Zingiber officinale: ginger: adrak

**Description**
A perennial herb with a subterranean, digitately branched rhizome producing stems up to 1.50 m in height with linear lanceolate sheathing leaves (5-30 cm long and 8-20 mm wide) that are alternate, smooth and pale green. Flower stems shorter than leaf stems and bearing a few flowers, each surrounded by a thin bract and situated in axils of large greenish yellow obtuse bracts, which are closely arranged at end of flower stem forming collectively an ovate-oblong spike. Each flower shows a superior tubular calyx, split part way down on side; an orange yellow corolla composed of a tube divided above into three linear-oblong, blunt lobes; six steamiiness in two rows, the outer row of three inserted at mouth of corolla; the posterior, small horn-like; the anterior petaloid, purple and spotted and divided into three rounded lobes; an inferior three celled ovary with tufted stigma. Fruit a capsule with small arillate seeds.

**Dried rhizome**

**General appearance**
Ginger occurs in horizontal, laterally flattened, irregularly branching pieces; 3-16 cm long wide, up to 2 cm thick; sometimes split longitudinally, pale yellowish buff or light brown externally, longitudinally striated, somewhat fibrous; branches known as "fingers" arise obliquely from the rhizomes are flattish, obovate, short about 1-3 cm long; fracture, short and starchy with projecting fibres; internally, yellowish brown, showing a yellow endodermis separating the narrow cortex from the wide stele and numerous scattered fibrovascular bundles, abundant scattered oleoresin cells with yellow contents and numerous larger greyish points, vascular bundles, scattered on the whole surface.

**Organoleptic properties**
Odour, characteristic aromatic; taste, pungent and aromatic; colour, internally pale yellow to brown.

**Microscopic characteristics**
Cortex of isodiametric, thin-walled parenchyma cells contains abundant starch granules, each with a pointed hilum up to 50 µm long and 25 µm wide and 7 µm thick and showing scattered fibrovascular bundles, abundant scattered secretion cells with suberized walls and yellowish brown oleoresinous content, and scattered bundles of the leaf-traces accompanied by fibres; endodermis of pale brown thin walled cells with suberized radial walls; stele with parenchymatous ground tissue. Numerous yellow oleoresin secretion cells and numerous scattered closed collateral vascular bundles with nonlignified, reticulate, scalariform and spiral vessels, often accompanied by narrow cells; containing a dark brown pigment and supported by thin-walled fibres with wide lumen, small oblique slit like pits, and lignified middle lamella; some of the fibres are septate.

**Powdered plant material**
Powdered ginger is yellowish white to yellowish brown; characterized by numerous fragments of thin-walled septate fibres with oblique slit-like pits; fragments of nonlignified scalariform reticulate and spiral vessels, often accompanied by dark pigment.
cells; oleoresin in fragments or droplets with oil cells and resin cells scattered in parenchyma; numerous starch granules, simple, flat, oval, oblong with terminal protuberance, in which the hilum is pointed, 5-60 µm usually 15-30 µm long, 5-40 µm (usually 18-25 µm) wide, 6-12 µm (usually 8-10 µm) thick with somewhat marked fine transverse striations.

**Origin and Distribution:**
It is being cultivated throughout India.

**Cultivating:**
The main cultivation of ginger takes place in zone 9. In cold-winter areas it must be grown indoors; as potted plants but they rarely bloom in winter. However, they do grow until they can be set outside in the spring.

They can be propagated from a small piece of the fresh rhizome that has at least one eye (sort of like the potato eye). Fill a small pot with professional potting soil and plant the root on its side parallel to the soil surface. Just barely cover the root with potting soil and pat down. Keep in a warm place until green stalks come from the eye. Transplant into a large pot filled with equal amounts of loam, sand, peat moss or compost. Fertilize and water regularly. Outdoors it likes a partially shaded location and to be moved indoors before the first frost.

This fragrant, lovely plant has given us much over the centuries. It is one of the most complex and complete medicinal favored by herbalists today. Research has shown our knowledge of its healing properties growing with new study. Certainly a gift from a bountiful Creator.

**Chemistry:**
The rhizome contains 1-4% essential oil and an oleoresin. The composition of the essential oil varies as a function of geographical origin, but the chief constituent sesquiterpene hydrocarbons (responsible for the aroma) seem to remain constant. These compounds include (-)-zingiberene, (+)-ar-curcumene, (-)-β-sesquiphellandrene and β-bisabolene. Monoterpenic aldehydes and alcohols are also present. The constituents responsible for the pungent taste of the drug and possibly part of its anti-emetic properties have been identified as 1-(3-methoxy-4-hydroxyphenyl)-5-hydroxyalkan-3-ones, known as [3-6]-, [8]-, [10]-, and [12]-gingerols (having a side-chain with 7-10, 12, 14, or 16 carbon atoms, respectively) and their corresponding dehydration products, which are known as shogaols.

**Traditional uses:**
In western herbal medicine ginger has been used for dyspepsia, flatulent colic, alcoholic gastritis and diarrhoea from relaxed bowel where there is no inflammation. As a circulatory stimulant, hot infusion of ginger was said to be beneficial for amenorrhoea due to cold. It was also used as a rubifacient. The Eclectics used ginger particularly as a stimulating tonic, stomachic, carminative and antispasmodic. It was used to treat nausea, gastrointestinal cramping, loss of appetite and cold extraintestinal cramping loss of
appetite and cold extremities. The hot infusion was used to 'break up' colds and to relieve painful menstruation.

Ginger was also described as a diffusive stimulant. The term 'stimulant' in this context means a metabolic (heating) and circulatory enhancing agent which also reinforces the therapeutic activity of other herbs. Being a diffusive stimulant, ginger was used to enhance those activities, which could be classified as 'diffuse' such as expectoration, digestion and diaphoresis.

Similar uses were observed for ginger in Ayurveda. It was also topically applied for headache, toothache and to improve circulation to the limbs. In Thai traditional texts the main uses described for ginger rhizome include sweetening the voice, enhancing appetite, dyspepsia, flatulence, fever, mouth ulcers and intestinal infections.

In traditional Chinese medicine, distinction is made between fresh and dried ginger rhizome. Dried ginger is more effective in expelling Interior Cold which is related more to the constitution of the patient, which fresh ginger promotes sweating and disperses Exterior Cold which is brought on by external agents, fresh ginger is pungent and hot and is used for vomiting, cough and debilitating sweating and to reduce the poisonous effect of other herbs. It cold characterized by severe intolerance to cold, slight fever, headache, general ache, nasal congestion and a runny nose. Dried ginger is pungent and hot and is used for Cold conditions characterized by pallor, poor appetite and digestion, cold limbs, vomiting, diarrhoea, pale tongue or thin, watery or white sputum. It is to be used cautiously during pregnancy.

**Pharmacological Activities and Clinical Trails**

**Antiemetic Activity**
The effect of powdered ginger root was compared with metoclopramide and placebo. In a prospective, randomised, double-blind trial the incidence of postoperative nausea and vomiting was measured in 120 women presenting for elective laparoscopic gynaecological surgery on a day stay basis. The incidence of nausea and vomiting was similar in patients given metoclopramide and ginger (27% and 21%) and less than in those who received placebo (41%). The requirement for postoperative antiemetics was lower in those who receiving ginger. The requirements for postoperative analgesia, recovery time and time until discharge were the same in all groups. There was no difference in the incidence of possible side effects such as sedation, abnormal movement itch and visual disturbance between the three groups. Zingerber officinale is an effective and promising prophylactic antiemetic, which may be especially useful for day case surgery.

Effect of ginger (Zingiber officinale Roscoe, Zingiberaceae) extracts (acetone, 50% ethanolic and aqueous) were investigated for antiemetic activity against emesis induced by 3 mg/kg cisplatin (the 100% emetic dose i.v.) in-healthy mongrel dogs. The acetone and 50% ethanolic extract at the doses of 25, 50, 100 and 200 mg/kg p.o. exhibited significant protection while aqueous extract at these doses was ineffective against
cisplatin emesis. The acetone extract was more effective than ethanolic extract. However both were less effective when compared to 5-HT3 receptors antagonist granisetron. Neither of the ginger extract was effective against apomorphine-induced emesis. The findings suggest that ginger could be an effective and cheap antiemetic adjunct to cancer chemotherapy.

Magnolol and honokiol, biphenyl compounds, were isolated as anti-emetic principles from the methanolic extract of Magnolia obovata bark. [6]-, [8]-, and [10]-shogaols and [6], [8]-, and [10]- gingerols were isolated from the methanolic extract of Zingiber officinale rhizome as anti-emetic principles. Some phenyl-propanoids with allyl side chains were found to show the same activity. They inhibited the emetic action induced by the oral administration of copper sulfate pentahydrate to leopard and ranid frogs.

The effectiveness of ginger (Zingiber officinale) as an antiemetic agent was compared with placebo and metoclopramide in 60 women who had major gynaecological surgery in a double-blind, randomised study. There were statistically significantly fewer recorded incidences of nausea in the group that received ginger root compared with placebo (p less than 0.05). The number of incidences of nausea in the groups that received either ginger root or metoclopramide were similar. The administration of antiemetic after operation was significantly greater in the placebo group compared to the other two groups (p less than 0.05).

**Antifeedant and Antifungal Activity**

Fresh rhizomes of Zingiber officinale (ginger), when subjected to steam distillation, yielded ginger oil in which curcumene was found to be the major constituent. The thermally labile zingiberene-rich fraction was obtained from its diethyl ether extract. Column chromatography of ginger oleoresin furnished a fraction from which [6]-gingerol was obtained by preparative TLC. Naturally occurring [6]- dehydroshogaol was synthesised following condensation of dehydrozingerone with hexanal, whereas zingerone and 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)butane were obtained by hydrogenation of dehydrozingerone with 10% Pd/C. the structures of the compounds were established by 1H NMR, 13C NMR and mass (EI-MS and ES-MS) spectral analysis. The test compounds exhibited moderate insect growth regulatory (IGR) and antifeedant activity against Spilosoma obliqua, and significant antifungal activity against Rhizoctonia solani. Among the various compounds, [6]-dehydroshogaol exhibited maximum IGRactivity (EC50 3.55 mg ml-1), while dehydrozingerone imparted maximum antifungal activity (EC50 86.49 mg liter-1).

**Antifilarial Activity**

Dogs, naturally infected with Dirofilaria immitis, were treated with the residues of the alcoholic extracts of the rhizomes of Zingiber officinale (ginger). Twelve subcutaneous injections of the extract given at 100 mg/kg reduce microfilarial concentration in blood by a maximum of 98%. Fifty five says after the last injection there was 83% reduction in microfilarial concentration suggesting partial destruction of adult worms. Half of the
treated dogs showed some lethargy at the beginning of treatment possibly due to the mass annihilation of microfilariae in blood.

**Antihyperlipidaemic Activity**

The effects of ethanolic extract of ginger (200 mg/kg, p.o.) were studies in cholesterol fed rabbits. The marked rise in serum and tissue cholesterol, serum triglycerides, serum lipoproteins and phospholipids that followed 10 weeks of cholesterol feeding was significantly reduced by the ethanolic ginger extract and results were compared with gemfibrozil, a standard orally effective hypolipidaemic drug. The severity of aortic atherosclerosis as judged by gross grading was more marked in pathogenic, i.e. the hypercholesterolemic group, while animals receiving ginger extract along with cholesterol showed a lower degree of atherosclerosis. The results indicate that ginger is definitely an antihyperlipidaemic agent.

**Antiinflammatory Activity**

The present study was carried out to elucidate the anti-inflammatory effect of the methanol extract obtained from the rhizomes of Zingiber cassumunar Roxb and its active principles. The methanol extract was partitioned between ether and water and then the ether-soluble fraction was extracted with n-hexane. The n-hexane-soluble fraction was chromatographed and part of the fraction was rechromatographed by silica gel column. Three compounds were identified as (E)-1-(3,4-dimethoxyphenyl)but-1-ene, (E)-1-(3,4-dimethoxy-phenyl) butadiene and zerumbone. The anti-inflammatory activity of these fractions was investigated on carrageenan-induced edema in rats, as well as on acetic acid-induced vascular permeability and writhing symptoms in mice. The methanol extract (p.o.) showed both anti-inflammatory activity and analgesic activity. These activities shifted successively to ether-soluble and n-hexane-soluble fractions and to (E)-1-(3,4-dimethoxyphenyl)but-1-ene. These results suggest that the anti-inflammatory action and analgesic action of Zingiber cassumunar is the result of the (E)-1-(3,4-dimethoxyphenyl)but-1-ene that it contains.

There is considerable emphasis on identifying potential chemopreventive agents present in food consumed by the human population. Ginger rhizome (Zingiber officinale) known commonly as ginger, is consumed worldwide in cookeries as a spice and a flavoring agent. In prior in vitro studies, it has been shown that the water or organic solvent extract of ginger possesses antioxidative and antiinflammatory properties. In this study, we evaluated whether ethanol extract of ginger (GE) possesses anti-tumor-promoting effects in a mouse skin tumor promoters induced epidermal ornithine decarboxylase (ODC), cyclooxygenase, and lipoxygenase activities and edema and hyperplasia are conventionally used markers of skin tumor promotion, first we assessed the effect of GE on these parameters. Preapplication of GE onto the skin of SENCAR mice resulted in significant inhibition of 12-0-tetradecanoylphorbol-13-acetate (TPA)-caused induction of epidermal ODC, cyclooxygenase and lipoxygenase activities and edema and hyperplasia are conventionally used markers of skin tumor promotion, first we assessed the effect of GE on these parameters. Preapplication of GE onto the skin of SENCAR mice resulted in significant inhibition of 12-0-tetradecanoylphorbol-13-acetate (TPA)-caused induction of epidermal ODC, cyclooxygenase and lipoxygenase activities and ODC mRNA expression in a does-dependent manner. Preapplication of GE to mouse skin also afforded significant inhibition of TPA-caused epidermal edema (56%) and hyperplasia (44%). In long-term tumor studies, topical application of GE 30 min prior to that of each TPA application to 7 12-dimethylbenz(a)anthracene-initiated SENCAR mice resulted in a
highly significant protection against skin tumor incidence and its subsequent multiplicity. The animals pretreated with GE showed substantially lower tumor body burdens compared with non-GE-treated controls. The results of our study, for the first time provide clear evidence that GE possesses anti-skin tumor-promoting effects and that the mechanism of such effects may involve inhibition of tumor promoter-caused cellular, biochemical and molecular changes in mouse skin.

Antimicrobial Activity
Dichloromethane and methanol extracts of 13 Zingiberceae species from the Alpinia, Costus and Zingiber genera were screened for antimicrobial and antioxidant activities. The antimicrobial activity of most of the extracts was antibacterial with only the methanol extract of Costus discolor showing very potent antifungal activity against only Aspergillus ochraceous (MID, 15.6 microg per disc). All the extracts showed strong antioxidant activity comparable with or higher that of alphatocopherol.

Antimotion Sickness Activity
The pharmacologic actions related to antimotion sickness effects of ginger (Zingiber officinal Roscoe.) were studied. There was no significant effect on parameters of rotatory movement-induced electronystagmogram of rabbit after intravenous (i.v.) infection of ginger juice. The low amplitude fast wave pattern of electrocorticogram of rabbit changed to high amplitude slow wave pattern after i.v. injection of ginger juice. Rabbit gastric contraction in situ was shortly suppressed after ginger juice i.v. administration. In the isolated rat fundus strip preparations, however, ginger juice reduced the spontaneous contractile frequency and enhanced the spontaneous contractile amplitude, which was followed by inhibition. Ginger juice produced longitudinal contraction of the guinea-pig isolated ileum, which was followed by rapid tachyphylaxis. This contraction effect was not affected by hexamethonium and 5-HT, but could be inhibited by cold storage, hyoscine, morphine, diphenhydramine, promethazine and substance P desensitization. Naloxone could eliminate this inhibition produced by morphine. By using dose response relationship plot, non-competitive antagonisms were observed between ginger juice and histamine in isolated guinea-pig ileum. It is suggested that the pungent constituents of ginger released substance P in turn either stimulates cholinergic and histaminic neurons to release Ach and histamine, respectively, or produces direct muscle contraction by activating M and H1 receptors correspondingly. It is proposed that after being excited by substance P, M an H1 receptors are inactive temporarily and unable to be excited by agonists, therefore, ginger juice exhibits anticholinergic and antihistaminic action. Ginger juice produces antimotion sickness action possibly by central and peripheral anticholinergic and antihistaminic effects.

The 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 111 or M-111). 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 1000 mg) or fresh ginger root (1000 mg) provided no protection against motion sickness. In contrast, subjects performed an average of 147.5 more head movements (p less than 0.01) after scopolamine (0.6 mg p.o.) than after placebo. The rate of gastric emptying was significantly (p less than 0.05) slowed when tested immediately after M-111. 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 (ECG) was increased after M-111 (tachygastria) and the normal increase in ECG 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.

**Antioxidant Activity**

Ginger (Z. officinale; 1% w/w) significantly lowered lipid peroxidation by maintaining the activities of the antioxidant enzymes-superoxide dismutase, catalase and glutathione peroxidase in rats. The blood glutathione content was significantly increased in ginger fed rats. Similar effects were also observed after natural antioxidant ascorbic acid (100 mg/kg, body wt) treatment. The results indicate that ginger is comparatively as effective as ascorbic acid as an antioxidant.

The antioxidative effect of more than 50 ethanol extracts of Chinese drugs were studied on the air oxidation of linoleic acid. Several ethanol extracts such as Glycyrrhiza uralensis, Magnolia officinalis and Zingiber officinale etc., were found having stronger antioxidative effect.

**Antiplatelet Activity**

The purpose of this investigation was to determine the antiplatelet mechanism of gingerol. Gingerol concentration-dependently (0.5-20 microM) inhibited the aggregation and release reaction of rabbit washed platelets induced by arachidonic acid and collagen, but not those induced by platelet-activating factor (PAF), U46619 (9, 11-dideoxy-9 alpha, 11 alpha-methano-epoxy-PGF2 alpha) and thrombin. Gingerol also concentration-dependently (0.5-10 microM) inhibited thromboxane B2 and prostaglandin D2 formation caused by arachidonic acid and completely abolished phosphoinositide breakdown induced by arachidonic acid but had no effect on that of collagen PAF or thrombin even at concentrations as high as 300 microM. In human platelet-rich plasma, gingerol and indomethacin prevented the secondary aggregation and blocked ATP release from platelets induced by adenosine 5'-diphosphate (ADP, 5 microM) and adrenaline (5 microM) but had no influence on the primary aggregation. The maximal antiplatelet effect was obtained when platelets were incubated with gingerol for 30 min and this inhibition was reversible. It is concluded that the antiplatelet action of gingerol is mainly due to the inhibition of thromoxane formation.
**Antirhinoviral Activity**
The dried rhizomes of Indonesian ginger, Zingiber officinale, were investigated for antirhinoviral activity in the plaque reduction test. Fractionation by solvent extraction, solvent partition, and repeated chromatography guided by bioassay, allowed the isolation of several sesquiterpenes with antirhinoviral activity. The most active of these was beta-sesquiphellandrene [2] with an IC50 of 0.44 microM vs. rhinovirus IB in vitro.

**Anti-thrombotic Activity**
Ginger (Zingiber Officinale Roscoe) has been claimed to exert an anti-thrombotic effect in humans as ginger extracts inhibit cyclo-oxygenase activity of platelets in vitro. Effects of ginger consumption on ex vivo platelet function, however, are contradictory. We therefore investigated whether daily consumption of raw or cooked ginger decreases platelet cyclo-oxygenase activity as assessed by ex vivo maximally stimulated platelet thromboxane B2 production. DESIGN: We carried out a randomized placebo-controlled cross-over study of 3 × 2 weeks. SUBJECTS: Eighteen healthy volunteers aged 22 3 y (means.d.) participated in the study; there were no dropouts. INTERVENTIONS: Subjects consumed 15 g of raw ginger root, 40 g of cooked stem ginger, or placebo daily for two weeks. We took fasted venous blood samples and measured thromboxane B2 production in maximally stimulated platelet-rich plasma at days 12 and 14 of each treatment period. RESULTS: Mean decrease in thromboxane B2 production relative to placebo was 1 9% for ginger root, and -1.8% for stem ginger with no effect of treatment order (P = 0.984). CONCLUSION: We cannot confirm the putative anti-thrombotic activity of ginger in humans.

**Anti-tumor Activity**
Zingiberaceae rhizomes commonly used in the Malaysian traditional medicine were screened for anti-tumour promoter activity using the short-term assay of inhibition of 12-O-tetradecanoyl phorbol-13-acetate (TPA)-induced Epstein-Barr virus early antigen (EBV-EA) in Raji cells. The inhibition of TPA-induced EBV-EA was detected using the indirect immunofluorescence assay (IFA) and Western blot technique. The indirect IFA detected the expression/inhibition of both EBV-EA-D and EA-R (restricted EA antigen). Seven rhizomes were found to possess inhibitory activity towards EBV activation, induced by TPA; they are: Curcuma domasticam, C. xanthorrhiza, Kaempferia galanga, Zingiber cassumunar, Z. officinale, Z.officinale (red variety) and Z. zerumbet. A cytotoxicity assay was carried out to determine the toxicity of the Zingiberaceae rhizome extracts. The rhizome extracts that exhibited EBV activation inhibitory activity had no cytotoxicity effect in Raji cells. Therefore the present study shows that several Zingiberaceae species used in Malaysian traditional medicine contain naturally occurring non-toxic compounds that inhibit the EBV activation, which if further investigated, could contribute in the development of cancer prevention methods at the tumour-promoting stage.

**Anti-ulcer Activity**
An anti-ulcer constituent, 6-gingesulfonic acid and three monoacylgalactosylglycerols, gingergly colipids A, B and C, were isolated from Zingiberis Rhizoma, the dried rhizome of Zingiber officinale Roscoe which was cultivated in Taiwan together with ()-
angelicoidenol-2-O-beta-D-glucopyranoside. Based on chemical reactions and physicochemical evidence the structures of 6-gingesulfonic acid, gingerglycolipids A, B and C have been determined. In addition the absolute stereostructure of (-)-angelicoidenol-2-O-beta-D-glucopyranoside was clarified on the basis of its synthesis from d-borneol. 6-Ginesulfonic acid showed weaker pungency and more potent anti-ulcer activity than 6-gingerol and 6-shogaol.

Use of Dipaniya Mahakasaya, a group consisting of 10 herbal drugs, has been suggested in Charaka Samhita to improve digestion. Out of these 10 plants three viz. P. longum (water decoction), Z. officinalis (water decoction) and Ferula species (colloidal solution) were studied for their antiulcer and mechanism of antiulcer effects in rats. All the drugs in the dose of 50 mg/kg p.o., 60 min prior to experiment, showed significant protection against gastric ulcers induced by 2 hr cold restraint stress, aspirin (200 mg/kg, 4 hr) and 4 hr pylorus ligation. The antiulcerogenic effect seemed to be due to the augmentation of mucin secretion and decreased cell shedding rather than offensive acid and pepsin secretion which however, were found to be increased by them.

Gastroprotective activity
The cytoprotective and gastric anti-ulcer studies of ginger have been carried out in albino rats. Cytodestruction was produced by 80% ethanol, 0.6M HCl, 0.2M NaOH and 25% NaCl. Whereas gastric ulcers were produced by ulcerogenic agents including indomethacin, aspirin and reserpine, beside hypothermic restraint stress and by pylorus ligated Shay rat technique. The results of this study demonstrate that the extract in the dose of 500 mg/kg orally exert highly significant cytoprotection against 80% ethanol, 0.6M HCl, 0.2M NaOH and 25% NaCl induced gastric lesions. The extract also prevented the occurrence of gastric ulcers induced by non-steroidal anti-inflammatory drugs (NSAIDs) and hypothermic restrain stress. These observations suggest cytoprotective and anti-ulcerogenic effect of the ginger.

Hyperemesis Gravidum.
Thirty women participated in a double-blind randomized cross-over trial of the efficacy of a natural product the powdered root of ginger (Zingiber officinale) and placebo in hypermesis gravidarum. Three patients had to be withdrawn. Each women swallowed capsules containing either 250 mg ginger or lactose q.i.d. during the first 4 days of the treatment period. Interrupted by a 2 days wash-out period the alternative medication was given in the second 4-day period. The severity and relief of symptoms before and after each period were evaluated by two scoring systems. The scores were used for statistical analyses of possible differences. Subjectively assessed 19 women (70.4%) stated preference to the period in which ginger as was later disclosed had been given (P = 0.003). More objectively assessed by relief scores a significantly greater relief of the symptoms was found after ginger treatment compared to placebo (P = 0.035). No side effects were observed. The possible mutagenic and antimutagenic characters of ginger reported in a study of E. coli have not been evaluated with respect to any significance in humans. Powdered root of ginger in daily doses of 1 g during 4 days was better than placebo in diminishing or eliminating the symptoms of hyperemesis gravidarum.
Mutagen and anti-mutagen Activity
When rhizome juice of ginger Zingiber officinale was added to a solution of 2(2-furyl)-3(5-nitro-2-furyl)acryl amide (AF2) or N-methyl-N'-nitro-N-nitrosoguanidine (NTG) mutagenesis by these chemicals was markedly increase. As a result of the component fractionation of the ginger juice, it was found that [6]-gingerol was a potent mutagen. However the ginger juice also contained anti-mutagenic component(s) against [6]-gingerol (CAS No. 58253-27-3) (present study) and tryptophan pyrolysates (kada et al., 1978; Morita et al., 1978). It is suggested, therefore, that the [6]-gingerol component may be mutagenicly activated by the presence of AF2 and NTG.

Molluscicidal and antischistosomal activities
Experiments were conducted to study the major constituents of Zingiber officinale responsible for its molluscicidal activity and the effect of the active component of different stages of Schistosoma mansoni. Gingerol and shogaol exhibited potent molluscicidal activity on Biomphalaria glabrata. Gingerol (5.0 ppm) completely abolished the infectivity of Schistosoma mansoni miracidia and cercariae in B. glabrata and mice, respectively indicating that the molluscide is capable of interrupting schistosome transmission at a concentration lower than its molluscicidal concentrations.

Migraine Headache.
Migraine is considered as a neurological disorder with little convincing evidence of the involvement of some vascular phenomenon. Recent understanding of the mechanisms behind migraine pain generation and perception have considerably helped the development of modern migraine drugs. Most migraine drugs in use, i.e., ergotamine and dihydroergotamine, iprazochrome, pizotifen and diazepam; and non-steroidal antiinflammatory drugs (i.e. aspirin, paracetamol, persantin, etc.) have side-effects and are prescribed with caution for a limited duration. Ginger is reported in Ayurvedic and Tibb systems of medicine to be useful in neurological disorders. It is proposed that administration of ginger may exert abortive and prophylactic effects in migraine headache without any side-effects.

Nausea and Vomiting
Ginger (Zingiber officinale) is often advocated as beneficial for nausea and vomiting. Whether the herb is truly efficacious for this condition is however, still a matter of debate. We have performed a systematic review of the evidence from randomized controlled trials for or against the efficacy of ginger for nausea and vomiting. Six studies met all inclusion criteria and were reviewed. Three on postoperative nausea and vomiting were identified and two of these suggested that ginger was superior to placebo and equally effective as metoclopramide. The pooled absolute risk reduction for the incidence of postoperative nausea, however, indicated a non-significant difference between the ginger and placebo groups for ginger 1 g taken before operation (absolute risk reduction 0.052 (95% confidence interval -0.082 to 0.186)). One study was found for each of the following conditions: seasickness, morning sickness and chemotherapy induced nausea. These studies collectively favoured ginger over placebo.
Patients undergoing photopheresis are required to ingest the drug 8-MOP as part of their treatment. This drug causes nausea as a side effect. Ginger taken prior to 8-MOP may substantially reduce this side effect. This study compared patients nausea when taking 8-MOP with and without ginger.

In a double-blind randomized placebo trial the effect of the powdered rhizome of ginger (Zingiber officinale) was tested on seasickness. Eighty naval cadets, unaccustomed to sailing in heavy seas reported during voyages on the high seas, symptoms of seasickness every hour for 4 consecutive hours after ingestion of 1 g of the drug or placebo. Ginger root reduced the tendency to vomiting and cold sweating significantly better than placebo did (p less than 0.05). With regard to vomiting a modified Protection Index (P1) = 72% was calculated. Remarkably fewer symptoms of nausea and vertigo were reported after ginger root ingestion, but the difference was not statistically significant. For all symptom categories, P1 = 38% was calculated.

**Rheumatism and Musculoskeletal disorders.**

One of the features of inflammation is increased oxygenation of arachidonic acid which is metabolized by two enzymic pathways—the cyclooxygenase (CO) and the 5-lipoxygenase (5-LO)—leading to the production of prostaglandins and leukotrienes respectively. Amongst the CO products, PGE2 and amongst the 5-LO products, LTB4 are considered important mediators of inflammation. More than 200 potential drugs ranging from non-steroidal anti-inflammatory drugs, corticosteroids, gold salts, disease modifying anti-rheumatic drugs, methotrexzte, cyclosporine are being tested. None of the drugs has been found safe; all are known to produce from mild to serious side-effects. Ginger is described in Ayurvedic and Tibb systems of medicine to be useful in inflammation and rheumatism. In all 56 patients (28 with rheumatoid arthritis, 18 with osteoarthritis and 10 with muscular discomfort) used powdered ginger against their afflications. Amongst the arthritis patients more than three-quarters experienced to varying degrees, relief in pain and swelling. All the patients with muscular discomfort experienced relief in pain. None of the patients reported adverse effects during the period of ginger consumption which ranged from 3 months to 2.5 years. It is suggested that at least one of the mechanism by which ginger shows its ameliorative effects could be related to inhibition of prostaglandin and leukotriene biosynthesis, i.e. it works as a dual inhibitor of elcosanoid biosynthesis.

Oxygenation of arachidonic acid is increased in inflamed tissues. In this condition products of two enzymic pathways—the cyclooxygenase and the 5-lipoxygenase producing respectively prostaglandins and leukotrienes—are elevated. Of the cyclooxygenase products, LTB4 are the strongest candidates for mediating inflammation. Non-steroidal anti-inflammatory drugs which inhibit the cyclooxygenase and corticosteroids are used to treat such disorders. Both types of drugs produce adverse side-effects on prolonged use. Ginger is reported in Ayurvedic and Tibb systems of medicine to be useful in rheumatic disorders. Seven patients suffering from such disorders reported relief in pain and associated symptoms on ginger administration.

**Teratogenic Effects**
The teratogenicity of EV.EXT 33, a patented Zingiber officinale extract was examined in Wister SPF rats according to GLP Guidelines. EV.EXT 33 was administered by oral gavage in concentrations of 100, 333 and 1000 mg/kg to three groups of 22 pregnant female rats from days 6 to 15 of gestation. For comparison a fourth group received the vehicle sesame oil. Body weight and food and water intake were recorded during the treatment period. The rats were killed on day 21 of gestation and examined for standard parameters of reproductive performance. The fetuses were examined for signs of teratogenic and toxic effects. EV.EXT 33 was well tolerated. No deaths or treatment-related adverse effects were observed. Weight gain and food consumption were similar in all groups during gestation. Reproductive performance was not affected by treatment with EV.EXT 33. The examination of fetuses for external, visceral and skeletal changes showed no embryotoxic or teratogenic effects of EV.EXT 33. Based on these results it was concluded that EV.EXT 33, when administered to pregnant rats during the period of organogenesis, caused neither maternal nor developmental toxicity at daily doses of up to 1000 mg/kg body weight.

Vertigo-reducing effect
The effect of powdered ginger root (Zingiber officinale) upon vertigo and nystagmus following caloric stimulation of the vestibular system was studied in 8 healthy volunteers in a double-blind crossover placebo trial. The results reported are based upon 48 vertigo scores and 48 electronystagmograms. Ginger root reduced the induced vertigo significantly better than did placebo. There was no statistically significant action upon the duration or the maximum slow phase velocity of nystagmus.

Pharmacokinetics
After injection, 90% of gingerol was found to serum protein and elimination was mainly via the liver. Oral or intraperitoneal dosage zingerone resulted in the urinary excretion of metabolites within 24 hours mainly as glucuronide and/or sulphate conjugates. Appreciable biliary excretion (40% in 12 hours) also occurred.

Interactions
Ginger may increase the absorption of pharmaceutical drugs. Although no problems have been reported in humans, ginger may increase the chance of bleeding. Daily doses of ginger in excess of 4 g should particularly be prescribed with caution in patients who are already taking blood thinning drugs such as warfarin or aspirin or who have increase risk of haemorrhage.

Current Regulatory Status in Selected Countries
Ginger was official in the second edition of the Indian Pharmacopoeia 1966, but was not included in the third edition 1985. It is also official in the "THEAYURVEDIC PHARMACOPEIA OF INDIA", edition 1990.

Ginger is covered by a positive Commission E. monograph and can be used for dyspepsia and the prevention of motion sickness. Ginger is on the UK General Sale List.

Ginger is also freely available as a dietary supplement in the USA under DSHEA legislation (1994 Dietary Supplement Health and Education Act). It has been present in the following OTC drug products: digestive aid drug products and as an ingredient in products offered for use as a smoking deterrent. The FDA, however advises: that based on evidence currently available there is inadequate data to establish general recognition of the safety and effectiveness of these ingredients for the specified uses.

Ginger is not included in Part 4 of Schedule 4 of the therapeutic Goods Act Regulations of Australia. However, products containing ginger with an equivalent dry weight per dosage unit of 2 g and above are required to carry warnings regarding concomitant use with anticoagulants and advising those with bleeding problems to seek medical advice.