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ZANJABEEL (*ZINGIBER OFFICINALE* ROSC.): A HOUSEHOLD RHIZOME WITH IMMENSE THERAPEUTIC POTENTIAL AND ITS UTILIZATION IN UNANI MEDICINE

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ABSTRACT: The tradition of home treatment is found in all cultures throughout the world whether in developed or developing countries. Few herbal drugs commonly appear in the home use as a medicine. One such drug is *Zanjabeel*, it is the rhizome of *Zingiber officinale* Rosc. It is a popular culinary spice that was used as an important medicine by ancient Unani physicians. It is a very important drug of house hold medicine kit used mainly as antifatulent, digestive, anti cough and other indications mentioned in traditional Unani text. Beside its traditional uses its new indications are as an, anti-emetic, hypocholesterolaemic antioxidant, antimicrobial, cardioprotective etc. Unani medicine has provided lot of information regarding this drug. Fresh look on the indications of *Zanjabeel* is needed in the light of current research performed on it and further scope of research can also be explored with the help of traditional knowledge exist in Unani medicine. This review is an attempt in this direction, so that *Zanjabeel* can become more beneficial to ailing people and particularly in contemporary lifestyle diseases which is an emerging concern.

INTRODUCTION: *Zanjabeel* is the rhizome of *Zingiber officinale* Rosc. of Zingiberaceae family.¹ It is described as root like underground stem that is commonly used in food products, it spreads underground, it is native to Oman and it is cultivated widely throughout India and China. Fresh is called Adrak (*Zanjabeele Ratab*) and dried one is known as Sonth (*Zanjabeele Yabis*) (**Fig. 1**), the characteristic odour and taste of Ginger is well known. Used in medicine as a decoction, infusion, powder of dried rhizome, grated fresh rhizome, tincturs.^{2, 3, 4, 5, 6}

They are dug in January February or when buds and upper part of rhizome get dried and this time is best to collect, after removing the buds and roots they are soaked overnight in water after peeling it with the help of especially designed knife then these peeled rhizomes are dried on leaf or mats for 5 to 6 days during which they lose about 80% of their weight, sometime they are treated with lime and some time it is masked with color for this purpose plaster of paris (*Kharya Mitti*) is used.^{1, 3, 5}

In some places its leaves are used as food remedy as Suddab is used. It is always cultivated but some people said that one wild and mountain type is also found which has larger leaves and roots. One variety namely *Sathuwa Sonth*, whitish and non fibrous is considered of good quality. One variety grow in Bengal is familiar with the name *Aam Sonth* because of its unripe mango flavor.³

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Fresh Zanjabeel from China is of best quality.⁷ In India it is cultivated on large scale, in the warmth and moist region, especially in Madras, Cochin, and Travancore and in Bengal and Punjab also which contributes to many of Unani formulations and is widely used in Unani and Ayurvedic System of Medicine.⁸

Historical Background: The most ancient literature points out the economic as well as medicinal importance of ginger in all great civilizations of the Middle East, Asia, and Europe dates back to 5000 BC to 2000 BC.⁹ Ginger is known to Chinese since 400 BC and it is cultivated in India from time immemorial. It was also used by Romans and Greeks as spice who considered it as an Arabian product¹⁰. *Ibne Baitar* described it as '*famous plant having very attractive odour*', it is described in Quran and poet made poetry about it; it has Ratoobat with pungency due to which it increases the semen volume".¹¹ It is being used in medicine and food remedies since very long.

In India it is cultivated since prehistoric era.¹² Its properties are described in ancient Ayurvedic text Charaka. About a Unani formulation Majoone Nankwah about which Hippocrates (460 BC) said that "it increases sexual power very much, if taken 10.5 gm daily for one week only in a year", in this formulation *Zingiber officinale* Rosc. constitutes with chief ingredient ie Nankwah.¹³ *Galen* (1st AD) advocated its use when heat production is needed in any particular organ instead of whole body.¹¹ He also described that it empowers the eyesight when applied locally or taken internally.¹⁴ *Dioscorides* has described properties of this drug claiming it has hot temperament and is similar to Filfil in its power (of action), *Rhazes* shows it is useful for stomach and liver having cold temperament. And *Ibne Masawiya* described its aphrodisiac property.¹¹

Scientific Classification^{15, 16}

Kingdom: Plantae

Subkingdom: Tracheobionata

Division: Magnoliophyta

Class: Liopsida

Sub Class: Zingiberidae

Order: Zingiberales

Family: Zingibraceae

Genus: Zingiber

Species: officinale

Botanical Name: *Zingiber officinale* Rosc.¹

Vernacular names: Arabic: Zanjabeel, Qafeer; Persian: Shangwez; Greek: Hotiyoon, Qasoomad, Quzmuyowun, Qiaras lulus, Qurmuyoos Soomai lamooloon Siryani: Zangabeel; Sanskrit: Adrakam⁸⁶ Mahashudhi, Sharank Veer; Hindi: Adrak, Adi (Fresh), Sonth (Dried); English: Ginger; French: Gingembre; Italian: Zenzero; German: Ingiver; Oriyan: Ada; Urdu: Zanjabeel, Sonth; Bengali: Ada (fresh), Sonth (Dry); Assamese: Ada; Gujrati: Sunth, Sundh; Marathi: Alen (Fresh), Sonth (Dry); Telgu: Allam (fresh) Sonti (dry), Sonthi, Allamu; Kaannada: Sunthi, Hasisunti (fresh), Vana Sunthi (Dry), Shunti; Tamil: Inji (Fresh), Shukku (dry), Sukkh, Chukku, Allam; Malyalum: Inchi (fresh), Chukka (dry)^{17, 11, 1, 12, 18, 4, 19, 3}

Habit and Habitat: It is native of southern Asia from tropical Asia it was introduced in West Indies and it is exported to Europe since very early times. It is being cultivated in England since the beginning of 17th century, it is now abundantly cultivated in Jamaica, Nigeria, China, India, Fiji, Sierra Leone, Australia, Bangladesh, Taiwan, Nigeria and Ceylon (Srilanka) and several east Asiatic countries. It is introduced in Australia mainly for pickling.^{20, 21} It is distributed in tropics of old world, mainly in India, East Asia, and Malaysia.¹⁰ It is grown all over India especially in Kerala, Assam, Himachal Pardesh, Orissa, West Bengal, and Karnataka also, mainly grown in the areas with heavy rainfall. It gives better yield at about 1000-1500 m above the sea level and is cultivated by sowing its rhizomes in the month of June.¹⁹

Botanical Description: Ginger when cultivated grew up to 90 cm in height having aromatic smell with pungent taste; it is herbaceous, rhizomatous perennial plant. Its rhizome is aromatic in nature, thick lobed, pale yellowish with narrow and distichous, sub-sessile, linear-lanceolate, dark green leaves measuring 17cm x 1.8 cm. Flowers are in spikes, greenish yellow with a small dark purple tip, ovary inferior, 3 celled, with numerous ovules;

style passing up behind and between the anther cells and extending beyond them; stigma tufted; its fruits are not seen.^{3, 10, 20} It differs in size, colour, flavor and appearance in different soils. Its shoots or knots give it palmate appearance that's why spice dealers called it *hands* or *races*. Rhizomes (**Fig. 1**) are laterally compressed having short, flatish, ovate, oblique, branches on its upper side, Each of which is having depressed scar on its apex, its pieces are about 15 cm (mostly 3 - 4 cm) in length and 1.5 - 6.5 cm (usually 1-1.5 cm) in width, Externally it is somewhat fibrous, pale yellow within covered with silvery brown peelings. When broken, transverse surface exhibits narrow cortex of area covering about one third of its radius, a well marked endodermis and wide stele showing numerous scattered fibro-vascular bundles and yellow secreting cells.^{1, 12, 21}

Microscopically transverse section of rhizome shows cortex of isodiametric thin walled parenchyma with scattered vascular strands and numerous isodiametric idioblasts, about 40 - 80 m in diameter which contain yellowish to radish brown oleo resin; endodermis slightly thick walled devoid of starch. Inside endodermis a row of parenchyma cells are found which are nearly arranged collaterally in bundles without fibres stele. Each of which is consisting of a few un lignified, reticulate or spiral vessels up to about 70 m in diameter; a group of phloem cells, un lignified, thin walled; septate fibers upto about 30 m in width and 600 m in length with small oblique, slit, like pits, present, numerous scattered idioblasts, similar to those of cortex, and associated with vascular bundles are also present. Idioblasts, present in single or in axial rows adjacent to vessels are about 8 - 20 m in width and 130 m in length with dark redish-brown contents. Cortex and stele having parenchyma with flattened, rectangular, ovate; starch grains, mostly 5 - 15 m, measuring 30 - 60 m in length about 25 m in width and 7 m in thickness, marked by five transverse striations.^{1, 19}

Description of Zanjabeel in Unani: *Zanjabeel* is called *Adrak* or *sonth* in Hindi²² is grown in *Oman* and west Asia.¹⁶ It is root like underground stem brownish to yellowish in colour which is used in many food recipes. It is brown and whitish with some yellowish shade in color, it has aromatic smell and pungent taste similar to that of *Filfil*

siyah. It is of two types fibrous and non fibrous. It leaves burning sensation on tongue when chewed. Its flowers are of *Jamuni* colour which are very few in number. Its leaves are narrow measuring up to one *balisht*. Its potency is restored upto 10 years. Its non fibrous type is described of best quality. While fresh rhizomes grown in China are unparallel in its quality.^{2, 3, 7, 4, 5}



FIG. 1: ZANJABEEL (ZINGIBER OFFICINALE ROSC.) RHIZOME

Part Used: Root (Rhizome)^{4, 5, 3, 2}

Mizaj (Temperament): Fresh: Har 2 Yabis 1,

Dried: Har 3 Yabis 2, Har in last stage of 3rd degree and yabis in 2nd degree, Har in last stage of 3rd degree and Tar in 1st degree.^{2, 23, 4, 11, 22, 3}

Afa'al (Pharmacological action mentioned in Unani Medicine): *Muqawwie Meda* (Stomachic), *mufatteh sudad jigar* (Remove obstruction of Liver), *hazim* (digestive), *Mushtahi* (appetizer), *muqawwie meda* (stomachic), *muqawwie jigar* (liver tonic), *kasir riyah / muhallile riyah* (carminative), *munaqqiye balgham*, *mulaiyine shikam* (laxative), *munaffise balgham* (expectorant), *muqawwiye bah / muhiyyije bah* (Aphrodisiac), *Jali*, *muhallile fuzlate balghami*, *muqawwiye hafiza* (cognitive enhancer), *tiryaaq* (antidote), *habise ishal* (Anti diarrhoeal), *mukhrije balgham wa sauda*, *mudirre baol* (diuretic), *muhallile aoram* (anti-inflammatory).^{22, 23, 11, 3, 1, 7, 16}

Uses as per Unani literature: Zanjabeel is used in the formulations intended to treat *Sue hazm* (Indigestion), *Zofe Jigar* (Liver debility), *amraze barda* (balghami) (Phlegmatic disorders), *Dofi bah* (Sexual debility), *Nisyan* (Oblivion), *suzak* (Gonorrhoea), chronic fevers, in pregnancy, in balghami wa saudawi amraz, *suaal* (cough), in *sailanur rahem* and *dardi pusht* (Leucorrhoea and backache), *Suda* (headache), *zeequnnafas* (asthma), *irqunnasa* (sciatica), *Wajaul mafasil* (arthritis), *Bawaseer* (haemorrhoids), *Istisqa* (ascites), *Gathiya* (rheumatism), *Ganda duhni* (bad breath), *Khuruje miqad* (rectal prolapse).^{2, 3, 5, 1, 23, 22, 11}

Dose (Miqdare khorak): 1 to 1 ½ gm, can be given up to 7 gm.^{2, 1, 3}

Muzir (Adverse effect): *Amraze halaq* (Diseases of throats) and person having hot temperament.^{2, 3, 23}

Reported adverse effect: Badreldin H. Ali *et al.*, in their review described that patented ginger preparation 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. Conversely, some adverse effects of ginger have been reported in pregnant rats. No maternal toxicity was observed, but embryonic loss in the treatment groups was double that of the controls. In one clinical trial that involved 12 healthy volunteers who received ginger orally at a dose of 400 mg of ginger (3 times per day for two week), one subject in the study reported mild diarrhea during the first 2 days of ginger pretreatment. Ginger may cause heartburn, and in doses higher than 6 gm may act as a gastric irritant. Inhalation of dust from ginger may produce IGE-mediated allergy.²⁴

Musleh (Corrective): *Roghane Badam* and *Shahed* (Honey), *Qurse Kafoor*, Juice of *Behi* fruit.^{2, 3;}

Badal (Substitute): *Dar filfil*, *Filfil Safed*, *Filfil Siyah*, *Rasan*, *Aqarqarha*.^{2, 3, 23, 11}

Murakkabat (Compound formulation): *Safoofe Kharkhasak*, *Habbe Hindi Zeeqi*, *Habbe Kabid naushadri*, *Jawarishe Kamooni*, *Jawarishe zanjabeel*, *Laboobe Kabeer*, *Laboobe Sagheer*, *Majoone Supari pak*, *Majoone Jograj Gugal*, *Jawarish Zarooni ambari ba Nushka Kalan*.^{13, 1}

Uses according to ethanobotanical and other literature: It is used in atonic dyspepsia due to its stimulating and aromatic and carminative properties. It is also used in griping, adjunct to purgative, chewed in the condition of relaxed uvula and tonsillitis, being a rubefacient it is frequently used in toothache and headache, used in flatulent colic.^{25, 26, 27} It is used in number of ailments like Alzheimers disease, anorexia, anxiety, allergy, aging, alcoholism, cholera,²⁸ irritable bowel syndrome, diarrhoea, colds and influenza, Migrain, cluster headache. In ayurveda it is used in dyspepsia, loss of appetite, tympanitis, anemia, rheumatism, cough, constipation, colic, edema, throat infectin and dyspepsia.¹⁵ *Trikatu* comprises of ginger along with black pepper and long pepper is used for cleaning tongue and throat and to increase appetite, ginger is taken with rock salt before meal.

In the condition of Biliousness and delirium ginger with cow milk is used after boiling with addition of sugar at bed time. Its juice with sugar-candy is used in diabetes type I and type II. In chronic rheumatism (infusion 1 in 24) gives good result. Juice in gradually increasing dose is useful in ascites, early cases of cirrhosis of liver and dropsy of lower limb.⁸ Having antihistaminic property it is used in urticaria.¹⁰ Its juice possesses potent antiviral, antibacterial activity and antifungal effect.²⁹ Alcoholic extract of dried ginger is found to be stimulant for respiratory center in cat and also stimulates heart.¹⁰

Chemical constituents: Chemical constituent of *Zingiber officinalis* varies according to agro climatic condition green/fresh ginger gives water 80.9 %, protein, fat, fibre, carbohydrate (starch, pentosans), minerals (Ca, P, Fe), trace of Iodine and fluorine Vitamin (thiamine, riboflavin, niacin, Vitamin C, carotene), fructose, sucrose, raffinose in trace.³⁰

Essential oils: car-3-ene, α -terpinene, α -terpineol, neurol, 1, 8-cineole, zingiberene, neral, geranial, geraniol and geranyl acetate were identified in essential oil obtained from rhizomes. Heptane, octane, isovaleraldehyde, nonanol, ethyl pinene, camphene, β -pinene, sabinene, myrecene, limonene, β -phellandrene and 1,8-cineole in essential oil were detected by GLC and by GC-MS

presence of gingediol, methylgingediol and their diacetates were confirmed.³¹

Sesquiterpenes sequithujene, cis-sequisabinene hydrate and zingiberenol were isolated and their structures were determined.³² Oil obtained from rhizome by steam distillation contains sesquiterpene hydrocarbons, sesquiterpene alcohols, monoterpenoids and associated compounds; Zingiberol (C₁₅H₂₆O) which is mixture of β -eudesmol stereoisomers is also present in oil. Oils extracted from ginger of Jamaica, Nigeria, Sierra Leone, China, India and Australia are same in quality but differs little in qualitative estimation eg. Zingiberene constitutes 20-30% and β -bisabolene 5-12% in all ginger's oils, while Australian oils are rich in citral (geranial and neral). Oleoresin (acetone extractives) which increases with maturity in Indian ginger contains pungent principles which are oxymethyl phenols and non pungent substances and essential oils. Starch, volatile oils and resin are the principal constituents of ginger East India ginger has 8% of oleoresin and Jamaica ginger yields only 5%. It may be extracted in alcohol, ether, or chloroform, benzene.²⁶

Free amino acids: Glutamic acid, aspartic acid, serine, glycine, threonine, alanine, glutamine, arginine, γ -aminobutyric acid, valine, phenylalanine are free amino acids present in rhizome and Asparagine and pipercolic acid were isolated from aqueous extract of ginger.^{26, 32}

Oleoresin: Preparation of oleoresin contains gingerol, shogaol and zingerone. In which gingerol is mainly present in freshly prepared oleoresin while oleoresin stored for long time contain shogaol, it is suggested that shogaol and zingerone do not occur in fresh rhizome naturally but they are synthesized by chemical changes during preparation and storage of the oleoresin, so oleoresin of poor quality and off flavored contain high level of shogaol and zingerone.¹⁰

Phenols: It has phenols in trace, esters of acetic and caprylic acids.^{119, 10}

Reported Pharmacological activity:

Aphrodisiac/Androgenic and Spermatogenic Activity: In study conducted to evaluate the effect of alcoholic extract of Ginger on the testes in rats in

busulfan induced infertility in rat model showed that *Zingiber officinale* increased the semen volume of seminiferous tubules in test group treated with 100mg/kg of the extract of ginger compared to control group. Sperm count and level of testosterone were also increased in test group treated with alcoholic extract of Ginger in dose of 100 mg/kg and 150 mg/kg body weight of rat, in comparison to control group.³¹ Study conducted on 30 male Sprague Dawley rats allotted in 3 groups 10 in each, for evaluation of androgenic activity of Ginger Showed Significant increase in testicular weight and body weight gain, serum testosterone in test group treated with 200mg/kg of aqueous extract of ginger for 28 and 56 days as compared to control group without any toxic effect on spermatogenesis in the testes.³³

A study reported in which aqueous extract of *Zingiber officinale* was administered orally in the Broiler breeder male in dose of 5 % and 10 % has demonstrated that aqueous extract of Ginger have an anti oxidant and androgenic activity and have good effects on spermatogenesis and sperm parameters as well as increase in ejaculatory volume, sperm concentration, count, movement, decrease in motility and abnormality. There was also significant increase in semen plasma cholesterol, glucose, and significant decrease in protein. Increase in testosterone, LH, FSH hormone level (P<0.05%).³⁴

In an experiment aqueous extract of *Zingiber officinale* was given orally to 2 groups of rats in dose of 500 mg / kg b.w. and 1000 mg / kg b.w. for 14 and 28 days then test groups were investigated for effect of Ginger on reproductive functions in the male rats in comparison to control group. It was revealed by the study that there was significant increase (P<0.05%) in the weight of the testis and epididymis, and dose and duration dependent increase in sperm count and motility (P<0.05%). There was significant increase (P<0.05%) in serum testosterone level noted.³⁵

In a study evaluating the effect of Ginger on spermatogenic and sperm parameters in Rats, it is found that in a dose of 100mg /kg/rat of Ginger rhizome powder administered for 20 days Made significant increase in Testosterone, percentage of sperm viability and motility in test group in

comperasion to control one. It was also reported that L.H., F.S.H. hormones, sperm count, morphology and weight of testes were same in control and experimental group.³⁶ Hosseini J *et al.*, investigate the effects of *Zingiber officinale* on sperm DNA fragmentation (SDF) in infertile men. 3-month oral treatment 250 mg capsule of ginger powder twice a day and a placebo in other group demonstrated that Zingiber in a controlled study of efficacy was effective in decreasing SDF.³⁷

Cytoprotective and Anti Ulcer Activity: Highly significant cytoprotective activity against Cytodestruction produced by 80% ethanol, 0.6M HCl, 0.2M NaOH and 25% NaCl in albino rats is reported when 96% ethanolic extract (Obtained by Soxhlet hot extraction method) of *Zingiber officinale* Rosc was administered orally in dose of 500 mg/kg body weight after passing the starvation period of 36 hrs. Beside this extract of Ginger was reported to have protective effect against gastric ulcers induced by Non steroidal anti inflammatory drugs (NSAIDs) and hypothythermic restraint stress.³⁸ Siddaraju *et al.*, studied ginger-free phenolic (GRFP) and ginger hydrolysed phenolic (GRHP) fractions of ginger (*Zingiber officinale*) as potent inhibitors of proton potassium ATPase activity (PPA) and *H. pylori* growth. GRFP (Constituted by syringic 38%, gallic 18% and cinnamic 14% acids as major phenolic acids) and GRHP (Constituted by cinnamic 48%, p-coumaric 34% and caffeic 6% acids as major phenolic acids) inhibited PPA at an IC 50 of 2.9 ± 0.18 and 1.5 ± 0.12 µg/mL, exhibiting six- to eight-fold better potency over lansoprazole. It exhibited free radical scavenging (IC50 1.7 ± 0.07 and 2.5 ± 0.16), inhibition of lipid peroxidation (IC 50 3.6 ± 0.21 and 5.2 ± 0.46), DNA protection (80% at 4 µg) and reducing power abilities (80 – 338 U/g) indicating strong antioxidative properties.

GRFP and GRHP may thus be potential low-cost multistep blockers against ulcer.³⁹ Nostro *et al.*, studied Propolis extract and *Zingiber officinale* extract to evaluate their effect when combined with clarithromycin on clinical *H. pylori* isolates (n = 25), characterized in respect to both clarithromycin susceptibility and the presence of the *cagA* gene. The results of combination exhibited improved inhibition of *H. pylori* with synergistic or additive

activity. Combination was significantly independent of the microbial clarithromycin susceptibility status and has the potential to help control *H. pylori* - associated gastroduodenal disease.⁴⁰ The rhizomes of *Zingiber officinale* is shown to be effective in preventing gastric ulcers induced by NSAIDs (indomethacin, and aspirin), reserpine, ethanol, stress (hypothermic and swimming), acetic acid and Helicobacter pylori-induced gastric ulcerations in laboratory animals and possess anti-emetic effects against different emetogenic stimuli in preclinical and clinical studies. Gastroprotective effects of ginger with diverse drug / factors highlight scope of future research and utility of ginger in human as a gastroprotective.⁴¹

Antiemetic activity: Powdered ginger root was compared with metoclopramide and placebo in a prospective, randomised, double-blind trial for the incidence of postoperative nausea and vomiting. Incidence of nausea and vomiting was similar in patients given metoclopramide and ginger, *Zingiber officinale* showed effective and promising prophylactic antiemetic, which may be especially useful for day case surgery.⁴² The benzene fraction (BF) of a petroleum ether extract of dried rhizomes of ginger, screened for anxiolytic and antiemetic activity. BF blocked lithium sulphate-induced conditioned place aversion indicating antiemetic activity. Findings of the complete study suggest that the fraction (BF) possesses anticonvulsant, anxiolytic and antiemetic activity.⁴³ Ginger can be a effective adjuvant in controlling nausea during cancer chemotherapy. In Patients receiving chemotherapy addition of ginger to conventional antiemetic medication causes further reduction in the severity of postchemotherapy nausea.⁴⁴

Antimicrobial activity: Antimicrobial activity of ethanolic extract of ginger in concentration of 20 mg/ml was reported in study performed against *Pseudomonas aeruginosa* and *Escherichia coli*. Although the extract had negligible inhibitory activity against *E.coli* most likely due to non liberation of active constituent of raw extract⁴⁵. Study of antifungal and anti-biofilm properties of ginger extract against *Candida* species indicate that ginger extract has good antifungal and antibiofilm formation by fungi against *C. albicans* and *C. Krusei*.⁴⁶

Zingiber officinale extract has displayed significant antibacterial activity against *S. mutans* and *S. sanguinis* cariogenic microorganisms.⁴⁷ Activity of extracts of *Zingiber officinale* (ginger) and *Curcuma longa* (curcumin) against *Giardia lamblia* *in vitro* and *in vivo* was studied. Faecal cyst and intestinal trophozoite counts reduction was seen and *in vivo* ginger was found more effective.⁴⁸

Antioxidant Activity: Stoilova I *et al.*, studied antioxidant effect and the total phenols of ginger, total phenols of the alcohol extract were found to be 870.1 mg/g dry extract. Ginger extract inhibited the hydroxyl radicals 79.6% at 37 °C and 74.8% at 80 °C, which showed a higher antioxidant activity than quercetin. The IC₅₀ concentration for inhibiting OH^{*} at 37 °C was slower than that at 80 °C -1.90 and 2.78 µg / ml respectively. The ginger extract chelated Fe³⁺ in the solution.⁴⁹ Significant antioxidant activity of volatile and non volatile compounds of fresh and dried ginger (N-hexane and methanolic extract) was noted in an experiment performed on rats by using DPPH and ferric reducing antioxidant power (FRAP) and it is found that methanolic extract of ginger especially of fresh ginger possesses appreciable amount of antioxidant compound within it which showed good inhibitory property against free radicals.⁵⁰ In a model of oxidative damage to pancreatic β cells, n-hexane extract exerts antiradical capacity. Protective potential of *Zingiber officinale* in a model of cytotoxic conditions imposed by diabetes in β cells was assessed in this study.⁵¹

Anti Diabetic: Sanjay *et al.*, have studied the effect of the juice of *Z. officinale* (4 mL kg⁻¹, p.o. daily) for 6 weeks on streptozotocin (STZ)-induced type I diabetic rats with particular reference to the involvement of serotonin (5-hydroxytryptamine; 5-HT) receptors in glycaemic control. *Z. officinale* produced a significant increase in insulin levels and a decrease in fasting glucose levels in diabetic rats. In an oral glucose tolerance test, treatment was found to decrease significantly the area under the curve of glucose and to increase the area under the curve of insulin in STZ-diabetic rats. Treatment also caused a decrease in serum cholesterol, serum triglyceride and blood pressure in diabetic rats. Data suggest a potential antidiabetic activity of the juice of *Z.*

officinale in type I diabetic rats, possibly involving 5-HT receptors.⁵² Ethyl acetate extract of ginger (EAG) was evaluated for its antioxidant activity in terms of DPPH radical scavenging potential with an IC₅₀ value of 4.59 µg/ml. Antidiabetic activity of EAG was evaluated by estimating antiglycation potential (IC₅₀ 290.84 µg/ml). Efficacy of extract to enhance glucose uptake in cell lines were checked in L6 mouse myoblast and myotubes. EAG was effective at 5 µg/ml concentration in both cases. Antibody based studies in treated cells revealed the effect of EAG in expressing Glut 4 in cell surface membrane compared to control. Activity is initiated by antioxidant, antiglycation and potential to express or transport Glut4 receptors from internal vesicles.⁵³

Polyphenol extracts of *Zingiber officinale* rhizome investigated for antidiabetic potential in pancreatic and renal tissues of diabetic rats at a dose of 500 mg/kg body weight. Revisited in histological examination of pancreas and kidney restoration of the structural derangements caused by streptozotocin in the polyphenol extracts treated diabetic rats compared to the control groups. Study suggests that it can ameliorate diabetes-induced pancreatic and renal derangements.⁵⁴ Akash MS *et al.*, in a review explain that *Zingiber officinale* used as a diet-based therapy showed that mechanistic rationale for antidiabetic effects of ginger includes the inhibition of several transcriptional pathways, lipid peroxidation, carbohydrate-metabolizing enzymes and HMG-CoA reductase and the activation of antioxidant enzyme capacity and low-density lipoprotein receptors (by targeting these pathways), It shows its antidiabetic therapeutic effects by increasing insulin sensitivity and synthesis, protecting pancreatic islets, reducing fat accumulation, decreasing oxidative stress, and also increasing glucose uptake by the tissues.

It also demonstrates protective effects against several complications related to diabetes like nephropathy and cataract probably by acting as an antioxidant and antiglycating agent.⁵⁵ Insulin resistance generally precedes the development of type 2 diabetes, effect of ethanol extract of ginger on insulin resistance in a high-fat and high-carbohydrate (HFHC) diet fed rat model of metabolic syndrome was studied.

Results suggest protection from HFHC diet-induced insulin resistance, this protection may be associated with the increased capacity of energy metabolism by its major active component (S)-[6]-gingerol.⁵⁶

Cardioprotective effect: In isoproterenol (ISO) induced myocardial necrosis in rats ethanolic extract of *Zingiber officinale* in dose of 200mg/kg pretreatment for 20 days in test group showed significant increase in levels of endogenous myocardial antioxidants as well as increase in myocardial lipid peroxides and decrease in levels of serum marker enzymes and exhibited cardio protective effect.⁵⁷ Methanol extract of rhizome of *Zingiber officinale* caused a dose-dependent positive inotropic effect on the guinea pig isolated atria. Fractionation of the methanol extract of ginger was performed, being monitored by the positive inotropic action, activity appears to be in the decreasing order: [8]- ginger 01 > [10]-gingerol > [6]-gingerol. cardiostimulant principles of ginger were identified as [6]-, [a]-, and (10)-gingerol.⁵⁸ Ghayur *et.al.*, and Suekawa *et al.*, studied hypotensive activity in hypertensive animals, ginger has a generally dose-dependent hypotensive effect, although temporary atrioventricular dissociation was documented shortly afterwards. Ginger caused vasodilation in rats and rabbits, following induced vasoconstriction, and exhibited calcium channel-blocking activity similar to verapamil.

Positive inotropic effect in guinea pig atrial muscle) and it promote the positive inotropic effect of adrenaline by stimulating its release from the adrenals was demonstrated by Kobayshi M *et al.*, and Iwasaki Y *et al.*,⁵⁹ Angiotensin-1-converting enzyme (ACE) inhibitors widely used in the treatment of cardiovascular diseases, the inhibition of ACE activity of two varieties of *Z. officinale* was investigated in a high cholesterol (2%) diet fed rats for 3 days to increase in the ACE activity.

Both ginger varieties exhibited anti-hypercholesterolemic properties in a high cholesterol diet fed to rats. Rats fed with 4% red ginger had the greatest reduction as compared with control diet. This activity of may be attributed to its ACE inhibitory activity. However, white ginger inhibited ACE better. Both gingers could serve as a

nutraceuticals in the management of hypertension and other cardiovascular diseases.⁶⁰

Antiplatelet and anti-inflammatory activity: Aqueous extract of Ginger (having pungent principles *eg.* [8]-Paradol, [8]-gongerol and [8]-Shogaol) were found to be potent platelet aggregation inhibitors induced by arachidonic acid, ADP, epinephrine and collagen, probably via inhibition of platelet cyclooxygenase-1/thromboxane synthase activity and may be via inhibition of induced platelet serotonin release. All {[8]-Paradol, [8]-gongerol and [8]-Shogaol} were found to be more potent than aspirin in the COX-I inhibitor assay.⁶¹ Aqueous extract of ginger (*Zingiber officinale*) was studied on serum cholesterol, triglyceride levels as well as platelet thromboxane-B2 and prostaglandin-E2 production for a period of 4 weeks, either orally or intraperitoneally (IP) to rats. Ginger administered orally caused significant changes in the serum PGE2 at this dose. High doses of ginger (500 mg/kg) were significantly effective in lowering serum PGE2 when given either orally or IP.

However, TXB2 levels were significantly lower in rats given 500 mg/kg ginger orally but not IP. A significant reduction in serum cholesterol was observed when a higher dose of ginger (500 mg/kg) was administered. At a low dose of ginger (50 mg/kg), a significant reduction in the serum cholesterol was observed only when ginger was administered IP. No significant changes in serum triglyceride levels were observed upon administration of either the low or high dose of ginger.⁶² Ginger appeared more effective for reducing pain severity than placebo, no significant difference was found between ginger and mefenamic acid (an NSAID), existing data suggest that oral ginger could be an effective treatment for menstrual pain in dysmenorrhea. Further study is needed in this regard with high methodological quality.⁶³

Ginger may reasonably reduce muscle pain due to eccentric resistance exercise and prolonged running; ginger may accelerate recovery of maximal strength after eccentric resistance exercise and reduce the inflammatory response. Further research is needed to evaluate its efficacy as an analgesic for a wide range of athletic activities.⁶⁴

Studies suggest that ginger could be used as an antithrombotic and anti-inflammatory agent.

Anti-Hyperlipidaemic activity: Ethanolic extract of *Zingiber officinale* (200 mg/kg) in streptozotocin (STZ)-induced diabetic rats fed orally for 20 days produced significant antihyperglycaemic effect, extract treatment also lowered serum total cholesterol, triglycerides and increased the HDL - cholesterol levels when compared with pathogenic diabetic rats ($P < 0.01$). *Zingiber officinale* extract treatment lowered the liver and pancreas thiobarbituric acid reactive substances (TBARS) values ($P < 0.01$) as compared to pathogenic diabetic rats.

The results of test drug were comparable to gliclazide (25 mg/kg, orally), a standard antihyperglycaemic agent. Extract can protect the tissues from lipid peroxidation and also exhibit significant lipid lowering activity in diabetic rats.⁶⁵ 50% EtOH extract of *Zingiber officinale* when studied in hyperlipidaemic rabbits showed a reduction in total cholesterol and serum LDL-cholesterol. A reduction in HDL ratio was also restored. An atherogenic index of 4.7 was brought down to 1.2. Tissue lipid profiles of liver, heart and aorta showed similar changes to those noticed in serum lipids. Zingiber extract feeding increased the faecal excretion of cholesterol thus suggesting a modulation of absorption⁶⁶. El Rokh ES *et al.*, Studied antihypercholesterolaemic effect of aqueous ginger (*Zingiber officinale*) infusion in hypercholesterolaemic rat models. Lipid profile measured at zero time and 2 and 4 weeks after ginger and atorvastatin treatment, revealed that the hypercholesterolaemic rats treated with aqueous ginger infusion in the three doses used after 2 and 4 weeks of treatment induce significant decrease in lipid profile and improved the risk ratio.⁶⁷

Anti Cancer activity: Antioxidant and anticancer activities of two Bangladeshi ginger varieties (Fulbaria and Syedpuri) at young age grown under ambient (400 $\mu\text{mol/mol}$) and elevated (800 $\mu\text{mol/mol}$) CO_2 concentrations against two human breast cancer cell lines (MCF-7 and MDA-MB-231) was studied. Results showed that enriched ginger extract (rhizomes) exhibited the highest anticancer activity on MCF-7 cancer cells with IC 50 values of 34.8 and 25.7 $\mu\text{g/ml}$ for Fulbaria and

Syedpuri respectively. IC₅₀ values for MDA-MB-231 exhibition were 32.53 and 30.20 $\mu\text{g/ml}$ for rhizomes extract of Fulbaria and Syedpuri accordingly. Both varieties possess antioxidant and anticancer properties and may have potential in the treatment and prevention of cancer.⁶⁸

Thermogenic activity: Pungent principles of Ginger stimulate thermoregulatory receptors, Zingeron induced catecholamine secretion from the adrenal medulla *in vivo* and thus induced warming action.⁶⁹

Hepatoprotective activity/ Anti liver fibrosis: *Zingiber officinale* rhizomes successive extracts (petroleum ether, chloroform and ethanol) were examined against liver fibrosis induced by carbon tetrachloride in rats. Antioxidant parameters; glutathione (GSH), total superoxide dismutase (SOD) and malondialdehyde (MDA) was measured. Liver marker enzymes were estimated and liver histopathological analysis and collagen content were evaluated. Ethanol extract displayed better result in the treatment of liver fibrosis induced by CCl_4 .⁷⁰ Efficacy of ginger was studied as pretreatment in alleviating acetaminophen (APAP) induced acute hepatotoxicity in rats. Ginger or Vitamin E treatment prior to APAP showed significant hepatoprotective effect by lowering the hepatic marker enzymes and total bilirubin. Histopathological examination of APAP treated rats showed alterations in normal hepatic histoarchitecture, with necrosis and vacuolization of cells.

These alterations were substantially decreased by ginger or Vitamin E. Results demonstrated that ginger can prevent hepatic injuries, alleviating oxidative stress in a manner comparable to that of Vitamin E.⁷¹ Hepatoprotective effects of polyphenols from *Zingiber officinale* was studied on streptozotocin-induced diabetic rats by assessing liver antioxidant enzymes, carbohydrate-metabolizing enzymes and liver function indices. There was significant increase in the antioxidant enzymes activities in the animals treated with polyphenols, polyphenols normalised the activities of some carbohydrate metabolic enzymes (hexokinase and phosphor-fructokinase) and the activities of liver function enzymes was significantly reduced.

Study suggest that polyphenol could ameliorate liver disorders caused by diabetes mellitus.⁷²

Cognitive enhancer: Antioxidants plants have gained a great deal of attention due to the role of oxidative stress-induced cognitive impairment. Study aimed to determine the effect of *Zingiber officinale* extract, on the cognitive function of middle-aged, healthy women. 60 participants receive a placebo or standardized plant extract at doses of 400 and 800 mg once daily randomly for 2 months. Participant were evaluated for working memory and cognitive function using computerized battery tests and the auditory oddball paradigm of event-related potentials at three different time periods: before receiving the intervention, one month, and two months. Ginger-treated groups had significantly decreased P300 latencies, increased N100 and P300 amplitudes, and exhibited enhanced working memory.

It is a potential cognitive enhancer for middle-aged women.⁷³ Study done by Wattanathorn J *et al.*, suggest that *Z. officinale* possessed the protective effect against focal cerebral ischemia induced by the occlusion of right middle cerebral artery. Cognitive enhancing effect and neuroprotective effect appeared to show almost the same magnitude as the positive control groups used in this study. The cognitive enhancing and neuroprotective effect occurred partly via the antioxidant activity of the extract. Study shows beneficial effect of ginger rhizome to protect against focal cerebral ischemia.⁷⁴

Activity of Gingerols: In laboratory animals its constituent gingerols increase the motility of the gastrointestinal tract and have analgesic, sedative, antipyretic and antibacterial properties.⁷⁵ Nurtjahja-Tjendraputra *et al.*, 2003 reported more potent anti-platelet and cyclo-oxygenase-1 (COX-1) inhibitors activity than aspirin in Gingerols derivatives, especially [8]-paradol. Tripathi *et al.*, tested that [6]-gingerol acts as an anti-inflammatory compound that may be useful to treat inflammation without interfering with the antigen presenting function of macrophages²⁴.

Nephroprotective activity: Renoprotective potential of 6-gingerol on cisplatin-induced oxidative stress and renal dysfunction was studied

and it revealed that 6-Gingerol treatment significantly and dose-dependently restored renal functions, reduced lipid peroxidation and enhanced the levels of reduced glutathione and activities of superoxide dismutase and catalase and it has a potential to be used as therapeutic adjuvant in cisplatin nephrotoxicity.⁷⁶ Study of the renal protective effects of ginger (*Zingiber officinale*) extract in lead induced toxicity rats indicate that its extract alleviated lead toxic effects by enhancing the levels of glutathione, glutathione peroxidase, glutathione-s-transferase and catalase.⁷⁷

Anthelmintic activity: Gingerenone A, [6]-dehydrogingerdione, [4]-shogaol, 5-hydroxy-[6]-gingerol, [6]-shogaol, [6]-gingerol, [10]-shogaol, [10]-gingerol, hexahydrocurcumin, 3*R*,5*S*-[6]-gingerdiol and 3*S*,5*S*-[6]-gingerdiol constituent from ginger, for studied against the parasite *Hymenolepis nana*. Findings of the study suggest that these constituents of ginger can be used as cestocidal agents against *H. nana*.⁷⁸ Fasciolosis is of considerable public health importance worldwide. The *in vitro* ovicidal effect of the methanolic extract of *Z. officinale* was found to be satisfactory in the study. It is a preliminary report on ovicidal effect of *Z. officinale* against *F. hepatica* eggs.⁷⁹

Anti-addictive activity: Influences of ginger on morphine-induced addictive behaviors was studied in Wister rats. Ginger extract indicated potential anti-addictive property against chronic usage of morphine.⁸⁰

Disease modifying effect in Alzheimer's disease (AD): The antioxidant activity, anti-amyloidogenic potential, cholinesterase inhibition and neuro protective properties of methanolic extract of dry ginger (GE) have been evaluated. Findings suggest that methanolic GE influences multiple therapeutic molecular targets of AD and can be considered as an effective nontoxic nutraceutical supplement for AD.⁸¹

Anti-cough activity: Water extracted poly saccharides (WEP) containing fraction from rhizome significantly inhibited the number of citric acid-induced cough efforts in guinea pigs. But it does not alter the specific airway smooth muscle reactivity significantly. Traditional aqueous

extraction method provides molecular entities, which induces antitussive activity without addiction.⁸²

Anti-allergic: Anti-allergic effects of ginger and 6-gingerol were investigated, using a mouse allergy model and primary/cell line culture system. Results demonstrate that 6-gingerol suppresses cytokine production for T cell activation and proliferation, thereby not causing B cell and mast cell activation and resulting in prevention or alleviation of allergic rhinitis symptoms.⁸³

Bioavailability improving activity: In view of prevalent deficiency of iron and zinc in populations dependent on plant foods, there is a need to improve the bioavailability of the same. Wistar rats were fed piperine, capsaicin and ginger containing diets for 8 weeks to check their influence on intestinal absorption of iron, zinc and calcium. Higher uptake of iron, zinc and calcium by the intestinal segments from spice-fed animals was observed. Consumption of pungent spices including ginger can reduce deficiency of these trace elements.⁸⁴

CONCLUSION: Present review revealed therapeutic importance of ginger rhizome as evident by the recent research performed on it. Several Unani formulations containing dry ginger is indicated in liver, kidney, stomach, joint diseases and as an aphrodisiac etc.^{1, 13} Recent researches also validated the indications of *Zingiber officinale* rhizome in Unani Medicine such as in liver debility, oblivion, sciatica, arthritis, rheumatism, as an liver tonic, anti-inflammatory, aphrodisiac etc. Beside traditional therapeutic utilization in Unani medicine its new indications such as anti-emetic, hypocholesterolaemic, antiplatelet, antioxidant, antimicrobial activity etc, make it more important easily available household drug. Further scope of research can also be explored with the help of traditional knowledge exist in Unani and other traditional medicine.

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