 3%. Over 50 components have been identified in this oil, most of which are monoterpenoid and sesquiterpenoid compounds. The pungency of fresh ginger is due to the group of phenolic compounds called gingerols, among which 6-gingerol is the most abundant. There are other gingerols in ginger with different length side chains. The shogaols that are responsible for the pungency of dried ginger, are the dehydrated form of gingerols (Arablou and Aryaeian, 2014; Wohlmuth et al., 2005). In fact, gingerols convert to shogaols during the thermal process and the degradation rate depends on environmental PH (Athari-Nikazm, 2009).

Other compounds found in ginger include 3-dihydroshogaols, paradols, dihydroparadols, acetylated gingerol derivates, gingerdiols, mono and diacetyl gingerdiol derivates, 1-dehydrogingerdiols, diaryl heptanoids, epoxide diaryl heptanoids, methyl ether derivates, ferollic acid derivates and terpenes such as zingerones and zingerols (Ali et al., 2008; Singh et al., 2010).

Despite a widespread use of ginger, there is little information about the bioavailability of its compounds, especially in human use. Intravenous injection of ginger to rats in the amount of 3 mg per kg of body weight, showed that its compounds were cleared rapidly from the blood (t 1/2 = 7. 2 min) due to their metabolism in the liver (Ding et al., 1991).

Also, oral administration of 6-gingerol (50 mg/kg) in rats leads to the production of its glucuronide conjugates and their excretion through the bile. Small amounts of its polar metabolites are also excreted in the urine within 60 h (Nakazawa and Ohsawa, 2002). Similar findings were observed by oral administration of zingerone and oleoresin of ginger in rats (Ahmed et al., 2000; Wang et al., 2009). Conjugation is done by UDP-glucuronosyltransferase enzyme in the liver and the mucus of the small intestine. Also, after 10 min of oral administration of 6-gingerol in the amount of 240 mg per kg of body

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http://dx.doi.org/10.1016/j.hermed.2017.09.005
Received 13 September 2015; Received in revised form 28 May 2016; Accepted 20 September 2017

weight in rats, its plasma concentration reached to 4.2 μg/ml. Its amount reached to the maximum level in tissues 30 min following consumption.

In one human study, healthy volunteers received different doses of ginger from 100 mg to 2 g. The results showed that the main pungent constituents of ginger root, 6-, 8-, 10-gingerol and 6-shogaol absorbed quickly and were detected in the serum as glucuronide and sulfate conjugates but not in their free forms. These constituents at concentrations normally found in the ginger root (0.5–2.5%), were detectable in the serum starting at a 1.0 g dose with the exception of 6-gingerol which is detectable at a 250 mg dose with maximum concentrations ranging from 0.1 to 1.7 μg/ml (Zick et al., 2008).

In another human study conducted by Yu et al., oral administration of 2.0 g ginger extracts, led to the detection of free 10-gingerol and 6-shogaol in plasma after 1 h, but no free 6-gingerol and 8-gingerol were detected in plasma from 0.25 to 24 h. This study also indicated that most of the 6-, 8-, and 10-gingerols and 6-shogaol existed in the form of glucuronide or sulfate conjugates with 1–3 h half-lives in the human plasma (Yu et al., 2011).

Ginger is known as a safe compound (Ali et al., 2008). The American food and drug administration recognized ginger as a GRAS (Generally Recognized As Safe) ingredient (Singletary, 2010). According to evidence from human studies, very few side effects have been reported after ginger consumption. Rare side effects include mild digestive disorders, heartburn, and diarrhea (Singletary, 2010; Arablou et al., 2014a,b). Clinical studies have shown that receiving ginger in the amount of 2 g per day has negligible toxicity for humans (Singletary, 2010).

Ginger's health properties were first documented more than 2000 years ago (Vasanthi and Parameswari, 2010). In the past, this plant was used for alleviation and treatment of different symptoms such as vomiting, pain, indigestion and upper respiratory tract infection (White, 2007; Wang and Wang, 2005). Nowadays, ginger is used in dietary supplements, drinks and food products like sweets, jams and soups (Singletary, 2010).

The main pharmacological activities of ginger and its segregated compounds include as an immune modulator, anti-tumorgenesis, anti-inflammatory, anti-apoptosis, and anti-vomiting. The plant is effective in improving nausea and vomiting induced by pregnancy, surgery, chemotherapy and motion sickness (Singletary, 2010). Also, scientific evidence shows that ginger has antioxidant and anticoagulation properties and can decrease pain (Li et al., 2012). Some studies have established the effect of ginger on reducing inflammation, especially in osteoarthritis (Naderi et al., 2015; Altman and Marcussen, 2001; Srivastava and Mustafa, 1992).

Additionally, ginger consumption is effective in the prevention of cancer (Singletary, 2010). This effect is attributable to the herb's action as a strong antioxidant that can prevent the damage caused by free radicals and decrease their activity (Ali et al., 2008; Nicoll and Henein, 2007).

In recent years, numerous animal and human studies have investigated the effect of ginger consumption on metabolic status, glycemia, blood lipids, and blood pressure. Most of these studies showed that ginger can improve some parameters of lipid profile, especially in diabetic patients (Arablou et al., 2014a,b; Khandouzi et al., 2015; Mahluji et al., 2013). In this paper, we review some of the studies regarding the effect of ginger on blood lipids.

2. Methodology

The information in this narrative review is obtained based on the results of the authors search in Pubmed, Google scholar, and Science Direct databases by using the keywords "ginger and Zingiber officinale" in combination with "lipid, cholesterol, triglyceride, and diabetes" without considering any time limitation. All relevant human studies (clinical trials) were included and discussed in this paper.

2.1. The effect of ginger on lipid profile

2.1.1. Human studies

In a randomized double-blind placebo-controlled clinical trial conducted by Khandouzi et al., 41 type 2 diabetic patients were assigned randomly to the ginger or placebo groups and received 2 g/day of ginger powder supplement or lactose as the placebo for 12 weeks. Ginger supplementation significantly reduced the levels of apolipoprotein B and apolipoprotein B/apolipoprotein A-I ratio (P value = 0.000) in comparison to baseline, as well as the control group, while it increased the level of apolipoprotein A-I (P value < 0.05) (Khandouzi et al., 2015).

In the last randomized double-blind placebo-controlled clinical trial uncovered in our literature search, 63 patients with type 2 diabetes were supplemented with 1600 mg of ginger for 12 weeks. A significant decrease in serum triglyceride and total cholesterol was observed in comparison to the placebo group (P value < 0.001 and P value = 0.02 respectively). However, there was no significant effect on LDL-c and HDL-c (P value < 0.05) (Arablou et al., 2014a,b).

Another clinical trial was conducted by Mahluji and colleagues on patients with type 2 diabetes. The results showed that supplementation with 2 g of ginger for 2 months reduced significantly serum triglyceride (P value = 0.03) and LDL-c (P value = 0.04), compared with the control group, but there were not significant changes in total cholesterol (P value = 0.20) and HDL-c (P value = 0.28) (Mahluji et al., 2013).

In Talaei's study on 81 patients with type 2 diabetes, daily consumption of 3 g of ginger powder for 8 weeks decreased serum LDL-c (P value = 0.03) and increased APO A1 (P value < 0.005), but had no effects on total cholesterol levels (P value = 0.47), triglyceride (P value = 0.46), HDL-c (P value = 0.37), and APO B100 (P value = 0.06) (Talaei et al., 2012).

Ayaz and Dabidi-Roshan's conducted a study on the effect of a 6 week water-based intermittent exercise program with and without ginger consumption on proinflammatory markers and blood lipids in overweight women with breast cancer. Supplementation with 3 g of ginger per day for 6 weeks resulted in only a statistically significant reduction of triglyceride in water-based intermittent exercise and water-based intermittent exercise + ginger groups (P value = 0.03 and P value = 0.003 respectively). However, the water-base exercise + ginger treatment was more effective than the water-base exercise treatment alone (Ayaz and DabidiRoshan, 2012).

Atashak et al. carried out another randomized, double-blind clinical trial to evaluate the effect of ginger supplementation and resistance exercise on cardiovascular disease risk factors and C-reactive protein in obese men. Participants in the ginger groups received 1 g of ginger daily for 10 weeks. Results showed that changes of triglyceride, HDL-c, LDL-c and total cholesterol were not significant in all groups, only total cholesterol decreased significantly in resistance exercise + ginger group (P value < 0.05) (Atashak et al., 2011).

A further study was conducted by Alizadeh-Navaei to evaluate the effect of ginger supplementation on blood lipids in 85 hyperlipidemic patients. It was observed that consumption of 3 g of ginger per day after 45 days reduced serum triglyceride (P value = 0.03) and total cholesterol (P value = 0.02) significantly compared with the controls. However, differences in the levels of HDL-c (P value = 0.058), LDL-c (P value = 0.09), VLDL (P value = 0.63), and lipoprotein a (P value = 0.45) were not statistically significant between the control and treatment groups (Alizadeh-Navaei et al., 2008) (Table 1).

2.1.2. In vivo studies

To date, several animal studies have been carried out on the effects of ginger on blood lipids. In these studies, the effect of different doses of ginger at different times was investigated in a variety of animal models, especially diabetic rats, obese rats, and high-fat diet fed rats. According to the results of most studies, ginger has improved lipid status,