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GINGER : ITS ROLE IN XENOBIOTIC METABOLISM

Plant derived products have been used for medicinal purposes for centuries. At present, it is estimated that about 80% of the world population relies on botanical preparations as medicines to meet their health needs. Herbs and spices are generally considered safe and proved to be effective against certain ailments. They are also extensively used, particularly, in many Asian, African and other countries. In recent years, in view of their beneficial effects, use of spices/herbs has been gradually increasing in developed countries also. Spices and herbs are widely used in phytotherapy, which is using plants and their chemical constituents to eliminate certain health problems. This form of treatment is common in Europe. Among these, Germany holds the largest share (49%). Italy, France and UK hold 10% each; Spain, Netherlands, Belgium 2% each and remaining 15% rest of Europe. About one third of the US adults use herbal remedies. In traditional Indian medicine or Ayurveda, ginger and many other spices have been used as medicine[1].

History

Ginger *(Zingiber officinale)* belongs to Zingiberaceae family. The part of the plant used is rhizome. The plant produces an orchid like flower with petals that are greenish yellow streaked with purple colour. Ginger is cultivated in areas of abundant rainfall. Even though it is native to southern Asia, ginger is cultivated in tropical areas also such as Jamaica, China, Nigeria and Haiti. It is an important spice crop in India. About 9000 metric ton (MT) of ginger valued at 4.5 crores was exported in 2001. It is mainly cultivated in Kerala, Karnataka, Tamil Nadu and North Eastern states.

In Sanskrit, ginger is known as *Sringavera* which has given way to *Zingiberi* in Greek and to the Latin *Zingiber*. Ginger has been used as medicine from vedic period and is called *"maha aushadhi"*, means the great medicine. In traditional medicine, it was used as a carminative or antiflatulent. The Greek physician Galen used ginger as a purificant of body. He used ginger to treat conditions caused by imbalances in body[1].

Nutrient Composition

Fresh ginger contains 80.9% moisture, 2.3% protein, 0.9% fat, 1.2% minerals, 2.4% fibre and 12.3% carbohydrates. The minerals present in ginger are iron, calcium and phosphorous. It also contains vitamins such as thiamine, riboflavin, niacin and vitamin C. The composition varies with the type, variety, agronomic

conditions, curing methods, drying and storage conditions[2].

Chemistry

In the fresh ginger rhizome, the gingerols were identified as the major active components and [6] gingerol [5-hydroxy-1-(4-hydroxy-3-methoxy phenyl) decan-3-one is the most abundant constituent in the gingerol series. 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 oil. The volatile oil consists of mainly mono and sesquiterpenes; camphene, beta-phellandrene, curcumene, cineole, geranyl acetate, terphineol, terpenes, borneol, geraniol, limonene, linalool, alpha-zingiberene (30-70%), beta-sesquiphellandrene (15-20%), beta-bisabolene (10-15%) and alpha-farmesene. In dried ginger powder, shogaol a dehydrated product of gingerol, is a predominant pungent constituent upto biosynthesis[3-5]. Oleoresin, which is isolated by acetone and ethanol extraction, contains 4-7.5% of dried powder, pungent substances namely gingerol, shogaol, zingerone and paradol. The oleoresin has also been found to contain zingiberol, the principal aroma contributing component as well as zingiberene, gingediol, diarylheptanoids, vitamins and phytosterols.

Ginger in Traditional Use

Ginger is an essential ingredient in many traditional Chinese medicines and has been used since the 4th century BC. Africans and West Indians also use ginger medicinally and the Greeks and Romans use it as spice[6]. The Chinese take ginger for a wide variety of medical problems such as stomachache, diarrhoea, nausea, cholera, asthma, heart conditions, respiratory disorders, toothache and rheumatic complaints[7]. In *Ayurveda*, ginger has been recommended for use as carminative, diaphoretic, antispasmodic, expectorant, peripheral circulatory stimulant, astringent, appetite stimulant, anti-inflammatory agent, diuretic and digestive aid[8]. In United States, ginger is recommended to relieve and prevent nausea caused by motion sickness and morning sickness[9].

Ginger in Foods

Ginger is an indispensable component of curry powder, sauces, ginger bread and ginger flavoured carbonated drinks. It is also used in some products like biscuits, pickles and confectionaries. It is extensively used in preparation of dietaries for its aroma and flavour. Dry ginger is used in the manufacture of oil, oleoresin, essence and processed meat[10,11].

Pharmacological Effects

Effects on the gastrointestinal tract

The active components of ginger is reported to stimulate digestion, absorption, relieve constipation and flatulence by increasing muscular activity in the digestive tract. The effectiveness of ginger (940 mg) in motion sickness was compared to that of dimenhydrinate (100 mg) in 18 male and 18 female college students, who were self rated as having extreme or very high susceptibility to motion sickness[12,13]. The study concluded that ginger was superior to dimenhydrinate in preventing motion sickness. Ginger administration (1g) prior to elective gynaecologic laparoscopy was also found to be effective in preventing postoperative nausea and vomiting. The effect of ginger was similar to that observed with 100 mg metoclopramide. In addition, a double blind study in 27 pregnant women suffering from morning sickness demonstrated that oral administration of 250 mg of powdered ginger 4 times daily over 4 days significantly reduced symptoms of nausea and vomiting[14-16].

Anti-inflammatory activity

Some of the characteristic features of rheumatic diseases are polyarthritis with inflammation, swelling, and pain accompanied by impaired mobility or even total loss of function of affected areas[17]. The condition is treated using medicines like corticosteroids or nonsteroidal anti-inflammatory drugs. These drugs sometimes produce undesirable side effects. One of the features of inflammation is increased oxygenation of arachidonic acid which results in the production of prostaglandins and leukotrienes[18]. In *Ayurveda*, ginger is reported to be useful in treating inflammation and rheumatism. One of the mechanisms by which ginger exerts its ameliorative effects could be related to inhibition of prostaglandin and leukotriene biosynthesis[19].

A study conducted in Denmark revealed that an average intake of 5 g of fresh ginger or 0.5 to 1 g powdered ginger reduced pain, swelling, morning stiffness in patients suffering from arthritis. None had

side effects due to ginger intake. In another study, administration of ginger for at least 3 months in patients with rheumatoid arthritis (n=28), osteoarthritis (n=18) and muscular complaints (n=10) produced ameliorative effect in all with no side effects[20].

Antimicrobial effects

Ginger has strong antibacterial and to some extent antifungal properties. *In vitro* studies have shown that active constituents of ginger inhibit multiplication of colon bacteria. These bacteria ferment undigested carbohydrates causing flatulence. This can be counteracted with ginger. It inhibits the growth of *Escherichia coli, Proteus sp*, Staphylococci, Streptococci and Salmonella[21,22]. The ginger extract has antimicrobial action at levels equivalent to 2000 mg/ml of the spice. Ginger inhibits aspergillus, a fungus known for production of aflatoxin, a carcinogen[23,24]. Fresh ginger juice showed inhibitory action against *A.niger, S.cerevisiae, Mycoderma SPP.* and *L. acidophilus* at 4, 10, 12 and 14% respectively at ambient temperatures[25].

Effects on cardiovascular system

In traditional Chinese medicine, ginger is used to improve the flow of body fluids. It stimulates blood circulation throughout the body by powerful stimulatory effect on the heart muscle and by diluting blood[26]. The improved circulation is believed to increase the cellular metabolic activity, thus contributing to the relief of cramps and tension[27]. A Japanese study showed that active constituents in ginger reduced the blood pressure and decreased cardiac workload[28]. Ginger reduced the formation of proinflammatory prostaglandins and thromboxane thus lowering the clotting ability of the blood[29]. The inhibition of platelet aggregation by ginger is more than the similar effects observed with garlic and onion[30-32]. Ginger can prevent the increase in cholesterol levels following intake of cholesterol-rich diet[33]. Ginger is also known to possess antioxidant properties[34-36].

Use in migraine

Ginger powder (500-600 mg) taken at the onset of migraine aura, followed by 4 hourly intake for 3-4 days, is reported to provide relief from migraine attacks[37].

Safety

The ginger has been listed in "Generally Recognised 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[1].

NIN studies

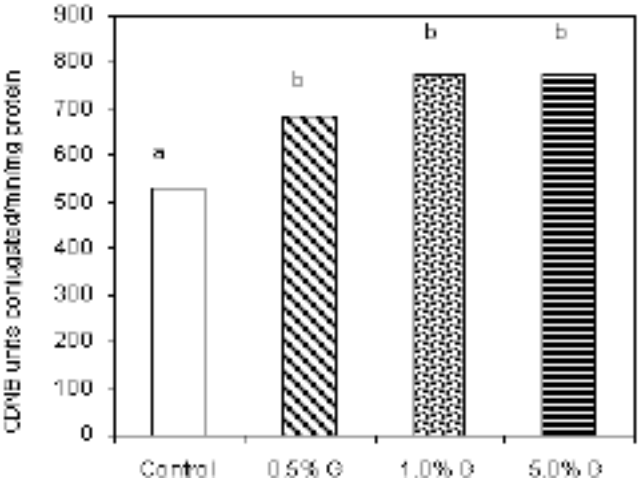
Both the nutritive and the non nutritive components of the diet play a significant role in the inhibition of carcinogenic process. The non-nutritive constituents exert their anticarcinogenic effect by various mechanisms *viz.* (i) by virtue of their antioxidant property; (ii) deactivating the carcinogens; or (iii) enhancing the tissue levels of protective enzymes in the body. Toxic metabolites of harmful drugs and chemicals are detoxified by the body's defense system. Phytochemicals in spices like turmeric, mustard and allium vegetables may act in more than one way to confer their beneficial effect[38].

Studies conducted at the National Institute of Nutrition (NIN), Hyderabad showed that some of the spices/vegetables stimulate, specifically, the levels of glutathione-s-transferases (GST), a group of enzymes which are known as cellular detoxification enzymes. There is a high correlation between the induction of these enzymes and inhibition of carcinogenesis.

Since ginger has the potential to inhibit chronic inflammation and arachidonic acid metabolism coupled with antioxidant property, studies were undertaken to evaluate the stimulation in drug metabolizing enzyme levels in rats, fed ginger through diet.

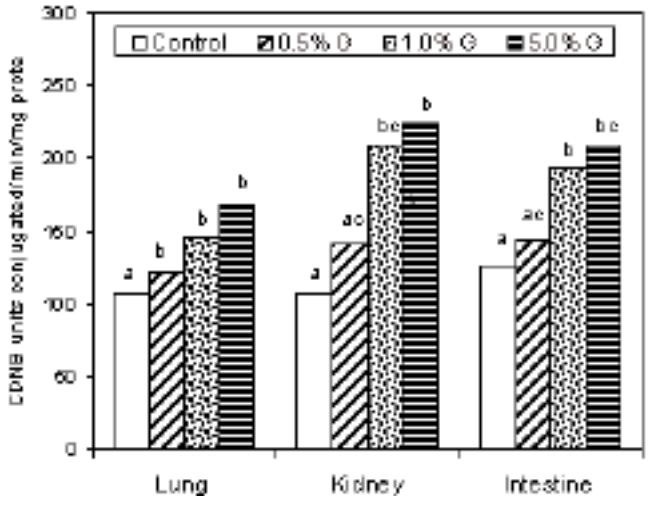
Wistar/NIN rats aged 8-10 weeks were divided into 4 groups of six rats per group. Ginger powder was fed at 0.5, 1 and 5% levels for one month. The fourth group was maintained as control without ginger feeding. The food intake of the animals was recorded every week throughout the study. The body weights of the animals were recorded at the beginning and end of the experiment. After one month of feeding, the animals were sacrificed and liver, kidney, lung and intestine were collected, processed and levels of drug metabolising enzymes measured. At all levels of ginger feeding (0.5, 1 and 5%) stimulation of GST activity was seen in liver and lungs whereas in intestine and kidney, a significant

increase was observed at 1 and 5% level of ginger feeding (Figs.1 & 2).



Values bearing different superscripts are significant (P<0.05)
Duncan's multiple range test
CDNB: 2-Chloro dinitro benzene

Fig.1. Effect of ginger on GST activity in rat hepatic cytosol.



Values bearing different superscripts are significant (P<0.05)
Duncan's multiple range test
CDNB: 2-Chloro dinitro benzene

Fig.2. Effect of ginger on GST activity in rat tissue cytosol

There was some increase (though statisticalliy non significant) in the activity of uridine diphospho–glucuronyl transferase (UDPGT) in liver, lung, kidney and intestine tissues (Fig. 3). There was almost no difference in the levels of arylhydrocarbon hydroxylase (AHH) in treated and control groups of rats showing thereby that ginger feeding does not stimulate

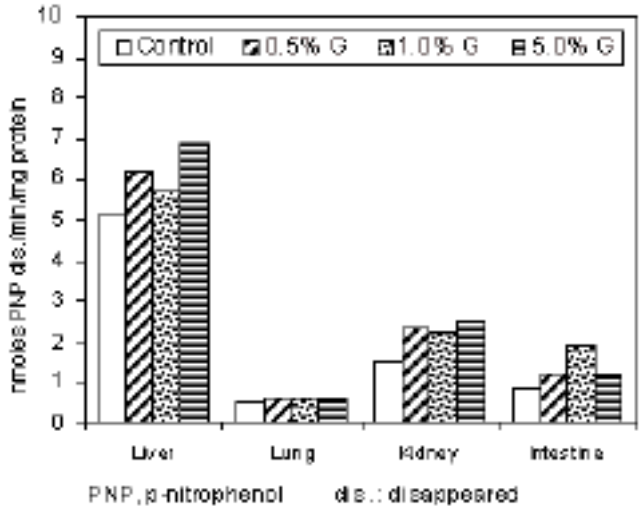


Fig.3. Effect of ginger on UDPGT activity in rat tissue microsomes

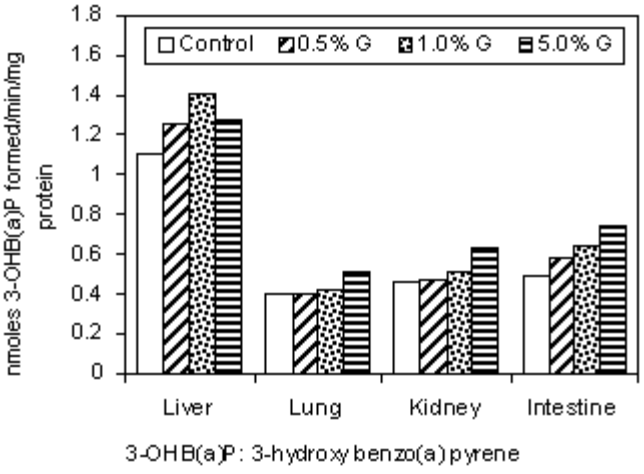


Fig.4. Effect of ginger on AHH activity in rat tissue microsomes

carcinogen metabolism (Fig.4). Significant stimulation in liver quinone reductase (QR) was noted with 1 and 5% ginger feeding compared to control. In lungs,

significant increase was observed in only 5% ginger fed group (Fig. 5).

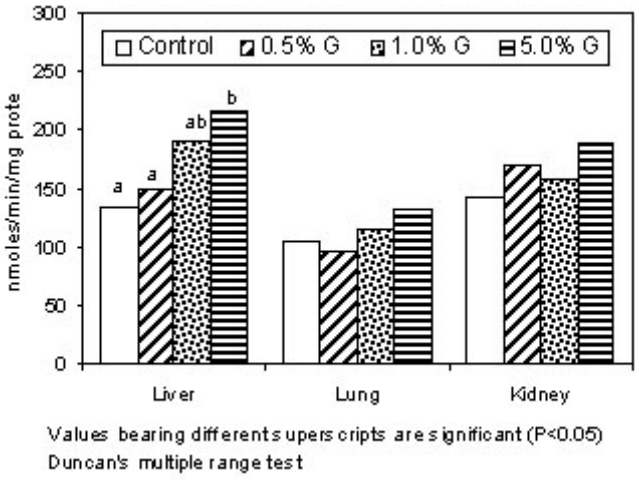


Fig.5. Effect of ginger on quinone reductase activity in rat tissue cytosol.

The stimulation of GST due to ginger feeding in liver and lungs and to some extent in intestine and kidney indicates that ginger feeding can confer protection against the toxic effect of xenobiotics. The GST group of enzymes play a major role in the detoxification pathway and help in the conversion of reactive chemicals to non reactive polar compounds which can be excreted from the body. Since liver is the major site of xenobiotic metabolism and transformation, stimulatory effect of ginger feeding on liver and intestine enzyme levels are significant. Other tissues namely lungs and kidney also play a role in the detoxification and elimination of xenobiotics. The increases in GST levels in all these tissues further support the hypothesis that regular intake of ginger through diet can enhance the activity of phase II detoxification enzymes. Quinone reductase is another important phase II enzyme which participates in the antioxidative process. Stimulation of the quinone reductase activity suggests that 5% ginger feeding can effectively counteract the oxidative damage in tissues of liver and lungs. However, significant differences were not observed in kidney and intestine.

Conclusions

Spices and condiments are an integral part of human diet, particularly in the orient. Besides their use to impart flavour, colour, food preservation and enhance palatability, they have been extensively used in view of their health beneficial effects. Fortunately, even long term consumption of these substances is not known to produce any side effects.

Ginger has been used extensively in folklore medicine to treat common ailments. Now scientific evidences in favour of some of these beneficial properties are emerging which would support their consumption and use to ameliorate certain disorders. Observations from studies on animals suggest that ginger has the ability to stimulate protective enzymes involved in xenobiotic metabolism. Thus, diets rich in some of these phytochemicals can play a major role in providing protection from xenobiotics.

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