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Original Research Article

Effect of Ginger on Isolated Intestine of Rat Establishing it's Action on Gastro-intestinal Motility and Peristalsis

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Abstract

The present study has been carried out to establish the effects of ginger-juice (*Zingiber officinale* Roscoe) on rat's intestine motility and peristalsis. Albino rats (n=6-12) were sacrificed to isolate intestine. Concentration of ginger is expressed in term of mg/ml of ginger rhizome. It was based on preparation of ginger-juice as detailed in material and methods section. Filtrate of 150 ml was used in the isolated experiment representing 500 g of ginger rhizome. The diluted filtrate was used in the experiment. The ginger-juice filtrate had no significant change in ulcer index. Intestinal stimulant activity was also exhibited in isolated rat intestine. It has been concluded in the present study that the intestinal stimulant activity was exhibited in isolated rat intestine.

Keywords

Atropine
Ginger-juice filtrate
Metochlopramide
Peristalsis
Tyrode solution

Introduction

A Ginger is one of the most important and oldest spices, consisting of the prepared and sun-dried rhizomes of *Zingiber officinale* (Zingiberaceae). It is cultivated in many tropical countries. It is produced all over India from ancient times. It has a good commercial value and is claimed to have many medicinal uses. Because of differences in cultivation pattern, harvesting technique and climatic conditions it's commercial value differs and so also the medicinal actions and uses. It is referred by different names in the languages of different regions and countries. It is widely consumed almost all over the world however in tropical countries or warm regions like Asia, it is more popular (Katiyar et al., 1996). Because of its typical taste and a pleasant odour it's widely used as flavoring agent in numerous food recipes, beverages, pickles, many popular soft drinks etc (Guenther, 1952).

From the ancient times it is included in many traditional medicinal systems for treatment of number of diseases. It is widely claimed as a Stomachic, aromatic, carminative, aphrodisiacs, diaphoretic, antiemetic, allergic rhinitis and gastric stimulant and for treating migraine headache. It is also used an antispastic against intestinal colic. Ginger oil is used in mouthwashes and liquors (Evans and Trease, 1989).

Many forms of ginger are marketed such as processed, coated or unscraped, unbleached (natural) and bleached

ginger. There are different types of active principles present in the ginger. Ginger oil is isolated by distillation of dried ginger. Many scientists have investigated the ginger oil and found about 50 constituents, mainly aroma, Starch, Volatile oil, Zingiberene, Gingerol, Oleoresin (Gingerin), Zingiberol, Zingerone, Shagaol etc. The acetone extract of ginger contains Zingerberone and ether extract contain Zingerone (Pungent principles).

In view of the available literature, we have tried to screen some actions of ginger-juice; as crude form of ginger. We presume that crude form contains majority of active principles, may be in very low concentrations. Keeping in mind some of its potential therapeutic applications we have carried out animal experiments to investigate the effects of ginger-juice on blood coagulation, gastrointestinal system, central nervous system, antioxidant status and lipid profile.

Antiemetic and gastric motility

Sharma et al. (1998) have investigated the activity of acetone, 50% ethanolic and aqueous ginger extracts against emesis produced by cisplatin (100% emetic dose i.v) in healthy mongrel dogs. The finding suggests that ginger could be an effective and cheap adjunct to cancer chemotherapy.

Sharma et al., (1996) studied that the acetone and 50% ethanolic extracts at the dose of 25, 50, 100 and 200 mg/kg, p.o exhibited significant protection, while the aqueous extract was more ineffective at these doses. The acetone extract was more effective than the ethanolic extract. However, both were less effective when compared with the 5-HT3 receptors antagonist, granisetron. Ginger extracts were not effective against apomorphine-induced emesis, ruling out mediation at the level of dopaminergic transmission. The finding suggests that ginger could be an effective and cheap anti-emetic adjunct to cancer therapy.

Yamahara et al. (1989) have studied the activity of dried acetone extract of ginger and its pungent constituent 6-gingerol against vomiting induced by cytotoxic drug in Suncus. The finding suggests that dried acetone extract and 6-gingerol inhibited the vomiting induced by cytotoxic drugs in the experimental animals, Suncusmurinus. Akita et al. (1998) had developed new assay method for screening the anti-emetic properties of compounds from Zingiber officinale in young chicks instead of frogs for screening anti-emetic compounds from natural sources, compared with previous method using leopard and ranid frogs. The advantages of new method included parallel results as well as decreasing standard errors.

Langner et al. (1998) have investigated the efficacy of rhizomes of Zingiber officinale for the prevention of nausea, dizziness and vomiting as symptoms of motion sickness (Kinetosis) as well as for postoperative vomiting and vomiting during pregnancy. Fudler et al. (1996) have shown that the ginger is safe for use as anti-emetic or anti-nausea remedy in pregnancy provided normal doses are consumed. It is permitted as an over-the-counter (OTC) medication in some countries for specific indications. There are no reports of adverse effects and toxicological evidence in Pharmacological literature.

Iwasaki et al. (1998) have investigated effect of BanxiaHoupo Tang (BHT) a traditional Chinese medicine on swallowing reflex among the elderly patient with aspiration pneumonia. *Zingiber officinale* is the main component of this preparation. The swallowing reflex was measured by a bolus injection of 1 ml of distilled water into the pharynx through a nasal catheter. The reflex was evaluated by the latency time of response, which was from the injection to the onset of swallowing. They suggested that BHT improves the impaired swallowing reflex and may help to prevent aspiration pneumonia in the elderly.

Sharma et al. (1993) had studied the "Shalpamyad Churna" an Ayurvedic preparation. Its main component is *Z. officinale*. It was administered in powder form (3 g 3 times a day for 1 month) to 15 patients. Reduction of irritable bowel syndrome (IBS) symptoms was observed in most cases. Comparison was made with placebo group.

Acetone extract of Zingiber officinale enhancing the gastro-intestinal motility. The effects of this extract were similar to or slightly weaker than those of equal doses of domperidone or metoclopramide (Yamahara et al., 1990).

Materials and methods

A keeping in view the aims and objectives, experiments were planned to study the effects of ginger juice filtrate on rat intestine and peristalsis.

Preparation of ginger-juice

The commercially available ginger was obtained from the local market. It was confirmed from the botanist that it was *Zingiber officinale*. The rhizome of ginger after cleaning and scrapping the superficial skin was cut into small pieces. With the help of mixer-grinder the pieces were made in to paste. The paste was taken on a white clean cloth and the liquid was squeezed out. The juice so obtained was used in the experiments. The stock of juice was kept in a refrigerator for maximum period of 15 days and the required quantity was used for the experiments after removing particulate matter from it. 500 g ginger rhizomes yielded about 250ml juice. 250ml juice was filtered which yielded about 120 - 150ml filtrate.

The liquid portion which was obtained in the course of filtration looked like yellowish hazy opalescent liquid. It was administered orally in acute or chronic experiments. The doses were either 2 ml to 4 ml per rat. This liquid portion was passed through the fine filter paper and golden coloured translucent liquid was obtained. This was used for isolated intestine experiments.

Gastrointestinal activity: Intestinal motility (*in vitro* study)

Rat intestinal activity was studied *in vitro* experiments in the term of (A) Pendular motility and (B) Peristaltic movement.

A. Pendular motility

Albino Wistar rats of either sex, weighing 150 to 280 g, fasted overnight were sacrificed by a sharp blow on the head. The abdominal cavity was quickly opened and intestinal loops of 5-6 cm (jejunum) was taken out caring to avoid damaging the gut muscles and placed in Tyrode solution (composition g/l: Glucose-1g, NaCl-8 g, KCl-0.2 g, $CaCl_2$-0.2 g, $MgSO_4.7H_2O$-0.26g, Na_2HPO_4-0.05 g, $NaHCO_3$-1 g at 32°C and gassed with oxygen. For each piece the mesentery was removed and the tissue was cleaned. The intestine was washed carefully through the pipette in order to expel the contents. About 4-5 cm length of intestine was mounted in a 40ml organ bath. The tissue was equilibrated for 30 minutes under resting tension 500 mg. Responses were recorded isometrically with a force displacement transducer of Physiograph which recorded the contraction (pendular movement) of the longitudinal muscles.

After initial stabilization, the responses of various doses of acetylcholine and various doses of fine filtrate of ginger-juice were recorded. Interaction of acetylcholine and ginger-juice with atropine was also studied.

B. Peristaltic movement of rat intestine (Trendelenburg's method)

About 5-6 cm length of intestine was mounted in a 50 ml organ bath as described in the previous experiment and illustrated in figure. Peristalsis induced by increase of intra-luminal pressure or drugs were recorded.

The distal end of the intestine piece was tied over an organ tube communicated to the reservoir containing Tyrode solution, which is attached to the pressure transducer of the Student physiograph (which record the change in pressure). The rise in internal pressure by increase of 1to 2 cm height of reservoir induces the peristalsis reflex and the intra-luminal fluid of intestine is propelled along with intestine to and fro in to the reservoir. The changes in pressure were produced by the contraction of both the longitudinal and the circular muscles.

The level of Tyrode solution in reservoir was same as the level of water in the organ bath to maintain the outside and inside pressure on intestine in organ bath. Both inside and outside of the intestine bathed in Tyrode solution but it was not possible to aerate with oxygen in reservoir. Only outside Tyrode solution was aerated with oxygen. During the experiment the drug was washed out of the organ bath by overflow to avoid the disturbances during emptying of the bath.

The stock of ginger-juice used in the experiment was filtered with filter paper and diluted as per need.
500g Ginger rhizome yielded about 250ml juice. 250ml juice was filtered yielded about 120 - 150ml filtrate. 150ml filtrate of ginger-juice (G.J.F) represents 500g of *Zingiber officinale* rhizome.

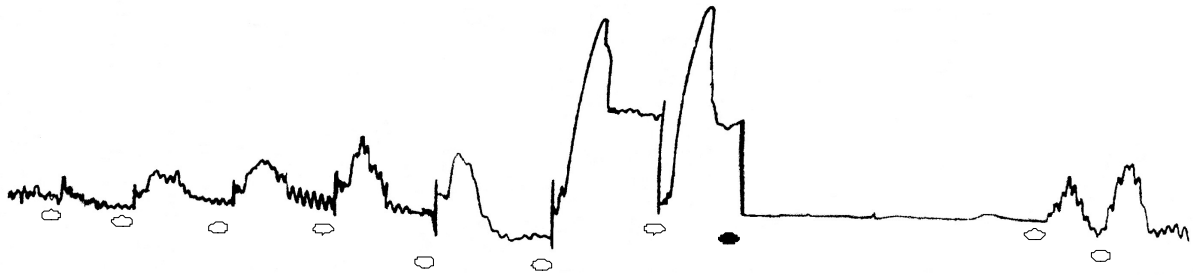
Results

Intestinal motility (*in vitro* study)

Pendular motility: In experimental set up in our laboratory acetylcholine dose response curve was illucidated in a range of (0.25 to 16 μg/ml). Atropine induced inhibition of acetylcholine action was also demonstrated. Acetylcholine in graded doses (0.25 to

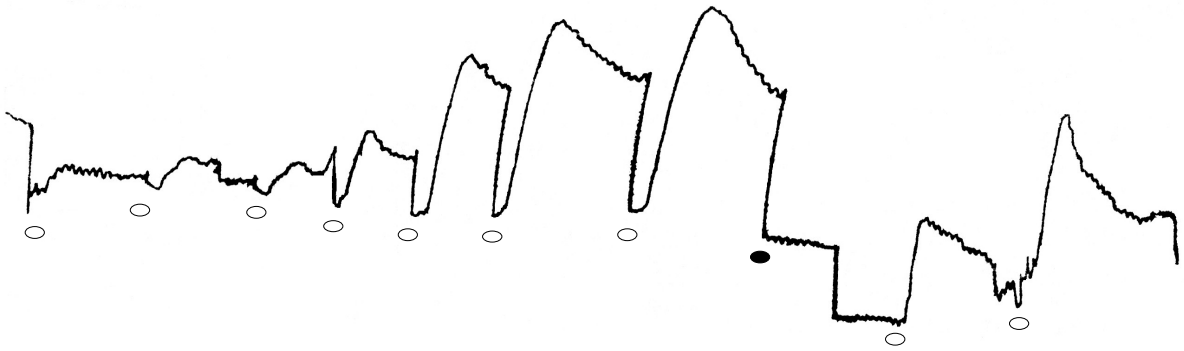
16μg/ml) caused dose related contraction of ileum. Ginger-juice filtrate (G.J.F) in graded doses (2.5 to 160 mg/ml calculated in term of raw ginger) also caused dose related contraction of ileum. Maximal contraction obtained was similar to that obtained with acetylcholine. Atropine of 1.6 μg/ml blocked the contraction of ileum induced by G.J.F. Contraction produced by smaller doses of G.J.F (2.5 to 20 mg/ml) were completely blocked by atropine at concentration of 1.6 μg/ml. Addition of higher doses of G.J.F (40 and 80 mg/ml) could overcome the blocked produced by atropine. The experiments conducted were of qualitative type and detailed quantitative study was not undertaken. Figs. 1 and 2 present an illustration based on findings of one of the three experiments conducted.

Fig. 1: Graded doses response of acetylcholine. Effect of graded doses of acetylcholine (0.25 to 16 μg/ml) on the rat intestine (*in vitro*) and responses are blocked by atropine (1.6 μg/ml) and overcome by higher doses of acetylcholine (8 and 16 μg/ml).



Acetylcholine 0.25μg/ml
Acetylcholine 0.5μg/ml
Acetylcholine 1μg/ml
Acetylcholine 2μg/ml
Acetylcholine 4μg/ml
Acetylcholine 8μg/ml
Acetylcholine 16μg/ml
Atropine 1.6μg/ml

Fig. 12: Graded doses response of ginger juice filtrate (G.J.F.). Effect of graded doses of Ginger Juice Filtrate (G.J.F- 2.5 to 160 mg/ml) in rat intestine (In vitro) and responses are blocked by atropine (1.6 μg/ml) and overcome by higher doses of G.J.F (40 and 80 mg/ml).



G.J.F - 2.5mg/ml
G.J.F - 5mg/ml
G.J.F - 10mg/ml
G.J.F - 20mg/ml
G.J.F - 40mg/ml
G.J.F - 80mg/ml
G.J.F - 160mg/ml
Atropine 1.6 μg/ml

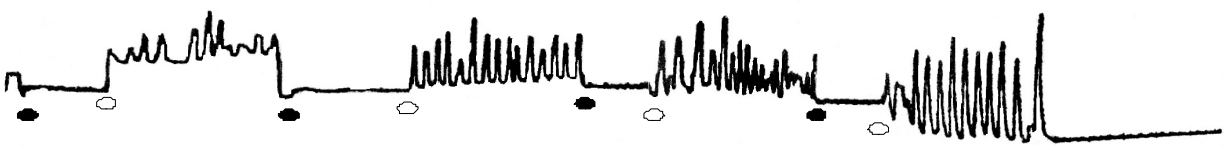
Concentration of ginger is expressed in term of mg/ml of ginger rhizome. It is based on preparation of ginger-juice as detailed in material and methods section. 150 ml of filtrate used in the isolated experiment represented 500 g of ginger rhizome. The diluted filtrate was used in the experiment.

B. Peristaltic movement of rat intestine [Trendelenburg's method cited Perry (1971); Laurence (1964)]

The rise in internal pressure by increasing the height of reservoir by 1 to 2 cm induced the peristalsis reflex. Under the normal conditions of intra-luminal pressure; addition of acetylcholine in different concentrations (0.25 to 16 μg/ml) also induced the peristalsis reflex. Similarly under normal conditions of intra-luminal pressure, addition of metoclopramide in the doses of (2.5 to 80 μg/ml) induced the peristalsis reflex.

Similar to acetylcholine, under normal condition of intra-luminal pressure, addition of G.J.F (2.5 to 160 mg/ml) also induced the peristalsis reflex. The result of this qualitative study is depicted in Fig. 3. The illustration is based on one of the three such experiments conducted.

Fig. 3: Recording of peristalsis induced by raising pressure, Ach., Meto, G.J.F. and blocked by atropine. Trendelenburg's preparation of rat intestine. Record of peristaltic movement by increasing the height of reservoir by 2 cm, Acetylcholine (1μg/ml), Metoclopramide (20 μg/ml) and Ginger Juice Filtrate (G.J.F–40 mg/ml) are shown the peristaltic movements induced by G.J.F are blocked by atropine (1.6 μg/ml).



- ● Under normal condition
- ○ Increasing the height of resv. by 2 cm
- ○ Acetylcholine 1μg/ml
- ○ Metoclopramide 20 μg/ml
- ○ G.J.F 40 mg/ml of ginger rhizome

Concentration of ginger is expressed in term of mg/ml of ginger rhizome. It is based on preparation of ginger-juice as detailed in material and methods section. 150 ml of filtrate used in the isolated experiment represented 500 g of ginger rhizome. The diluted filtrate was used in the experiment.

Discussion

Our data and that of Goso et al. (1996) suggest that ginger does contain certain active principles, which are orally bio-available from crude preparation. The tonic contractions induced by the ginger-juice filtrate were inhibited by atropine. This is suggestive of some muscarinic principle. However detailed quantitative study was not under taken. Possibility of involvement of other contractile substances could not be ruled out in the present experimental set up.

Experiments to exhibit peristaltic movement in rat intestine were successfully mounted. Raising intra-luminar pressure or addition of acetylcholine or metoclopramide-induced the peristalsis, indicating the validity of the experimental set up. However these experiments exhibited qualitative response, quantitative analysis was difficult to carry out.

On these experiments ginger-juice filtrate showed peristalsis, this was inhibited in presence of atropine.
Induction of peristalsis by ginger may be considered as stimulation of Auerbach's plexus. This kind of prokinetic activity was also reported by various authors (Yamahara et al., 1990; Langer et al., 1998; Sharma et al., 1998).

Both kinds of experiments on rat intestine are supportive to each other, highlighting muscarinic effect of ginger-juice. Antiemetic use of *Zingiber officinale* as suggested by Akita et al. (1998) can be supported by above observation.

Yamahara et al. (1990) have reported that acetone extract of *Z. officinale* enhanced the gastro-intestinal motility, similar to or slightly weaker than those of equal doses of domperidone or metoclopramide.
Sharma et al. (1998) also have reported that acetone and 50% ethanolic extract significantly reversed cisplatin induced delay in gastric emptying. The reversal produced by the acetone extract of Zingiber officinale was similar to that caused by the 5-HT3 receptor antagonist ondensetron. They carried positive impression that ginger-juice produced better reversal than ondensetron.

Langer et al. (1998) reported usefulness of ginger-juice to prevent the symptoms of motion sickness. Prokinetic effect exhibited in the present study may explain possible effectiveness in motion sickness.
Observations on amphetamine-induced locomotor activity may give some clue about effects of ginger-juice treatment on central dopaminergic action. Amphetamine in the dose (1mg/kg i.p) administered to the rats exhibited enhanced locomotor activity this may be considered by virtue of stimulation of central dopamine receptors (Shigenabu et al., 1994).

This indicates that there is neither prodopamenergic nor antidopaminergic effect on part of ginger. This point is important from the angle that ginger has been shown to have antiemetic effect (Sharma et al., 1996). Many

antiemetic compounds produce their antiemetic activity by virtue of central antidopaminergic effect; usually at CTZ (Chemoreceptor trigger zone) of Borrison and Wang (1953). It is clear from the present observations that there appears no contribution of central antidopaminergic mechanism for its reported antiemetic effect. Further, lack of antidopaminergic effect may also possibly rule out the possibility of acute dystonia as is the case with anti-dopaminergic antiemetics.

The role of dopaminergic mechanisms in the regulation of stress responses has been studied in experimental animals. The complex dopaminergic mechanisms are involved in the regulation of visceral, endocrinological and immune responses during stress (Puri et al., 1994). As ginger-juice is not affecting the central dopaminergic system.Any speculation that ginger-juice treatment may modify stress or endocrinal and immune responses may not be sustained.

Conclusion

Intestinal stimulant activity was exhibited by the filtrate of zinger juice, in isolated rat intestine.

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