Pharmacology 1991;42:111–120

0031–7012/91/0422–0111$2.75/0

Effects of Ginger on Motion Sickness Susceptibility and Gastric Function[1]

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Key Words. Motion sickness · Ginger · Scopolamine

Abstract. This study was designed to evaluate the antimotion sickness activity of ginger root *(Zingiber officinale)* and to characterize the effects of ginger on gastric function. Twenty-eight human volunteers participated in the project. Subjects made timed head movements in a rotating chair until they reached an endpoint of motion sickness short of vomiting (malaise III or M-III). Each subject was tested with either ginger or scopolamine and a placebo. A substance was judged to possess antimotion sickness activity if it allowed a greater number of head movements compared to placebo control. Gastric emptying of a liquid was measured by nuclear medicine techniques in normal and motion sick subjects. Gastric electrical activity was monitored by cutaneous (surface) electrodes positioned over the abdominal area. Powder ginger (whole root, 500 or 1,000 mg) or fresh ginger root (1,000 mg) provided no protection against motion sickness. In contrast, subjects performed an average of 147.5 more head movements ($p < 0.01$) after scopolamine (0.6 mg p.o.) than after placebo. The rate of gastric emptying was significantly ($p < 0.05$) slowed when tested immediately after M-III but was inhibited less when tested 15 min after M-III. Powdered ginger (500 mg) had no effect on gastric emptying in normal or motion-sick subjects. Gastric motility was also changed during motion sickness. The frequency of the electrogastrogram (EGG) was increased after M-III (tachygastria) and the normal increase in EGG amplitude after liquid ingestion was reduced in motion sick subjects. Although powdered ginger (500 mg) partially inhibited tachygastria in motion sickness, it did not enhance the EGG amplitude in motion sick subjects. We conclude that ginger does not possess antimotion sickness activity, nor does it significantly alter gastric function during motion sickness.

[1] This work was supported by NASA grant NAG-9-167.

Introduction

Ginger *(Zingiber officinale)* has been used as a condiment and medicine for centuries. The rhizome contains a family of chemicals called gingerols which produce the characteristic taste and exert the pharmacological effects. Results of recent studies show that ginger or ginger extracts stimulate calcium uptake in skeletal and cardiac muscle [1], inhibit thromboxane synthesis and platelet aggregation [2–4], enhance bile secretion [5], and increase gastrointestinal propulsion [6].

Health food stores in the United States sell preparations containing ginger root as a motion sickness remedy. Scientific confirmation of its antimotion sickness activity is limited. Two studies report some protection against motion sickness after ginger. In one study, subjects remained on a rotating chair longer and experienced fewer gastric sensations after ginger than after dimenhydrinate [7]. In another study, ginger significantly reduced the incidence of vomiting among naval cadets on the open sea [8]. Holtmann et al. [9] speculated that the antimotion sickness properties of ginger result from effects on the gastrointestinal tract rather than effects on the central nervous system.

The symptoms of motion sickness are associated with abnormal pacemaker activity in the gastric musculature. The increased frequency of pacesetter potentials, called tachygastria [10, 11], suggests that there is a period of disordered gastric motility during motion sickness. In addition, there is a prolonged and severe inhibition of gastric emptying during motion sickness [12] which may be the functional consequence of the gastric dysrhythmia. The role of the stomach in the initiation and progression of motion sickness is unknown, but in some cases, gastric contents can enhance motion sickness susceptibility [13]. Substances that prevent tachygastria or enhance gastric emptying may reduce the incidence or severity of motion sickness.

In this study we assessed the antimotion sickness activity of ginger using techniques that have in the past successfully predicted useful antimotion sickness drugs. In the tests of antimotion sickness activity we compared ginger to the well-known antimotion sickness drug, scopolamine. In addition, we investigated ginger's effects on gastric electrical activity and gastric emptying in normal and motion sick subjects.

Methods

Human volunteers ranging in age from 18 to 40 years participated in this project. Before acceptance into the program, each subject was given a physical examination, a standard clinical laboratory test (SMA-20) and a urine analysis to screen for interfering substances. Informed consent was obtained from all participants. The study was approved by the Institutional Review Committee for Human Experimentation.

Tests of Motion Sickness Susceptibility

Susceptibility to motion sickness was determined in one series of experiments using the stair case protocol. Seated subjects were blindfolded and rotated (clockwise) around the vertical axis in a rotating chair (Contraves-Goerz Corporation, Philadelphia, Pa.). The initial rotational velocity of the chair was set to 1 rpm. While rotating, subjects made five head movements (forward, right, back, left and forward) every 25 s. After each 40 head movements, the rotational velocity of the chair was increased by 2 rpm. As symptoms developed, they were reported to an experienced and trained technician. The test continued until the subject reached a score of 16 points (malaise III or M-III) on the Graybiel scale of motion sickness symptoms [14], or until the rotational velocity reached 35 rpm. The number of head movements

required to reach the M-III endpoint measured motion sickness susceptibility.

Another protocol for testing motion sickness susceptibility employed simultaneous vestibular and visual stimuli. In this test, subjects were rotated in the chair at a constant velocity of 7 rpm. Visual stimuli were produced by a surrounding drum, painted with alternating, 10 cm, black and white stripes. The drum was rotated at a constant 12 rpm in the same direction as the chair. The subjects made timed head movements and reported symptoms as described above.

In the tests of motion sickness susceptibility, each subject was challenged with the test agent and a placebo control. The test agent was judged to possess antimotion sickness activity if it significantly increased the number of head movements required to reach the M-III level of motion sickness compared to placebo. Differences between test and placebo treatments were determined using a paired Student's t test. Levels of $p < 0.05$ were considered significantly different.

Gastric Emptying

The rate of gastric emptying was determined using nuclear medicine techniques. Subjects drank 300 ml of a commercially available sugar and electrolyte solution (Gatorade, Stokely-Van Camp, Chicago, Ill.) to which 1 mCi of ^{99m}Tc diethylenetriaminepentaacetic acid (DTPA) was added. Sequential gastric scintigraphy was performed with the patient supine utilizing a Picker small field of view gamma camera. Images and counts were obtained over the gastric region every 30 s for 1 h. The data were recorded on an A^3 Medtronic Data System computer using the region of interest format over the stomach. The percentage of liquid remaining in the stomach was calculated after the first minute and for every 10 min thereafter for the entire 60-min test period. The data were analyzed with ESTRIP, a computer program designed to calculate parameters of polyexponential equations [15]. Gastric emptying parameters were evaluated using grouped t tests. Levels of $p < 0.05$ were considered significantly different.

Electrogastrography

Gastric electrical activity was monitored from surface (cutaneous) electrodes during the measurement of gastric emptying. Four disposable, silver-silver chloride electrodes (Red Dot, St. Paul, Minn.) were affixed to the abdominal surface of each subject. Electrodes were positioned to obtain the best recording. In general, the electrodes were applied in a rectangular configuration. Two electrodes were placed on each costal margin, approximately 2 cm below the xiphoid, while the remaining two electrodes were positioned approximately 2–5 cm on each side of midline along Addison's Line. Two bipolar EGG recordings were obtained using a Grass Recorder with specially modified 7P122D amplifiers. Recordings were conducted using a sensitivity of 0.1 or 0.05 mV/cm, a time constant of 5 s, and an upper frequency 3-dB cutoff of 0.1 Hz.

The electrogastrograms (EGGs) were analyzed by one of investigators (J.J.S.) without prior knowledge of the treatment administered. The recordings were analyzed for both frequency and amplitude. Control recordings were obtained for a 30-min period before tests of motion sickness susceptibility. Test recordings were conducted for the entire period of gastric emptying. EGG frequency was simply counted for each 5-min period. EGG amplitude was averaged from three waves for each 5-min period. Results are reported as percent of control.

Experimental Protocols

Motion Sickness

All subjects were instructed to arrive at the laboratory after having fasted for the previous 12 h. Treatments were either randomized or assigned using a Latin square design. All tests were conducted at weekly intervals.

Eight male subjects participated in the first study. The subjects received capsules containing 500 or 1,000 mg of ground ginger root (McCormick & Co., Hunt Valley, Md.), 0.6 mg of scopolamine HBr, or lactose on separate test days. The capsules were swallowed with a small quantity of water. One hour after ginger and lactose, or 30 min after scopolamine, the subjects were tested for motion sickness susceptibility using the staircase test.

Eight additional male subjects were evaluated for motion sickness susceptibility after 1,000 mg of fresh ginger obtained from a local grocery store. The product was cleaned, chopped into small particles, weighed and placed in a single gelatin capsule for oral administration. Because of the moisture of the prepa-

ration, the capsule was prepared immediately before administration. A capsule filled with lactose served as control. The staircase test was conducted as described above.

In a third test, ground ginger (940 mg) was tested using the combined emetic stimuli. Motion sickness susceptibility was determined in 4 subjects (3 males, 1 female) 15 min after ginger or brown sugar. Lactose was mixed with the brown sugar to match the color of ginger.

Gastric Function

Eight subjects (5 males and 3 females) participated in a study of gastric emptying and gastric electrical activity after ginger. The fasted subjects reported to the laboratory for a 30-min baseline recording of EGG. Subjects then received either ginger (500 mg in 2 capsules) or placebo (brown sugar in 2 capsules) under normal conditions (without the presentation of motion sickness stimuli) or immediately after reaching the M-III endpoint of motion sickness. Motion sickness was induced using the staircase test described above. Fifteen minutes later, gastric emptying and motility were evaluated as described above.

In a separate test, gastric emptying was evaluated in 8 male subjects immediately after reaching the M-III level motion sickness. Gastric emptying was measured as described.

Results

Motion Sickness Susceptibility

The number of head movements required to reach the M-III level of motion sickness after various treatments is shown in table 1. Neither powdered nor fresh ginger (1,000 mg) significantly increased the number of head movements required to reach the M-III of motion sickness over control. In contrast, subjects given scopolamine (0.6 mg) tolerated significantly ($p < 0.01$) more head movements than subjects given placebo. Figure 1 compares the number of head movements performed by individuals after ginger and scopolamine.

Gastric Emptying

Figure 2 shows gastric emptying of Gatorade in subjects given powdered ginger (500 mg) or placebo 15 min before testing. Under normal (non-motion sick) conditions gastric emptying was relatively rapid and was not changed by ginger. When tested 15 min after M-III, gastric emptying was noticeably slowed, but again did not differ for ginger and control treatments. When tested immediately after the induction of motion sickness the rate of gastric emptying was significantly ($p < 0.05$) reduced compared to normal gastric emptying. The parameters calculated by ESTRIP are shown in table 2.

Electrogastrography

Figure 3 shows EGG frequency following the ingestion of Gatorade during normal conditions for 15 min after M-III. In non-motion sick subjects, ginger tended to inhibit the reduction in EGG frequency which normally occurs after liquid ingestion. The effect was not significant. During motion sickness, ginger generally inhibited the increased EGG frequency (tachygastria) which occurred after M-III. This inhibition was significantly ($p < 0.05$) different at the 10- and 35-min time periods.

The EGG amplitude generally increased after liquid ingestion in normal but not in motion sick subjects (fig. 4). Ginger enhanced EGG amplitude significantly ($p > 0.05$) for the first 5-min period in normal subjects but did not alter the EGG amplitude response during motion sickness.

In addition to the effects noted above, 3 of 8 subjects given ginger reported gastric burning during the gastric emptying procedure. In addition, 2 of the 8 subjects spontaneously reported an intense urge to urinate

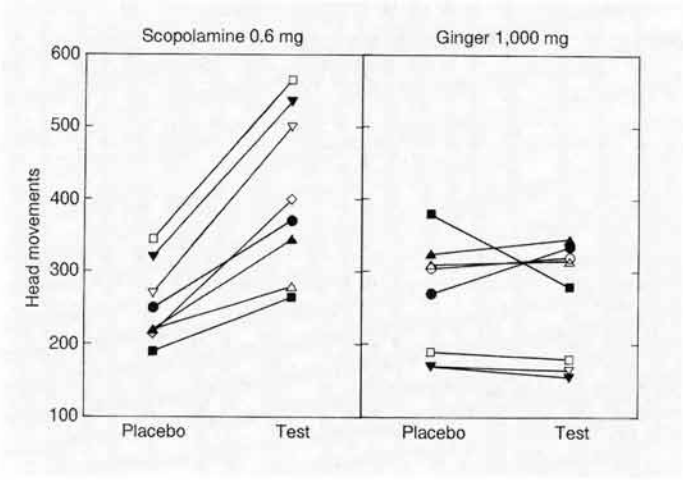

Fig. 1. The number of head movements tolerated by 8 individual subjects after ginger or scopolamine and placebo. Notice that after scopolamine all subjects made more head movements than after placebo. After ginger subjects made either more or less head movements than after placebo.

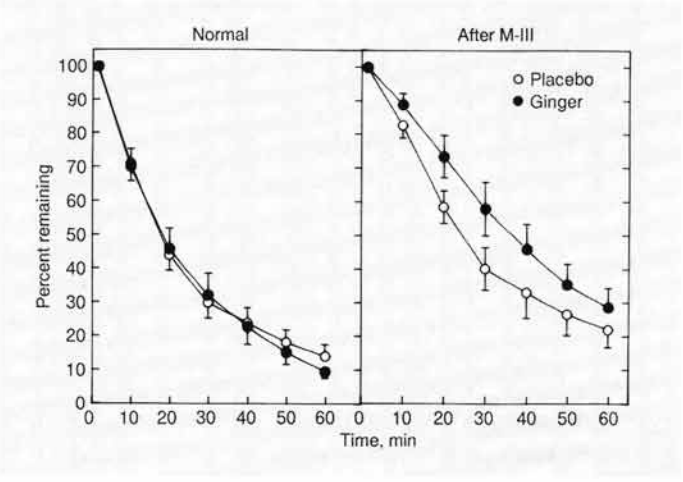

Fig. 2. Percentage (mean ± SEM) of liquid remaining in the stomach at various times after ingestion in non-motion sick (normal) and motion sick subjects. Motion sick subjects were tested 15 min after M-III. Gastric emptying was slowed during motion sickness. Ginger did not influence gastric emptying during normal and motion sick conditions.

Table 1. Test minus placebo head movements for various treatments

Test – placebo	Staircase test				Vestibular + visual test with ginger 940 mg
	ginger 500 mg	ginger 1 g	fresh ginger 1 g	scopolamine 0.6 mg	
Mean	−8.8	−3.1	−0.4	147.5	−7.50
SEM	30.4	16.5	11.5	22.1	4.8
n	8	8	8	8	4
p	NS	NS	NS	$<.01$	NS

Table 2. Parameters of gastric emptying (mean ± SEM)

Condition	Treatment	Rate constant min^{-1}	Half life min	Correlation coefficient
Normal	placebo (n = 7)	0.038 ± 0.01	20.71 ± 2.69	0.99 ± 0.01
	ginger (n = 8)	0.040 ± 0.01	18.47 ± 1.93	0.97 ± 0.02
15 min after M-III	placebo (n = 7)	0.032 ± 0.01	27.43 ± 4.81	0.87 ± 0.11
	ginger (n = 7)	0.024 ± 0.01	34.32 ± 6.50	0.96 ± 0.01
Immediately after M-III	placebo (n = 9)	0.021* ± 0.01	49.48* ± 15.32	0.95 ± 0.02

* Significantly ($p < 0.05$) different from normal placebo.

approximately 30 min after ginger. The remaining subjects volunteered no comments.

Discussion

In this study, two different preparations of ginger were tested for antimotion sickness activity. Neither commercially prepared ginger root, nor the fresh product, obtained locally, significantly reduced motion sickness susceptibility. Subjects tolerated approximately the same number of head movements in the rotating chair after either ginger or a placebo control. In contrast, subjects tolerated significantly more head movements after the well-known antimotion sickness drug, scopolamine [16], than after placebo.

Ginger provided no protection against motion sickness under various test conditions. We tested doses of ginger in the range reported previously to protect against motion sickness [7, 8]. We conducted tests either 15 or 60 min after oral dosing, in case ginger exerted local effects on the stomach or small intestine. Sixty minutes should also provide enough time for absorption and distribution of gingerols. Neither location along the bowel or time for systemic absorption was an important factor. Finally, we tested the substance using two different protocols to induce motion sickness. In one protocol the subjects were blindfolded and received vestibular stimulation only. In the other, the subjects received a combination of vestibular and visual stimuli. Ginger showed no antimotion sickness activity in all tests performed.

Our results conflict with two previous studies which reported significant antimotion sickness activity for ginger. The study of Mowrey and Clayson [7] compared dimenhydrinate, ginger root and a placebo control. They found that subjects given ginger spent more time on a rotating chair and experi-

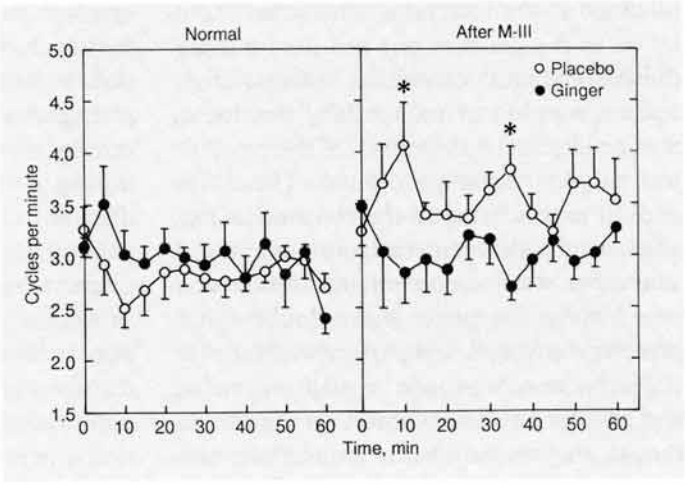

Fig. 3. EGG frequency (mean ± SEM) at various times after ingestion of liquid in normal and motion sick subjects. Ginger (500 mg) tended to inhibit the frequency reduction after liquid ingestion in normal subjects and inhibit the tachygastria associated with motion sickness. * $p < 0.05$.

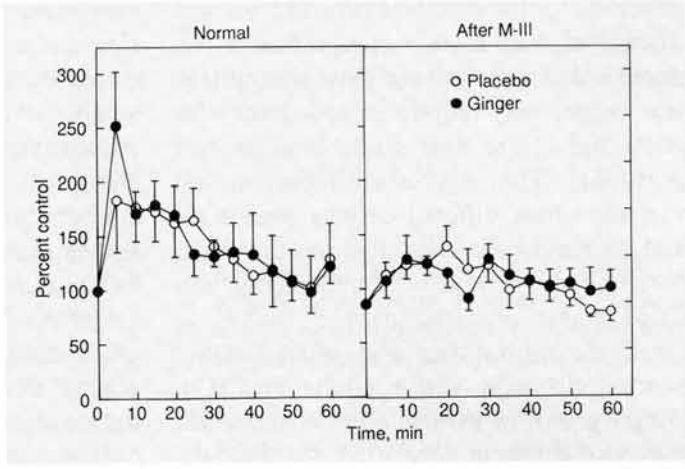

Fig. 4. Percentage of control EGG amplitude (mean ± SEM) at various times after ingestion of liquid in normal and motion sick subjects. Ginger briefly increased EGG amplitude in normal subjects but did not affect the amplitude recorded in motion sick subjects.

enced fewer gastric sensations than subjects given placebo or dimenhydrinate. Their study differed from ours in at least two ways. First, their subjects were assigned to test groups based upon a self-appraisal of motion sickness susceptibility and each group received only one experimental treatment. We took a different approach and tested each subject with both a test agent and a placebo. Thus each of our subjects served as his/her own control and innate differences in motion sickness susceptibility between subjects were eliminated statistically. Secondly, their criteria for motion sickness susceptibility was different from ours. They asked subjects to report gastric sensations and determined the total time spent on the rotating chair. Their test was terminated if the subject vomited, requested that it stop, or if the gastric sensations increased too rapidly. We ap-

plied gradually increasing vestibular stimulation in the staircase test and used a reproducible endpoint of motion sickness based upon a number of sequentially developing motion sickness symptoms [15]. None of our test subjects actually vomited. The difference in results between the two studies may relate to the different endpoints employed. The other study reporting antimotion sickness activity for ginger was a double-blind, placebo-controlled trial performed at sea [8]. Subjects scored nausea, vertigo, vomiting and sweating at hourly intervals for 4 h. Although ginger significantly reduced the incidence of vomiting and sweating, it did not affect the incidence of nausea and vertigo. Total symptom score was significantly reduced only for the 4th and final hour of testing. Ginger may require extended time for onset and future tests might evaluate this possibility. The only other important test variable which differed between our study and the previous studies cited was the ginger preparation employed. Commercially prepared ginger preparations vary widely in chemical composition and often contain pharmacologically active adulterants [17]. Ginger grown in various areas of the world may also differ in content. Unfortunately, many studies, including the studies cited, fail to include a source, or provide the specific details of the ginger preparation tested.

We monitored gastric motility using the noninvasive technique of EGG [18]. Under normal conditions, the ingestion of a liquid is associated with a decrease in frequency and an increase in amplitude of the EGG [19]. The increase in EGG amplitude is thought to result from the additional electrical activity associated with gastric contractions and increased gastric work [20, 21]. During motion sickness, EGG frequency increases from the normal rate of approximately 3 cycles/min, to rates of between 4 and 9 cycles/min [10, 11]. This so-called tachygastria occurs in fasted or fed subjects during motion sickness [13]. In addition, during motion sickness the EGG amplitude does not increase after the ingestion of liquids or solids [13, 22]. In this study we confirmed many of these previous observations. In normal subjects ingestion of liquid produced a reduction in EGG frequency and relatively brief enhancement of EGG amplitude. During motion sickness, we recorded tachygastria which persisted for a relatively long period. In addition, we noted that EGG amplitude did not increase after liquid ingestion in motion sick subjects. Ginger produced little change in the EGG in normal subjects. Although it did tend to inhibit the reduced frequency after liquid ingestion, the effect was not significant. In motion sick subjects, ginger partially inhibited the tachygastria associated with motion sickness and EGG frequency seemed more stable after ginger than after placebo treatment. On the other hand, ginger did not affect the depressed EGG amplitude response after liquid ingestion in motion sick subjects.

This study also confirms that gastric stasis accompanies motion sickness. In addition, the results offer some insight into the temporal characteristics of the inhibition. Gastric emptying was measured both immediately and 15 min after the M-III endpoint of motion sickness. As reported previously [12], gastric emptying was severely reduced immediately after M-III, during the period of maximum motion sickness symptoms. In the other test of gastric emptying, the subjects waited 15 min after M-III before they drank the isotope-containing liquid. Subjects rested in the supine position during this

15-min interval. Symptoms diminished rapidly during this waiting period and subjects reported 'feeling better' immediately before the ingestion of tracer. Although gastric emptying was still noticeably slowed during these tests, partial recovery of gastric activity had occurred. It appears, therefore, that the gastric stasis associated with motion sickness subsides rapidly after the termination of motion sickness stimuli. The degree of gastric stasis appeared to parallel the incidence and severity of other motion sickness symptoms. Ginger did not alter gastric emptying in motion sick subjects.

The relationship between EGG and gastric emptying is not established. The present results, however, suggest that tachygastria may not be the primary indicator of gastric stasis. In spite of its tendency to reduce tachygastria, ginger did not affect gastric emptying. On the other hand, the inhibition of tachygastria by ginger was only partial and the exact relationship between gastric emptying and EGG frequency is not clear from our data. EGG amplitude, however, may be a more important indicator of gastric emptying. As mentioned previously [13], the temporal relationship between tachygastria and gastric emptying is inconsistent, whereas EGG amplitude is more consistently depressed during clinical states associated with gastric stasis. Thus, patients with diabetic gastroparesis have brief, intermittent periods of tachygastria, but consistently fail to respond with increased amplitude EGG after food [22]. In the present study, EGG amplitude changed little after liquid ingestion in motion sick subjects, suggesting that during motion sickness gastric muscle fails to respond to either the physical or chemical stimuli associated with gastric contents. Whether this is a specific or generalized depression of gastric smooth muscle is unknown.

The partial inhibition of tachygastria by ginger implies that the symptoms of motion sickness can be dissociated from this gastric electrical event. It also suggests that partial inhibition of the tachygastria does little to relieve the onset or severity of motion sickness symptoms. Several subjects complained of gastric burning after ginger and this seemed to be associated with the supine position required for the measurement of gastric emptying. Certain subjects may be predisposed to this effect of ginger because of pre-existing or ginger-induced reduction in lower esophageal sphincter tone. Our results indicate that ginger would be of little value to subjects anticipating motion sickness stimuli.

References

1 Kobayashi M, Shoji N, Ohizumi Y: Gingerol, a novel cardiotonic agent, activates the Ca^{++}-pumping ATPase in skeletal and cardiac sarcoplasmic reticulum. Biochim Biophys Acta 1987;903:96–102.

2 Backon J: Ginger: Inhibition of thromboxane synthetase and stimulation of prostacyclin. Relevance for medicine and psychiatry. Med Hypotheses 1986;20:271–278.

3 Srivastava KC: Aqueous extracts of onion, garlic and ginger inhibit platelet aggregation and alter arachidonic acid metabolism. Biomed Biochim Acta 1984;43(suppl):335–346.

4 Srivastava KC: Isolation and effects of some ginger components of platelet aggregation and eicosanoid biosynthesis. Prostaglandins Leukot Med 1986;25:187–198.

5 Yamahara J, Miki K, Chisaka T, Sawada T, Fujimura H, Tomimatsu T, Nakano K, Nohora T: Cholagogic effect of ginger and its active constituents. J Ethnopharmacol 1985;13:217–225.

6 Yamahara J, Huang Q, Li Y, Xu L, Fujimura H: Gastrointestinal motility enhancing effect of gin-

ger and its active constituents. Chem Pharm Bull 1990;38:430–431.
7 Mowrey DB, Clayson DE: Motion sickness, ginger, and psychophysics. Lancet 1982;ii:655–657.
8 Grøntved A, Brask T, Jørgen K, Hentzer E: Ginger root against seasickness. Acta Otolaryngol 1988;105:45–49.
9 Holtmann S, Clarke AH, Scherer H, Hohn M: The anti-motion sickness mechanism of ginger. Acta Otolaryngol 1989;108:168–174.
10 Stern RM, Koch KL, Leibowitz HW, Lindblad IM, Shupert CL, Stewart WR: Tachygastria and motion sickness. Aviat Space Environ Med 1985; 56:1074–1077.
11 Stern RM, Koch KL, Stewart WR, Lindblad IM: Spectral analysis of tachygastria recorded during motion sickness. Gastroenterology 1987;92:92–97.
12 Wood MJ, Wood CD, Manno JE, Manno BR, Redetzki HM: Nuclear medicine evaluation of motion sickness and medications on gastric emptying. Aviat Space Environ Med 1987;58: 1112–1114.
13 Stewart JJ, Wood MJ, Wood CD: Electrogastrograms during motion sickness in fasted and fed subjects. Aviat Space Environ Med 1989;60:214–217.
14 Graybiel A, Wood C, Miller EF, Cramer DB: Diagnostic criteria for grading the severity of acute motion sickness. Aerospace Med 1968;39: 453–455.
15 Brown RD, Manno JE: ESTRIP, a BASIC computer program for obtaining initial polyexponential parameter estimates. J Pharm Sci 1978;67: 1687–1691.
16 Wood CD, Manno JE, Wood MJ, Manno BR, Redetzki HM: Mechanisms of antimotion sickness drugs. Aviat Space Environ Med 1987;58: A262–A265.
17 Osisiogu IU: Detection of adulteration in ginger galenicals by thin-layer chromatography. J Chromatogr 1973;84:200–203.
18 Stern RM: A brief history of the electrogastrogram; in Stern RM, Koch KL (eds): Electrogastrography: Methodology, Validation, and Applications. New York, Praeger, 1985.
19 Stewart JJ, Wood CD, Wood MJ, Woods TW, Mims ME: Effects of liquid ingestion on the electrogastrogram recorded during motion sickness. Aviat Space Environ Med 1989;60:505.
20 Smout AJPM, van der Schee EJ, Grashuis JL: What is measured in electrogastrography? Dig Dis Sci 1980;25:179–187.
21 Koch KL: Gastric motility: Electromechanical considerations; in Stern RM, Koch KL (eds): Electrogastrography: Methodology, Validation, and Applications. New York, Praeger, 1985.
22 Hamilton JW, Bellahsene BF, Rechelderfer M, Webster JG, Bass P: Human Electrogastrograms: Comparison of surface and mucosal recordings. Dig Dis Sci 1986;31:33–39.

Received: July 6, 1990
Accepted: September 18, 1990

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