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The study of the antispasmodic effect of Ginger (*Zingiber officinale*) in vitro

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ABSTRACT

Ginger herb is grown in many areas around the world it is used as medicinal herb. However, only a limited amount of research exists to support their efficacy. The aim of the present work is to demonstrate the antispasmodic effect of ginger (Zingiber officinale) on rat intestine in vitro. *Methods Rats (150–200 g) were used throughout the experiment, Sacrificing was done by cervical dislocation The abdomens excised immediately, the jejunum Segments 2 cm long are cut mounted in a 10 ml tissue automatic organ bath containing Tyrode's solution at 37◦C and aerated with carbogen (oxygen + 5 % carbon dioxide) gas, where one end is attached to the hook and the other is tied by a thread to the transducer. The transducers were connected to an amplifier to amplify the magnitude of contractions; these in turn were interpreted by a data acquisition system to obtain the final results by computer system. Results The results revealed that the effect of low doses of ginger on exogenous acetyl choline (ACh) induced contraction is spasmogenic as a dose of 0.2ml=20µg of ginger / tissue bath produced increase in the magnitude of ach induced contraction from 0.91 to 1.17 , while doses of 0.4 ml = 40µg of ginger/of tissue bath produced decrease in magnitude of ach induced contraction from 0.61 to 0.45 , and a dose of 0.8 ml=80µg of ginger / tissue bath produced decrease in magnitude of ach induced contraction from 0.85 to 0.11.*

Keywords: *Zingiber officinale*, in vitro, rats, antispasmodic.

INTRODUCTION

Ginger herb is grown in many areas around the world. Over centuries of cultivation, ginger rhizome (ginger root) has made its way into our daily food and more important it is used as medicinal herb. The Latin name is Zingiber. Ginger (*Zingiber officinale*) belongs to

Zingiberaceae family; the part of the plant used is rhizome. The ginger has been listed in "Generally Recognized as Safe" (GRAS) document of the US FDA. A dose of 0.5 – 1.0 g of ginger powder ingested 2-3 times for periods ranging from 3 months to 2.5 years did not cause any adverse effects [12]. In a human study, ginger showed no teratogenic effects [3], 1.2% minerals, 2.4% fiber and 12.3% carbohydrates. On the other hand the powdered rhizome contains 3-6%fatty oil, 9% protein, 60-70% carbohydrates, 3-8% crude fiber, about 8% ash, 9-12% water and 2-3% volatile oils as curcumin, zingiberene , terpinene, etc…The minerals present in ginger are iron, calcium and phosphorous. It also contains vitamins such as thiamine, riboflavin, niacin and vitamin A and C. The composition varies with the type, variety, agronomic conditions, curing methods, drying and storage conditions [8]. Compounds gingerols ; i.e. 6-gingerol, 8-gingerol and zingerone were identified as the major active components [9].

Pharmacological Effects

It has positive inotropic effect on cardiovascular system [17].Its content of Gingerols and diarylhepatanoids which are anti-prostaglandin compounds exhibit anti-inflammatory activity [11]. Effects on the gastrointestinal tract includes carminative, appetite stimulant and amelioration of nausea associated with motion sickness effects [13]. Having also anti-oxidant effect due to its content of polyphenols [4].

MATERIALS AND METHODS

Animals

Sprague-Dawley albino rats weighing (175-200gm) were used for in vivo study. All animals were housed in standard metal cages in an air conditioned room at 22 ± 3°C, 55 ± 5% humidity and were provided with a standard laboratory diet and water *ad libitum*. They were obtained from animal house colony of the national research center, Dokki, Giza, Egypt. Animal procedures were performed in accordance with the Ethics Committee of the National Research Centre and followed the recommendations of the National Institutes of Health Guide for Care and Use of Laboratory Animals (Publication No. 85-23, revised 1985) [15].

Experimental animals: albino rats weighing (150-200gm) were obtained from the animal house colony of the National Research Center.

Drugs and chemicals: Ginger powder (Mepaco), acetyl choline (Sigma).

Method

Rats (150–200 g) were given tap water ad libitum and a standard diet consisting of (g/kg): flour, 380; fiber, 380; molasses, 12; NaCl, 5.8; nutrivet L, 2.5; potassium meta bisulfate, 1.2; vegetable oil, 38 and powdered milk, 150. They were fasted for 24 hr before the experiment. Sacrificing was done by cervical dislocation. The abdomens excised immediately, the jejunum is identified by following the back of the stomach, a suitable length is cut and transferred to a dish containing Tyrode's solution .The composition of Tyrode's solution (mM) was: KCl, 2.7; NaCl, 136.9; $MgCl_2$, 1.1; $NaHCO_3$, 11.9; NaH2PO4, 0.4; glucose, 5.6; and $CaCl_2$, 1.8 (pH 7.4) [14] **.**

Segments 2 cm long are cut and freed from mesenteric attachments then each is mounted in a 10 ml tissue bath containing Tyrode's solution at 37◦C and aerated with carbogen (oxygen + 5 % carbon dioxide) gas, where one end is attached to the hook and the other is tied by a thread to the transducer. Care should be taken that the lumen of the jejunum is kept open. A preload of 1 g was applied to each tissue and the tissues kept undisturbed for an equilibrium period of 30 min.

The apparatus used was automatic organ bath (LSI Letica Scientific instruments) (Fig12). The transducers were connected to an amplifier to amplify the magnitude of contractions; these in turn were interpreted by a data acquisition system to obtain the final results by computer system.

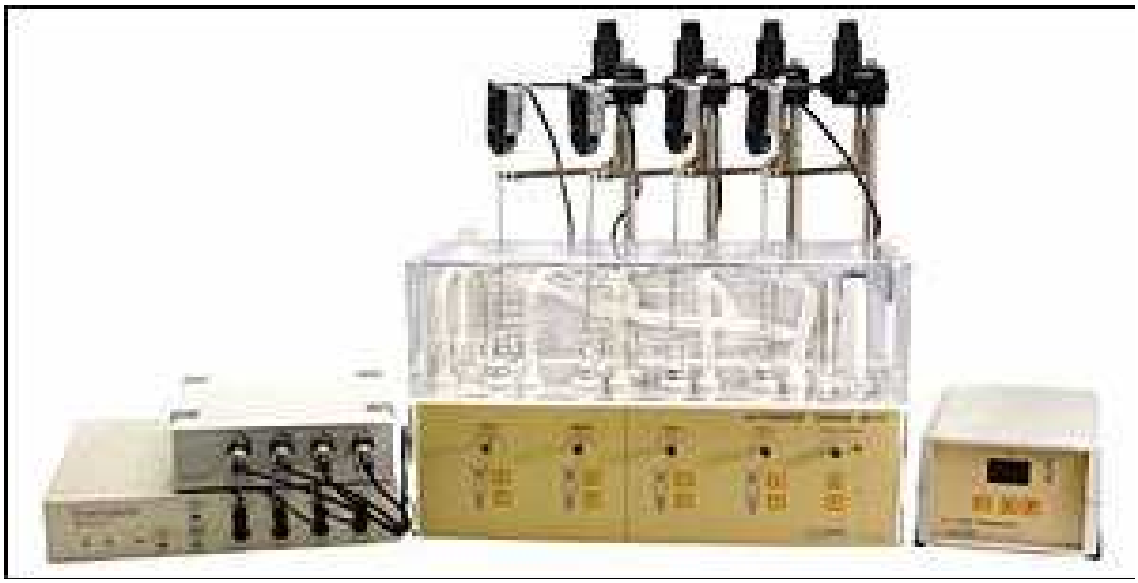

Fig-1. Automatic Organ Bath

RESULTS

Dose response curve of acetyl choline (ACh):
ACh solution of concentration 1/100,000 is used .Doses of 0.0125, 0.025, 0.05, 0.1 and 0.2 ml were used wash was done after each contraction obtained. The magnitude of each contraction was measured using the computer system by means of data acquisition system. The sub-maximal dose obtained was 0.05 ml =0.5δ/tissue bath. (Fig. 2 & 3)

Dose response curve of ginger (*Zingiber officinale*):
This preparation is known to exhibit spontaneous rhythmic contractions and thus allows studying spasmolytic activity without using any agonist [7].

Ginger is dissolved in distilled water. Its concentration is 1/10,000.Doses of 0.1, 0.2, 0.4, 0.8 ml/tissue bath =10, 20, 40, 80 δ/tissue bath respectively .were used. Each dose was kept in contact with the tissue for five minutes before starting the apparatus. The effect of each dose on

the jejunum was measured using the computer system by means of data acquisition system. (Fig. 4 & 5)

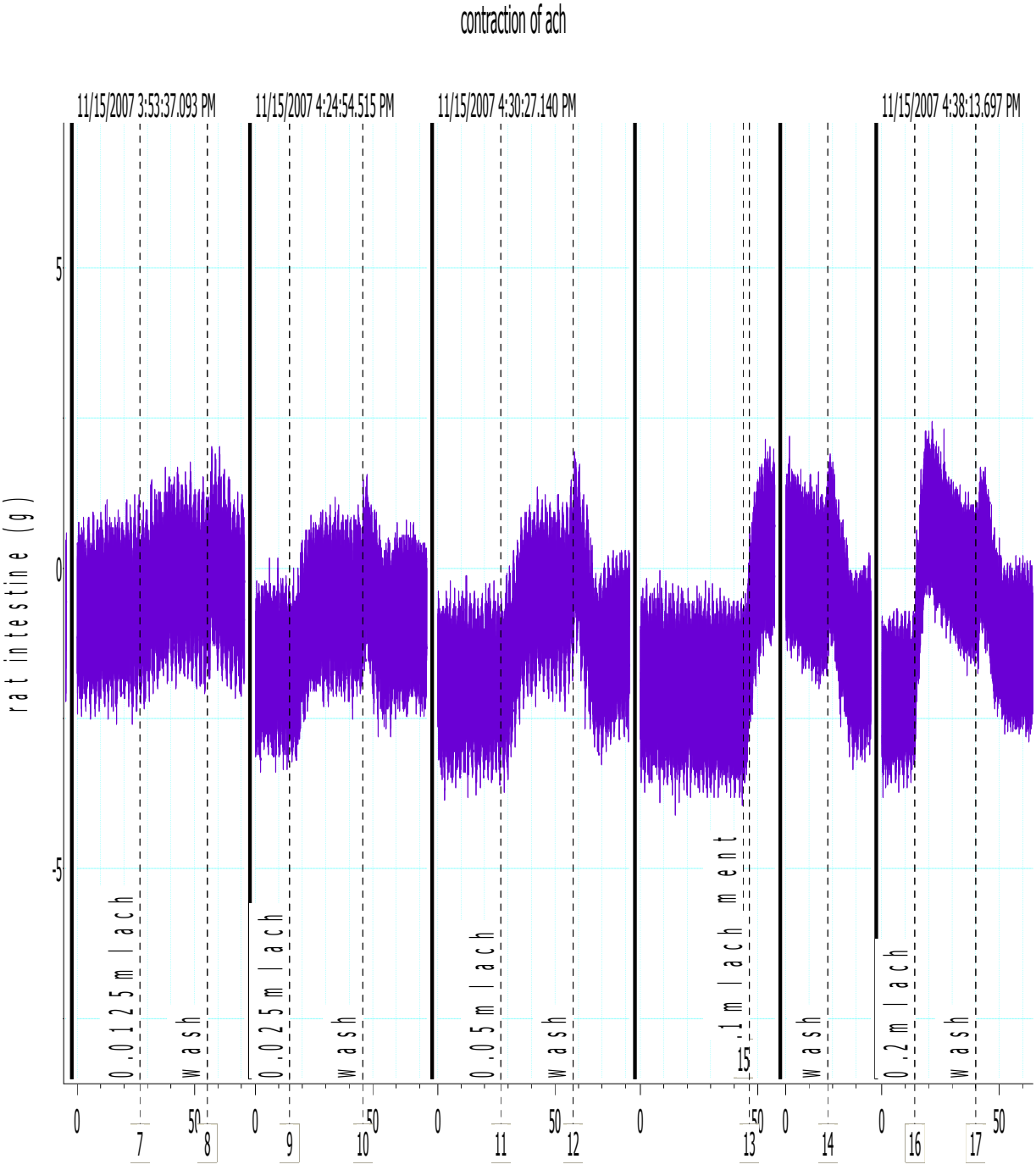

Figure 2: Dose response of acetylcholine on rat jejunum in vitro

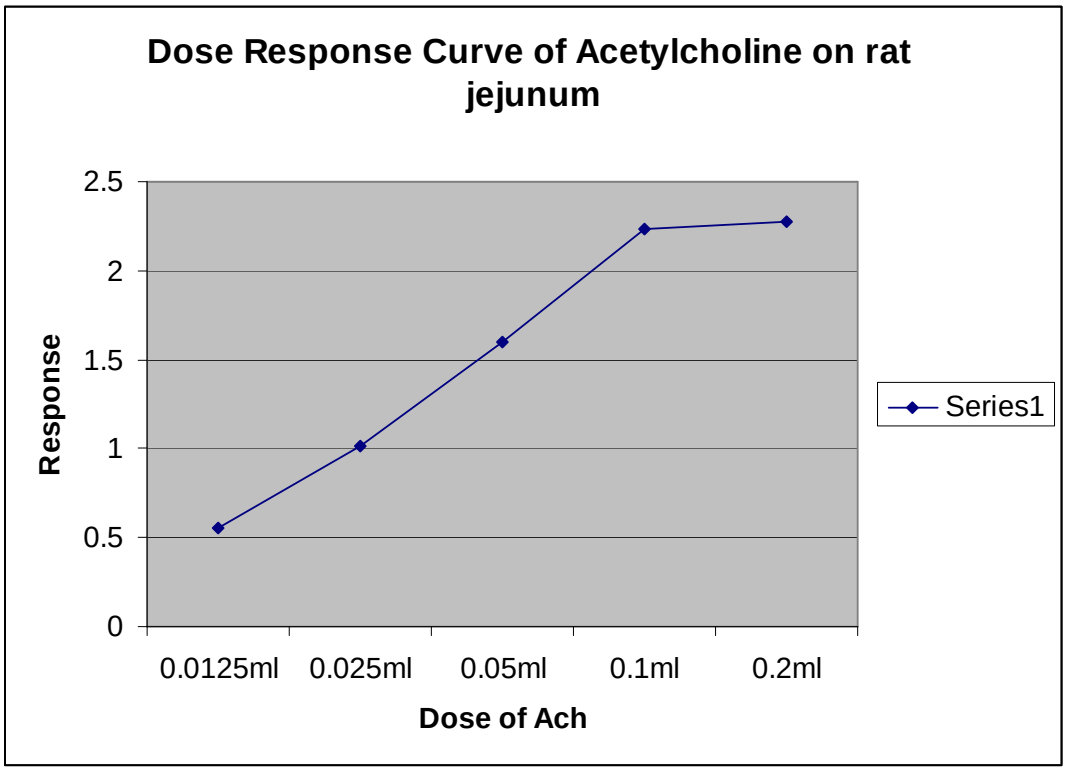

Figure 3: Semi log curve of dose response of acetylcholine on rat jejunum in vitro

Studying the effect of ginger on ACh induced contraction of rat jejunum :

Sub-maximal dose of ACh 0.05ml is used then washing is done, followed by giving 0.2 ml of ginger , on top f ginger dose of ach 0.05ml is added followed by wash. The same steps are repeated with 0.4 and 0.8 ml ginger. Ginger was kept in contact with the tissue for five minutes before starting the apparatus then adding ACh. The magnitude of ach induced contraction before and after using ginger as well as the effect of ginger alone on the jejunum were measured using the computer system by means of data acquisition system. (Fig. 6 & 7).

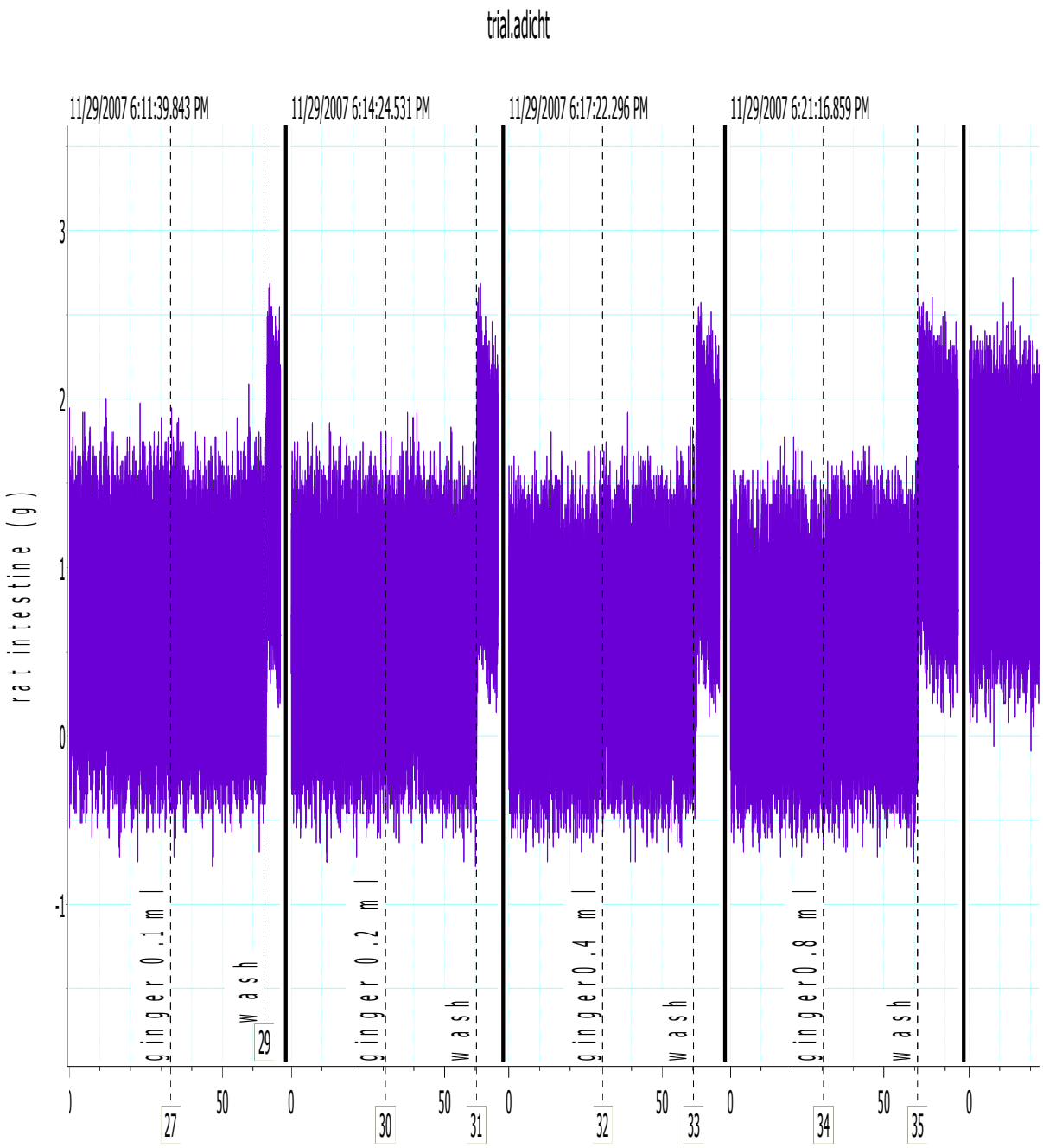

Figure 4: Effect of ginger on rat jejunum in vitro

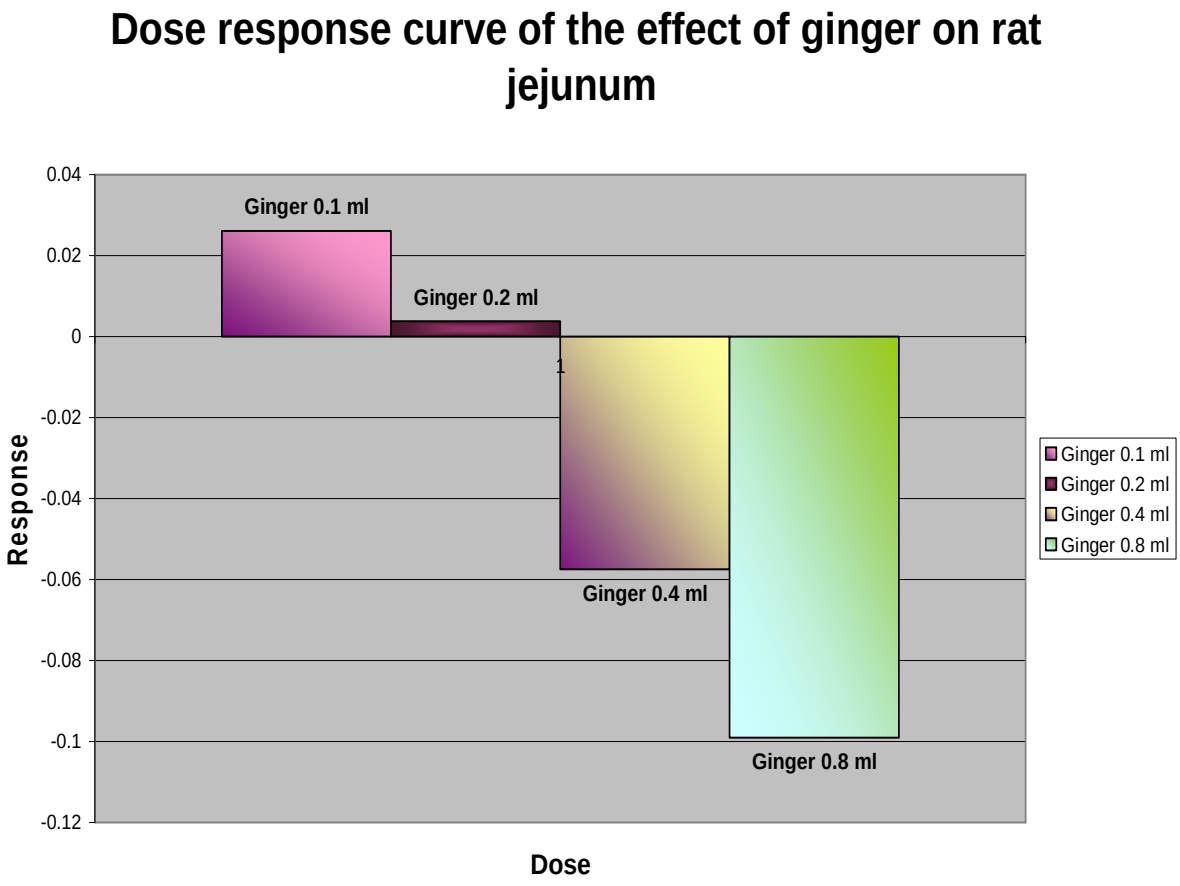

Figure 5: Effect of ginger on spontaneous contractions of rat jejunum in vitro.

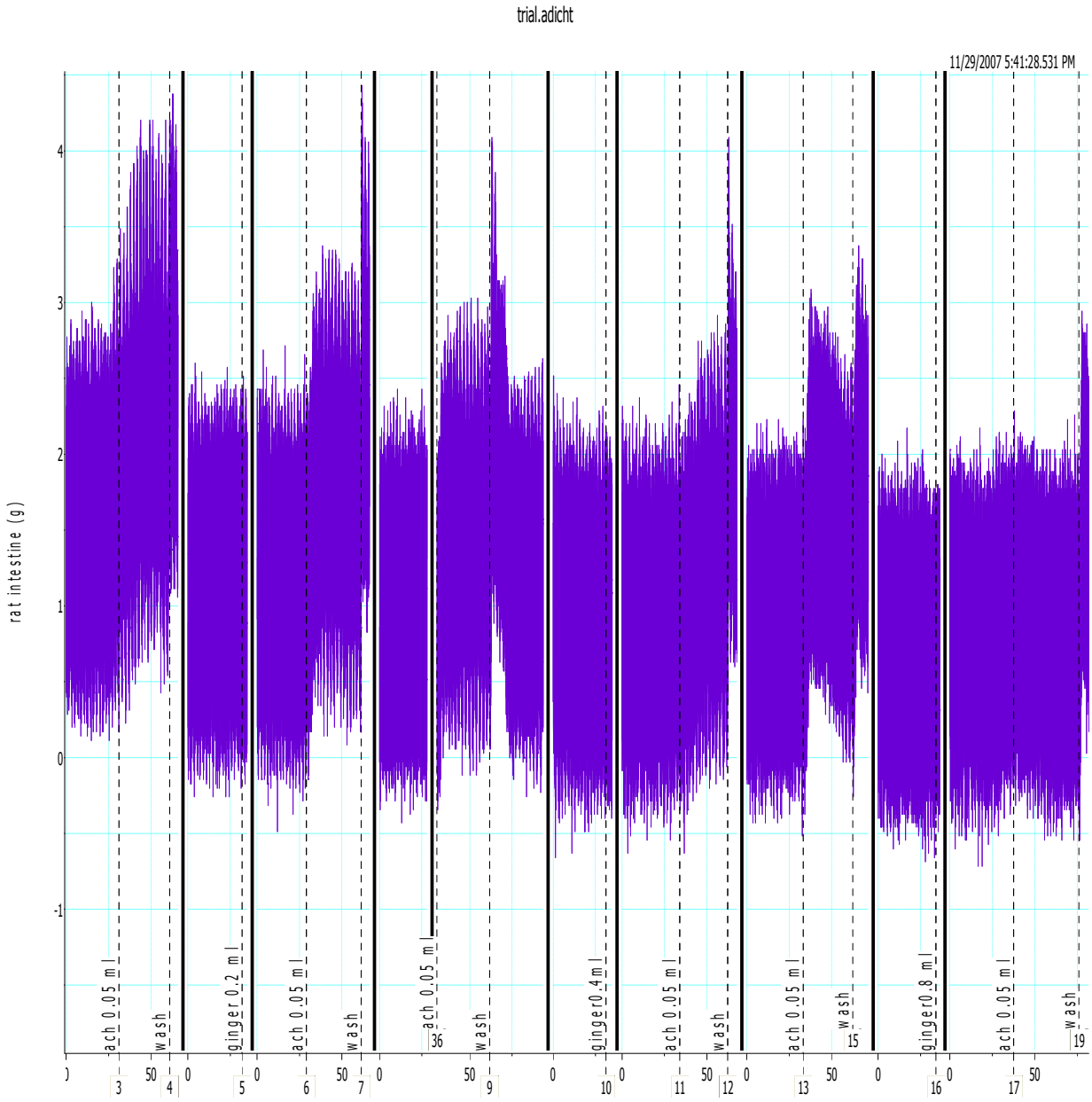

Figure 6: Effect of ginger on Ach on rat jejunum in vitro

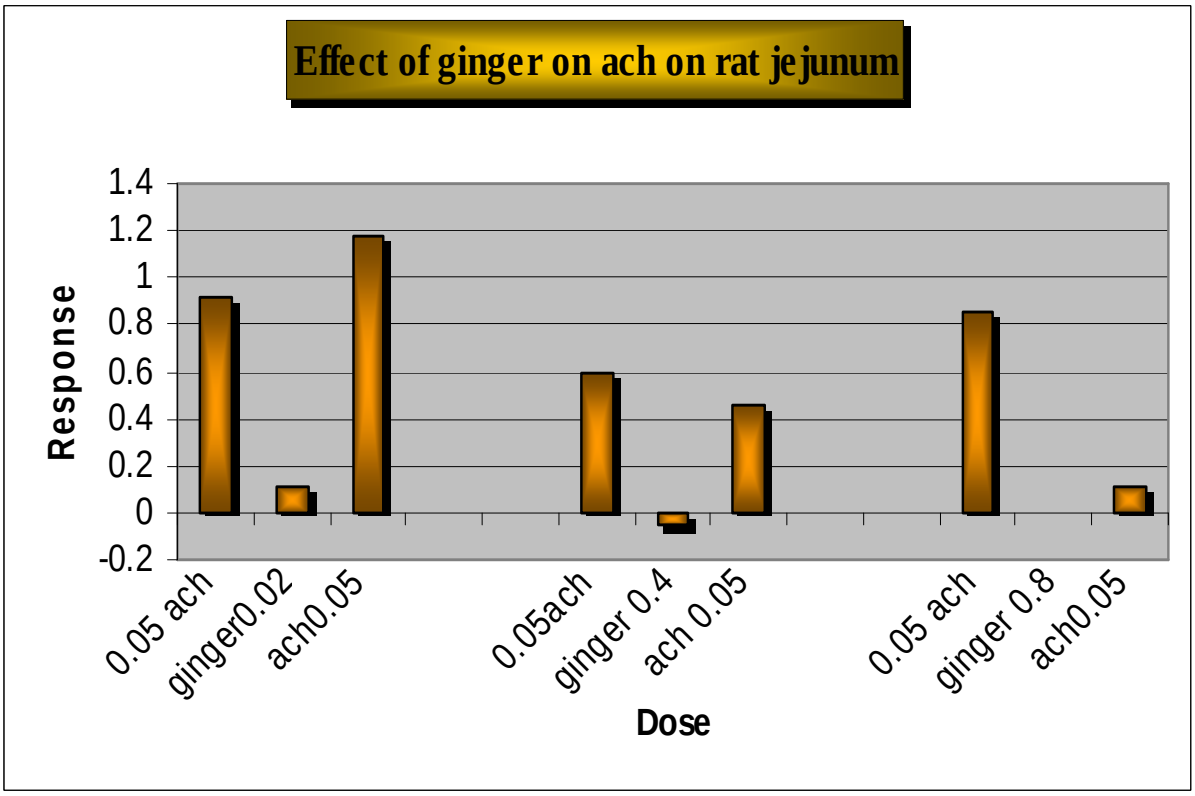

Figure 7: Effect of ginger on ach on rat jejunum

DISCUSSION

Concerning the effect of ginger on in vitro on rat jejunum ;the present study demonstrated that the effect of low doses of ginger on exogenous acetyl choline (ACh) induced contraction is spasmogenic as a dose of 0.2ml=20µg of ginger / tissue bath produced increase in the magnitude of ach induced contraction from 0.91 to 1.17 , while doses of 0.4 ml = 40µg of ginger/of tissue bath produced decrease in magnitude of ach induced contraction from 0.61 to 0.45 , and a dose of 0.8 ml=80µg of ginger / tissue bath produced decrease in magnitude of ach induced contraction from 0.85 to 0.11. Also the effect of low doses of ginger alone without an agonist on the jejunum was stimulatory ,as dose of 0.1 ml=10µg of ginger/tissue bath produced increase in the magnitude of jejunum contraction to be 0.026,dose of 0.2 ml=20µg of ginger /tissue bath produced increase in the magnitude of jejunum contraction to be 0.003, while doses of 0.4 ml = 40µg of ginger /tissue bath reduced the magnitude of jejunum contraction to be -0.0572,and the highest dose of ginger 0.8 ml=80µg/ tissue bath produced decrease in magnitude of jejunum contraction to be -0.099.The mechanism of the results of this study is most probably explained by Chrubasik etal., [2] in their study, as they demonstrated that [11]-gingerol inhibited or enhanced contraction depending on the dose and that it acts by noncompetitive antagonisms to acetylcholine. It has also been reported in an earlier study, that ginger and its constituents have a spasmolytic effect, and the mode of action reported has been speculated to be anticholinergic,

antihistaminergic,or antiserotonergic [16]**.** Borrelli etal., [1] studied the effect of ginger on rat ileum, which demonstrated that addition of ginger (0.01–1000 μg/ml) produced concentration-dependent inhibition of acetylcholine-evoked contractions. The inhibitory effect was significant starting from the 300 μg /ml concentration. They concluded that ginger inhibitory effects on rat ileal motility, could explain, at least in part, the anti-diarrhea activity attributed to ginger. Ghayur and Gilani [6] tested ginger alone on the spontaneous movements of rabbit jejunum, it was found to be devoid of any stimulant effect and instead caused a dose-dependent (0.1 to 3.0 mg/ml) spasmolytic effect .Ginger was also studied for its interaction with ACh. It produced a dose dependent (0.1–0.3 mg/mL) shift in the ACh dose–response curve to the right in a nonparallel manner, with suppression of the maximal response. They found that the ginger crude extract dose dependently relaxed not only rat and mouse stomach fundus but also rabbit jejunum, rat ileum, mouse ileum, and guinea pig ileum and colon. In their study they observed that the spasmolytic component(s) present in ginger is (are) of a nonspecific type, such as calcium channel blocker (CCB). They revealed that the earlier proposed mechanism through anticholinergic, antihistaminergic,or antiserotonergic action were still questionable. On the contrary the ginger extract exhibited a stimulant and then a spasmolytic effect in atropinized rat and mouse stomach fundus preparations, yet it showed generalized spasmolysis in all other intestinal tissues tested. They explained that the relaxation mediated by the extract in rat and mouse stomach fundus was weak compared with that in the other tissues, thus allowing the muscarinic mediated stimulation to dominate over the CCB-type relaxant in the fundic preparation, while owing to the relaxant component being more potent in the other tissues, no muscarinic-mediated stimulant effect was seen. Possibility of the presence of some additional relaxant component(s) in ginger that might be more active in the rat or mouse ileum could not be ruled out. Their study showed the presence of a combination of spasmogenic (cholinergic) and spasmolytic (calcium antagonist) constituents in ginger. Ghayur and Gilani [5] demonstrated that 70% aqueous-methanolic extract of ginger (Zo.Cr) exhibits prokinetic activity in rats via activation of post-synaptic muscarinic M(3) receptor in rat stomach fundus. In view of the physiological significance of pre-synaptic muscarinic M(1) and M(2) auto receptors, their study was undertaken to further look into the possible mode of action of the prokinetic effect of ginger through inhibition of pre-synaptic muscarinic receptors. Isolated tissue bath experiments were performed with Sprague-Dawley rat stomach fundus strip preparations. Their results show that ginger, in addition to having a direct cholinergic agonistic effect on the post-synaptic M3 receptors, also has a possible inhibitory effect on pre-synaptic muscarinic auto receptors, similar to standard muscarinic antagonists, thus reiterating the gastric stimulant effect of this age-old plant**.**On the other hand one study found that intragastrically administered acetone extracts of ginger or one of its constituents: [6]-shogaol, and [6], [8]-, and [10]-gingerols (2.5 mg /kg),all enhanced gastrointestinal motility in mice to a similar extent as did metoclopramide (10 mg /kg) and domperidone **.**This depends on the route of administration as intravenous administration of ginger extract inhibits gastrointestinal motility [18].Although previous studies by this same Japanese group demonstrated that diterpenoid and galanolactone, isolated from ginger inhibited contractions induced by serotonin (5-HT3) in guinea pig ileum likely acting as a 5-HT3 receptor antagonist [10].

CONCLUSION

Over centuries of cultivation, ginger rhizome (ginger root) has made its way into our daily food and more important it is used as medicinal herb. Ginger herb is grown in many areas around the world.In China, the use of Ginger in the Traditional Chinese Medicine is documented back to 2,500 years. Ginger is also well established in the Ayurvedic system of medicine. Ginger has antipyretic, anti-inflammatory, antimicrobial, antiparasetic, antiplatelet aggregation, antioxidant and analgesic effect as it is used to ameliorate pain in migraine ,osteoarthritis and dysmenorrheal . It also has several cardiovascular and gastrointestinal effects as its anti-ulcer, antispasmodic and anti-emetic effects. Its effects are due to its various constituents. Most of the therapeutic focus is on the pungent taste compounds, called Gingerols and Shoagols,as they are responsible for most effects of ginger particularly its antioxidant and anti-inflammatory effects.Ginger is marketed for its antispasmodic effect which was evident in vitro studies on animal intestine and was revealed to be due to its anticholinergic, antihistaminic, antiserotonergic or calcium channel blocking effect. The antispasmodic effect of ginger was apparent in vitro experiment on rat jejunum as it reduced the magnitude of ACh induced contraction. From this study as well as what was mentioned in other studies ,we can conclude that ginger appears to be a herb that can be used for several purposes besides its use for its aroma in cooking, because it has nutrient and medical values. But still more studies should be done to evaluate its effects more.Also further studies involving animals and more studies involving human volunteers should be done before approving its use as a supplement for treatment of the diseases that this study was done for. Moreover precautions should be done before its trial on patients who have diseases that ginger may worsen, this is because natural substances can interact with medicine, be inappropriate for many health conditions and be harmful in high doses.

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