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# The use of ginger (*Zingiber officinale* Rosc.) as a potential anti-inflammatory and antithrombotic agent

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**Summary** The effect of an aqueous extract of ginger (*Zingiber officinale*) on serum cholesterol and triglyceride levels as well as platelet thromboxane-$B_2$ and prostaglandin-$E_2$ production was examined. A raw aqueous extract of ginger was administered daily for a period of 4 weeks, either orally or intraperitoneally (IP) to rats. Fasting blood serum was investigated for thromboxane-$B_2$, prostaglandin-$E_2$, cholesterol and triglycerides. A low dose of ginger (50 mg/kg) administered either orally or IP did not produce any significant reduction in the serum thromboxane-$B_2$ levels when compared to saline-treated animals. However, ginger administered orally caused significant changes in the serum $PGE_2$ at this dose. High doses of ginger (500 mg/kg) were significantly effective in lowering serum $PGE_2$ when given either orally or IP. However, $TXB_2$ levels were significantly lower in rats given 500 mg/kg ginger orally but not IP. A significant reduction in serum cholesterol was observed when a higher dose of ginger (500 mg/kg) was administered. At a low dose of ginger (50 mg/kg), a significant reduction in the serum cholesterol was observed only when ginger was administered IP. No significant changes in serum triglyceride levels were observed upon administration of either the low or high dose of ginger. These results suggest that ginger could be used as an cholesterol-lowering, antithrombotic and anti-inflammatory agent. © 2002 Published by Elsevier Science Ltd.

## INTRODUCTION

*Zingiber officinale* Roscoe known as ginger is widely used in foods as a spice around the world. For centuries, it has been an important ingredient in Chinese, Ayurvedic and Tibb-Unani herbal medicine.[1,2] In the Tibb and Ayurvedic systems of medicine preventive and ameliorative effects of ginger have been described in the treatment of catarrh, rheumatism, nervous diseases, gingivitis, toothache, asthma, stroke, constipation and diabetes.[2]

Ginger contains a number of different pungent and active ingredients. Steam distillation of powdered ginger produces ginger oil which contains a high proportion of sesquiterpene hydrocarbons predominantly zingiberene.[3,4] The major pungent compounds found in ginger are the gingerols which can be converted into shogaol, zingerone and paradol.[3,4] Zingerone and shogaol are found in small amounts in fresh ginger and in large amounts in stored products.[3,4] 6-gingerol and 6-shogaol have been shown to have a number of pharmacological activities including antipyretic, analgesic, antitussive and hypotensive effects.[5]

Ginger has shown to exhibit antithrombotic activity,[6] because its extract inhibits platelet aggregation and thromboxane-$B_2$ ($TXB_2$) production in vitro.[6,7] In addition, gingerdione has been shown to inhibit the formation of 5-hydroxyeicosatetraenoic acid (5-HETE) and prostaglandin-$E_2$ ($PGE_2$) from arachidonic acid, shogal appeared to be a preferential inhibitor of 5-HETE formation and gingerol and dehydroparadol favored the inhibition of cyclooxygenase.[8] However, reports on the effects of ginger consumption on blood platelet function, and

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specifically on cyclooxygenase activity are few and contradictory.[9–14]

One of the most interesting properties of ginger shown is its antirheumatic activity.[15] A few studies have focussed on the effect of ginger on blood lipids in animals and humans. The results of those studies show that ginger significantly reduces plasma cholesterol in animals,[16,17] but not in patients with coronary artery disease.[18]

In the present study, we investigated the ex vivo effect of an aqueous extract of ginger on the synthesis of thromboxane-$B_2$, prostaglandin-$E_2$, and cholesterol and triglyceride levels in the serum of normal rats. We have chosen an aqueous extract of raw ginger for this study as this preparation most clearly corresponds to ingestion of fresh ginger. In addition, previous studies have suggested that blockade of thromboxane-$B_2$ synthesis in humans is likely to occur only with the consumption of fresh ginger.[13]

We would expect the results of this study to indicate the effectiveness of raw ginger administration on the lipid profile in rats. Two routes of administration, oral and intraperitoneal, and two doses (50 mg/kg and 500 mg/kg) were studied for comparison purposes.

## MATERIALS AND METHODS

Adult female Sprague–Dawley rats weighing 200–250 g were used in this study. Rats were fed a normal diet and were divided into six groups, each group consisted of six rats. Group 1 served as control and received normal saline orally. Group 2 also served as control and were given normal saline intraperitoneally (IP). Group 3 received a low oral dose of ginger extract via stomach gavage daily. Group 4 received a high oral dose of ginger via stomach gavage daily. Group 5 received a low dose of ginger (50 mg/kg) IP daily. Group 6 received a high dose of ginger (500 mg/kg) IP daily.

After 4 weeks of treatment, the rats were sacrificed under urethane anesthesia. The blood was collected by cardiac puncture and allowed to clot for 30 min at room temperature. The clotted blood was then centrifuged at 3500 rpm for 30 min. The serum was separated and stored for determination of $TXB_2$, $PGE_2$, cholesterol and triglycerides. The serum cholesterol and triglycerides were determined using kits supplied by Randox Co., USA. The $TXB_2$ and $PGE_2$ were estimated by ELISA kits supplied by Amersham, UK. Optimal dilutions of serum were established employing a serial dilution. A dilution of 80–100 fold for $TXB_2$ and 4–5 fold for $PGE_2$ were found to be optimal. The levels of $TXB_2$ and $PGE_2$ were expressed as ng/ml serum.

Aqueous ginger extract was prepared from locally available ginger roots. The ginger roots were peeled on crushed ice, and 50 g of ginger was cut into small pieces and homogenized in 75 ml of cold, sterile 0.9% NaCl in the presence of some crushed ice. The homogenization was carried out in a blender at high speed using 2 min bursts for a total of 12 min. The homogenized mixture was filtered 3 times through cheesecloth and the filtrate was centrifuged at 2000 rcf for 10 min and the clear supernatant was made up to 100 ml with normal saline. The concentration of this ginger preparation was considered to be 500 mg/ml on the basis of the weight of the starting material (50 g/100ml). The aqueous extract of ginger root was stored in small aliquots at $-20^{\circ}C$ until use. Lower concentrations of ginger were prepared by dilution of this solution with cold, sterile 0.9% NaCl.

The data are expressed as mean $\pm$ SEM. Readings within a group were compared using the one-way ANOVA analysis and readings between groups were compared using the independent sample test. Statistical analysis was done with the SPSS program (Version 7.1). A level for $P < 0.05$ was considered to be significant.

## RESULTS AND DISCUSSION

Figures 1 and 2 show the effects of administration of the aqueous extract of ginger on the synthesis of $PGE_2$ (Fig. 1) and $TXB_2$ (Fig. 2). When ginger was administered orally at low doses (50 mg/kg), the levels of serum $PGE_2$ were significantly reduced. However, high oral doses of ginger (500 mg/kg) were more effective in reducing the synthesis of $PGE_2$. $PGE_2$ levels were significantly lower than the saline control in rats given 500 mg/kg ginger extract either orally or IP. The low dose of ginger (50 mg/kg) had no effect on the synthesis of $TXB_2$, but the higher oral dose of ginger (500 mg/kg) significantly reduced $TXB_2$ levels in serum. A non-significant reduction in the level of $TXB_2$ was observed when ginger was injected IP. However, due to the large standard deviation, these

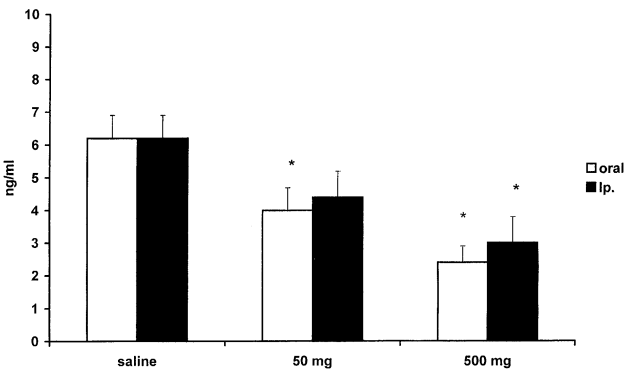


**Fig. 1** Effect of aqueous extracts of ginger on the serum levels of $PGE_2$ in rats. *Significantly different from control (normal saline) using Student's *t*-test, $P < 0.05$. IP=intraperitoneal.

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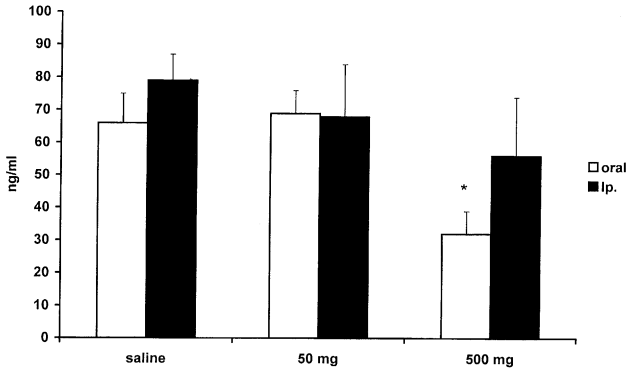


**Fig. 2** Effect of aqueous extracts of ginger on the serum levels of $TXB_2$ in rats. *Significantly different from control (normal saline) using Student's *t*-test, $P < 0.05$. IP=intraperitoneal.

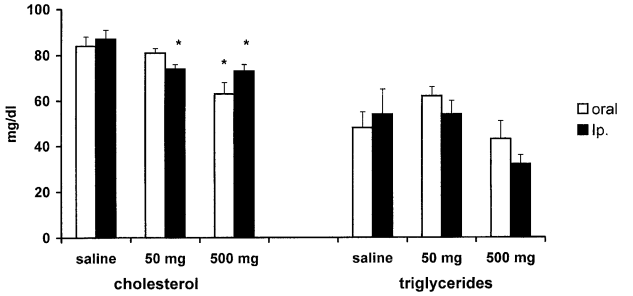


**Fig. 3** Effect of aqueous extracts of ginger on the serum levels of cholesterol and triglycerides in rats. *Significantly different from control (normal saline) using Student's *t*-test, $P < 0.05$. IP=intraperitoneal.

levels were not significantly different from the $TXB_2$ levels in control rats receiving normal saline.

There is some evidence that ginger consumption may provide relief to arthritic patients by reducing joint pain.[19] This soothing action was suggested to be due to the dual inhibition of the cyclooxygenase[9,20] and lipooxygenase pathways.[8] Elevated levels of $PGE_2$, $PGF_{2\alpha}$ and $TXB_2$ have been reported in the synovial fluid of patients with rheumatoid arthrithis.[21] Of these prostanoids, $PGE_2$ is most likely to play an important role in this inflammatory process.[22] In the present study, we have evaluated the efficacy of an aqueous extract of ginger on the inhibition of $PGE_2$ synthesis during ex vivo whole blood clotting of rats. When assessed ex vivo, daily oral or intraperitoneal administration of an aqueous extract of ginger (50 and 500 mg/kg doses) significantly inhibited the synthesis of $PGE_2$ (Fig. 1). These results suggest that ginger could possibly be used as anti-inflammatory agent to reduce inflammation, and therefore relieve pain. A number of non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin were shown to inhibit these metabolites in different tissues by blocking the cyclooxygenase activity.[23,24] To our knowledge, no previous studies have reported the effect of aqueous extract of ginger on ex vivo synthesis of $PGE_2$ in rats.

The antithrombotic property of ginger has been previously reported.[6] This property has been correlated with the ability of ginger to inhibit platelet aggregation and thromboxane formation in vitro.[7,8] Previous reports have indicated that consumption of ginger does not affect ex vivo platelet thromboxane production in humans.[14] Our results showed a significant reduction (50%) of thromboxane $B_2$ when 500 mg/kg of an aqueous extract of ginger was given orally to rats daily for a 4-week period. However, no significant reduction in the synthesis of $TXB_2$ was observed when the same dose of ginger was administered IP (Fig. 2). The reasons for this variation of effect with route of ginger administration are unclear, but may be due to conversion of ginger components to active metabolites during the process of digestion. Similarly, it is not clear why there is a difference in the effects of ginger on ex vivo thromboxane formation in rats as observed in the present study and as previously reported in humans.[14] It is possible that this may be a result of dose dependence since in the present study the rats were given a oral dose of 500 mg/kg, whereas in the human study the subjects consumed 15 g of raw ginger root per day. In addition, the present study was conducted over a period of 4 weeks, whereas the human study involved only 2 weeks of ginger ingestion.

Figure 3 summarizes the levels of cholesterol and triglycerides in the serum of rats receiving ginger orally and IP. A significant reduction in levels of cholesterol was observed in the rats given a high dose of ginger (500 mg/kg) either orally or IP. No significant change in triglyceride levels was observed in the serum of rats receiving either oral or intraperitoneal ginger.

The anti-hypercholesterolemic effect of ginger was previously shown in rats fed with a high-cholesterol diet for 24 days.[16] These workers also reported that there was no immediate effect of ginger on serum cholesterol. This confirms our finding that ginger given daily for a period of 4 weeks orally or IP significantly reduced the serum cholesterol in the normal rats (Fig. 3). In another study in patients with coronary artery disease, ginger failed to lower blood lipids when it was given in powdered form (4 g) daily for a period of 3 months.[18] We have observed no significant reduction in serum triglyceride levels in our study (Fig. 3). The significant reduction in serum cholesterol by ginger could possibly play an important in the prevention and development of atherosclerosis.

The unique ability of ginger to inhibit the synthesis of $PGE_2$ and $TXB_2$, and to lower serum cholesterol levels is clinically important, because its daily intake for a prolonged period will neither lead to side-effects nor to complications as normally occurs with non-steroidal anti-inflammatory drugs.

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