Chapter- 1

Bulbus allii sativi

Definition
Bulbus Allii Sativi consists of the fresh or dried bulbs of Allium sativum L. (Liliaceae)

Synonyms
Porvium sativum Rehb.

Selected vernacular names
It is most commonly known as "garlic". Ail, ail commun, ajo, akashneem, allium, alubosa elewe, ayo-ishi, ayu, banlasun, camphor of the poor, dai toan, dasuan, dawang, dra thiam, foom, Gartenlauch, horn khaao, horn kia, horn thiam, hua thiam, kesumphin, kitunguu-sumu, Knoblauch, kra thiam, krathiam, krathiam cheen, krathiam khaao, I'ail, lahsun, lai, lashun, lasan, lasun, lasuna, Lauch, lay, layi, lehsun, lesun, lobha, majo; naharu, nectar orthe gods, ninniku, pa-se-waa, poor man's treacle, rason, rasonam, rasun, rustic treacles, seer, skordo, sluon, stinking rose, sudulunu, ta-suam, ta-suan, tafanuwa, tellagada, tellagaddalu, thiam, toi thum, turn, umbi bawang putih, vallaip- pundu, velluli, vellulli

Description
A perennial, erect bulbous herb, 30-60 cm tall, strong smelling when crushed. The underground portion consists of a compound bulb with numerous fibrous rootlets; the bulb gives rise abovc ground to a number of narrow, keeled, grass- like leaves. The leaf blade is linear, flat, solid, 1.0-2.5cm wide, 30-60 cm long, and has an acute apex. Leaf sheaths form a pseudostem. Inflorescences are umbellate; scape smooth, round, solid, and coiled at first, subtended by membraneous, long-beaked spathe, splitting on one side and remaining attached to umbel. Small bulbils are produced in inflorescences; flowers are

variable in number and sometimes absent, seldom open and may wither in bud. Flowers are on slender pedicels; consisting of perianth of 6 segments, about 4-6mm long, pinkish; stamens 6, anthers exerted; ovary superior, 3-locular. Fruit is a small loculicidal capsule..Seeds are seldom if ever produced

Plant material of interest: fresh or dried bulbs

General appearance
Bulbus Allii Sativi consists of several outer layers of thin sheathing protective leaves which surround an inner sheath. The latter enclose the swollen storage leaves called "cloves". Typically.. the bulb possesses a dozen sterile scathing leaves within which are 6-8 cloves bearing buds making a total of 10-20 cloves and 20-40 well-developed but short and embedded roots. The cloves are asymmetric in shape, except for those near the centre.

Organoleptic properties

Odor strong, characteristic alliaceous taste very persistently pungent and acrid.

Geographical distribution
Bulbus Allii Sativi is probably indigenous to Asia **(India)** but it is commercially cultivated in most countries.

General identity tests
Macroscopic and microscopic examinations and microchemical analysis are used to identify organic sulfur compounds, thin-layer chromatographic
analysis to determine the presence of alliin.

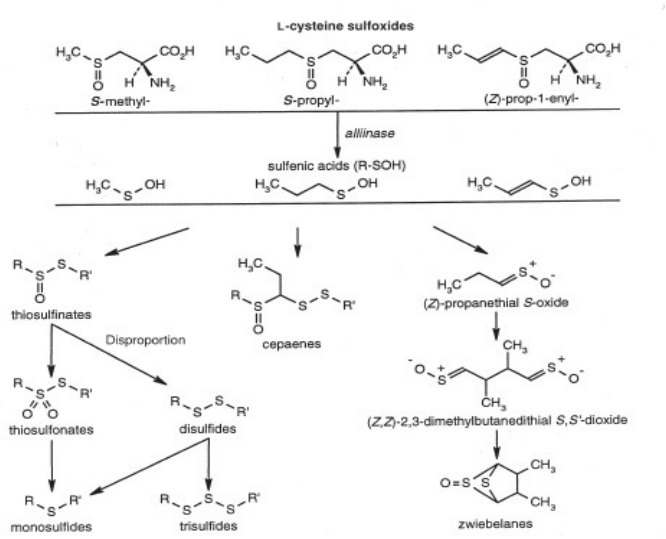
Chemical assays
Qualitative and quantitative assay for sulfur constituents (alliin, allicin etc.) content by means of high-performance liquid chromatography or gas chromatography-mass spectroscopy methods.

Major chemical constituents
The most important chemical constituents reported from Bulbus Allii Sativi are the sulfur compounds. It has been estimated that cysteine sulfoxides (e.g. alliin)and the non-volatile y-glutamylcysteine peptides make up more than 82% of the total sulfur content of garlic.

The thiosulfinates (e.g. allicin) ajoenes (e.g. E-ajoene, Z-ajoene). vinyldithiins (e.g. 2-vinyl-(4H)-1,8-dithiin [5], 8-vinyl-(4H)-1.2-dithiin [6]), and sulfides (e.g.diallyl disulfide, diallyl trisulfide), however, are not naturally occurring compounds,. Rather, they are degradation products from the naturally occurring cysteeine sulfoxide, alliin . When the garlic bulb is crushed, minced, or otherwise processed, alliin is released from compartments and interacts with th eoenzyme alliinase in adjacent vacuoles. Hydrolysis and immediate condensation of the reactive intermediate (allylsulfenic acid) forms alicin . One milligram of alliin is considered to be equivalent to 0.45mg of allicin. Allicin itself is an unstable product and will undergo additional reactions to form other derivatives

(e.g. products), depending on environmental and processing condition. Extraction of garlic cloves with ethanol at <0 o C gave alliin; extraction with ethanol and water at 25o C led to allicin and no allin; and steam distillation (100o C) converted the alliin totally to diallyl sulfides. Sulfur chemical profiles of Bulbus Allii Sativi products reflected the processing procedure: bulb, mainly alliin, allicin; dry powder, mainly alliin. allicin; volatile oil, almost entirely diallyl sulfide, diallyl disulfide, diallyl tisul fide, and diallyl tetrasulfide; oil macerate, mainly 2-vinyl-[4H]-1.8-dithiin, 8-vinyl-[4H]-1,8-dithiin, E-ajoene, and Z-ajoene .The content of alliin was also affected by processing treatment: whole garlic cloves (fresh) contained 0.25-1.15% alliin, while material carefully dried under mild conditions contained 0.7-1.7% alliin.

Gamma-glutamylcysteine peptides are not acted on by alliinase. On prolonged storage or during germination, these peptides are acted on by y-glutamyl transpeptidase to forn1 thiosilfinates.



Dosage forms

Fresh bulbs, dried powder, volatile oil, oil macerates, juice, aqueous or alcoholic extracts, aged garlic extracts (minced garlic that is incubated in aqueous alcohol (15-20%) for 20 months, then concentrated), and odorless garlic products (garlic products in which the alliinase has been inactivated by cooking; or in which chlorophyll has been added as a deodorant; or aged garlic preparations that have low concentrations of water-soluble sulfur compounds).

The juice is the most unstable dosage form. Alliin and allicin decompose rapidly, and those products must be used promptly.

Dried Bulbus Allii Sativi products should be stored in well-closed containers, protected from light, moisture, and elevated temperature.

Medicinal uses

Uses supported by clinical data

As an adjuvant to dietetic management in the treatment of hyperlipidaemia, and in the prevention of atherosclerotic (age-dependent) vascular changes. The drug may be useful in the treatment of mild hypertension.

Uses described in pharmacopoeias and in traditional systems of medicine

The treatment of respiratory and urinary tract infections, ringworm and rheumatic conditions. The herb has been used as a carminative in the treatment of dyspepsia.

Uses described in folk medicine, not supported by experimental or clinical data

As an aphrodisiac, antipyretic, diuretic, emmenagogue, expectorant, and sedative, to treat asthma and bronchitis, and to promote hair growth.

Pharmacology

Experimental pharmacology

Bulbus Allii Sativi has a broad range of antibacterial and antifungal activity.The essential oil, water, and ethanol extracts, and the juice inhibit the in vitro growth of Bacillus species, *Staphylococcus aureus*, *Shigella sonnei*, *Erwinia carotovora*, *Mycobacterium tuberculosis*, *Escherichia coli*, *Pasteurella multocide*, *Proteus species*, *Streptococcus faecalis*, *Pseudomonas aeruginosa*, *Candida species*, *Cryptococus species*, *Rhodotorula rubra, Toruloposis species, Trichosporon pullulans*, and *Aspergillus niger*.Its anti microbial activity has been attributed to allicin, one of the active constituents of the drug. However, allicin is a relatively unstable and highly reactive compound and may not have antibacterial activity in vivo. Ajoene and diallyl trisulfide also have antibacterial and anti fungal activities. Garlic has been used in the treatent of roundworm (*Ascaris strongyloides*) and hookworm (Ancylostoma caninum and Necator americanus) (44=45). Allicin appears to be the active anthelminthic constituent, and diallyl disulfide is not effective.

Fresh garlic, garlic juice, aged garlic extracts, or the volatile oil all lowered chlesterol and plasma lipids, lipid metabolism, and athero9genesis both in vitro and in vivo. In vitro studies with isolated primary rat hepatocytes and human HepG2 cells have shown that water-soluble garlic extracts inhibited cholesterol biosynthesis in a dose-dependent manner . Anti hyperchlesterolaemic and anti hyperlipidameic effects were observed in various animal models (rat, rabbit, chicken, pig) after oral (in feed) or intragastric administration of minced garlic bulbs; water, ethanol, petroleum ether, or methanol extracts, the essential oil; aged garlic extracts and the fixed oil. Oral administration of allicin to rats during a 2-month period lowered serum and liver levels of total lipids, phospholipids, triglycerides, and total cholesterol.Total plasma lipids and cholesterol in rats were reduced after intraperitoneal injection of a mixture of diallyl disulfide and diallyl trisulfide .The mechanism of garlic's anti hypercholesterolaemic and anti hyperlipidaemic activity appears to involve the inhibition of hepatic hydroxymethylglutaryl-CoA (HMG-CoA) reductase and remodeling of plasma lipoproteins and cell membranes.At low concentrations (<0.5mg/ml), garlic extracts inhibited the activity of hepatic HMG-CoA reductase, but at higher concentrations (>0.5mg/ml)cholesterol biosynthesis was inhibited in the later stages of the biosynthetic pathway (68). Alliin was not effective, but allicin and ajoene both inhibited HmG-CoA

reductase in vitro (IC 50 = 7 and 9 mmol/l respectively) . Because both allicin and ajoene are converted to allyl mercaptan in the blood and never reach the liver to affect cholesterol biosynthesis, this mechanism may not be applicable in vivo. In addition to allicin and ajoene, allyl mercaptan (50mmol/l) and diallyl disulfide (5mmol/l) enhanced palmitate-inducedinhibition of chgolesterol biosynthesis in vitro. It should be noted that water extracts of garlic probably do not contain any of these compounds; therefore other constituents of garlic, such as nicotinic acid and adenosine, which also inhibit HmG-CoA reductase activity and cholesterol biosynthesis, may be involved.

The anti hypertensive activity of garlic has bee demonstrated in vivo. Oral or intragastric administration of minced garlic bulbs, or alcohol or water extracts of the drug, lowered blood pressured in dogs, guinea pigs, rabbits, and rats. The drug appeared to decrease vascular resistance by directly relaxing smooth muscle.The drug appears to change the physical state functions of the membrane potentials of vascular smooth muscle cells. Both aqueous garlic and ajoene induced membrane hyperpolarization in the cells of isolated vessel strips. The potassium channels opened frequently causing hyperpolarization, which resulted in vasodilatation because the calcium channels were closed.The compounds that produce the hypotensive activity of the drug are uncertain. Allicin does not appear to be involved, and adenosine has been postulated as being associated with the activity of the drug. Adenosine enlarges the peripheral blood vessels, allowing the blood pressure to decrease, and is also involved in the regulation of blood flow in the coronary arteries; however, adenosine is not active when administered orally. Bulbus Allii Sativi may increase production of nitric oxide, which is associated with a decrease in blood pressure. In vitro studies using water or alcohol extracts of garlic or garlic powder activated nitric-oxide synthase, and these results have been confirmed by in vivo studies

Aqueous garlic extracts and garlic oil have been shown in vivo to alter the plasma fibrinogen level, coagulation time, and fibrinolytic activity. Serum fibrinolytic activity increased after administration of dry garlic or garlic extracts to animals that were artificially rendered arteriosclerotic. Although adenosine was thought to be the active constituent, it did not affect whole.

Garlic inhibited platelet aggregation in both in vitro and in vivo studies. A water, chloroform, or methanol extract of the drug inhibited collagen-, ADP-, arachidonic acid-, epinephrine-, and thrombin-induced platelet aggregation in vitro. Prolonged administration (intragastric, 3 months) of the essential oil or a chloroform extract of Bulbus Allii Sativi inhibited platelet aggregation in rabbits. Adenosine, alliin, allicin, and the transformation products of allicin, the ajoenes; the vinyldithiins; and the dialkyloligosulfides are responsible for inhibition of platelet adhesion and aggregation. In addition methyl allyl trisulfide, a minor constituent of garlic oil, inhibited platelet aggregation at least 10 times as effectively than allicin. Inhibition of the arachidonic acid cascade appears to be one of the mechanisms by which the various constituents and their metabolites affect platelet aggregation. Inhibition of platelet cyclic AMP phosphodiesterase may also be involved.

Ajoene, one of the transformation products of allicin, inhibited in vitro plate-let aggregation induced by the platelet stimulators-ADP, arachidonic acid, calcium

ionophore A28187, collagen, epinephrine, platelet activating factor, and thrombin. Ajoene inhibited platelet aggregation in cows, dogs, guinea- pigs, horses, monkeys, pigs, rabbits, and rats. The antiplatelet activity of ajoene is potentiated by prostacyclin, forskolin, indometacin, and dipyridamole. The mechanism of action involves the inhibition of tllc metabolism of arachidonic acid by both cyclooxygenase and lipoxygenase, thereby inhibiting the formation of thromboxane A2 and 12- . hydroxyeicosatetraenoic acid.Two mechanisms have been suggested for ajoene's antiplatelet activity. First, ajoene may interact with the primary agonist-receptor complex with the exposure of fibrinogen receptors through specific G-proteins involved in the signal transduction system on the platelet membrane.Or it may interact with a haemoprotein involved in platelet activation that modifies the binding of the protein to its ligands.

Hypoglycaemic effects of Bulbus Allii Sativi have been demonstrated in vivo. Oral administration of an aqueous, ethanol, petroleum ether, or chloroform extract, or the essential oil of garlic, lowered blood glucose levels in rabbits and rats. However, three similar studies reported negative results, In one study, garlic bulbs administered orally (in feed) to normal or streptozotocin-diabetic mice reduced hyperphagia and polydipsia but had no effect on hyperglycaemia orhypoinsulinaemia . Allicin administered orally to alloxan-diabetic rats lowered blood glucose levels and increased insulin activity in a dose-dependent manner,Garlic extract's hypoglycaemic action appears to enhance insulin production, and allicin has been shown to protect insulin against inactivation.

Intragastric administration of an ethanol extract of Bulbus Allii Sativi decreased carrageenin-induced rat paw oedema at a dose of 100 mg/k,g, The anti-inflammatory activity of the drug appears to be due to its antiprostilglanlin activity.

A water or ethanol extract of the drug showed antispasmodic activity against acetylcholine, prostaglandin E2 and barium-induced contractions in guinca-pig small intestine and rat stomach. The juice of the drug relaxed smooth muscle of guinea pig ileum, rabbit heart and jejunum, and rat colon and fundus. The juice also inhibited norepinephrine-. acetylcholine- and histamine-induced contractions in guinea pig and rat aorta, and in rabbit trachea.

Clinical pharmacology

The efficacy of Bulbus Allii Sativi as a carminative has been demonstrated in human studies, A clinical study of 29 patients taking two tablets daily (1000mg/day) of a dried garlic preparation demonstrated that garlic relieved epigastric and abdominal distress, belching, flatulence, colic, and nausea. as compared with placebo. It was concluded that garlic sedated the stomach and intestines, and relaxed spasms, retarded hyperperistalsis, and dispersed gas.

A meta-analysis of the effect of Bulbus Allii Sativi on blood pressure re- viewed a total of 11 randomized, controlled trials (published and unpublished). Each of the trials used dried garlic powder (tablets) at a dose of 600- 900mg daily (equivalent to 1.8-2.7 g/day fresh garlic). The median duration of the trials was 12 weeks. Eight of the trials with data from 415 subjects were included in the analysis; three trials were excluded owing to a lack of data. Only, three of the trials specifically used hypertensive subjects, and many of the studies suffered from methodological flaws. Of the seven studies that compared garlic

with placebo, three reported a decrease in systolic blood pressure, and four studies reported a decrease in diastolic blood pressure. The results of the meta-analysis led to the conclusion that garlic may have some clinical usefulness in mild hypertension, but there is still insufficient evidence to recommend the drug as a routine clinical therapy for the treatment of hypertension.

A meta-analysis of the effects of Bulbus Allii Sativi on serum lipids and lipoproteins reviewed 25 randomized, controlled trials (published and unpub- lished) and selected 16 with data from 952 subjects to include in the analysis. Fourteen of the trials used a parallel group design, and the remaining two were cross- over studies. Two of the studies were conducted in an open- label fashion, two others were single- blind, and the remainder were double- blind. The total daily dose of garlic was 600-900 mg of dried garlic powder, or 10 g of raw garlic, or 18 mg of garlic oil, or aged garlic extracts (dosage not stated). The median duration of the therapy was 12 weeks. Overall, the subjects receiving garlic supplementation (powder or non-powder) showed a 12% re- duction (average) in total cholesterol, and a 13% reduction (powder only) in serum triglycerides. Meta-analysis of the clinical studies confirmed the lipid-lowering action of garlic. However, the authors concluded that the overall quality of the clinical trials was poor and that favorable results of better- designed clinical studies should be available before garlic can be routinely recommended as a lipid-lowering agent. However, current available data support the hypothesis that garlic therapy is at least beneficial. Another meta- analysis of the controlled trials of garlic effects on total serum cholesterol reached similar conclusions. A systematic review of the lipid-lowering potential of a dried garlic powder preparation in eight studies with 500 subjects had similar findings. In seven of the eight studies reviewed, a daily dose of 600-900 mg of garlic powder reduced serum cholesterol and triglyceride levels by 5-20%. The review concluded that garlic powder preparations do have lipid-lowering potential.

An increase in fibrinolytic activity in the serum of patients suffering from atherosclerosis was observed after administration of aqueous garlic extracts, the essential oil, and garlic powder. Clinical studies have demonstrated that garlic activates endogenous fibrinolysis, that the effect is detectable for several hours after administration of the drug, and that the effect increases as the drug is taken regularly for several months. Investigations of the acute haemorheological (blood flow) effect of 600-1200mg of dry garlic powder demonstrated that the drug decreased plasma viscosity, tissue plasminogen activator activity and the haematocrit level.

The effects of the drug on haemorheology in conjunctival vessels were determined in a randomized, placebo-controlled, double- blind, cross- over trial. Garlic powder (900 mg) significantly increased the mean diameter of the arterioles (by 4.2%) and venules (by 5.90;0) as compared with controls. In another double- blind, placebo-controlled study, patients with stage II peripheral arterial occlusive disease were given a daily dose of 800 mg of garlic powder for 4 weeks. Increased capillary erythrocyte flow rate and decreased plasma viscosity and plasma fibrinogen levels were observed in the group treated with the drug. Determinations of platelet aggregation ex vivo after ingestion of garlic and garlic preparations by humans, suffers from methodological difficulties that may account for the negative results in some studies. In one study in patients with hypercholesterolinaemia treated with a garlic-oil macerate for 3 months, platelet adhesion

and aggregation decreased significantly. In a 3-year intervention study, 482 patients with myocardial infarction were treated with either an ether-extracted garlic oil (0.1 mg/kg/day, corresponding to 2g fresh garlic daily ora placebo. In the group treated with garlic, there were 35%, fewer new heart attacks and 45% fewer deaths than in the control group. The serum lipid concentrations of the treated patients were also reduced.

The acute and chronic effects of garlic on fibrinolysis and platelet aggregation in 12 healthy patients in a randomized, double- blind, placebo-controlled cross-over study were investigated. A daily dose of 900 mg of garlic powder for 14 days significantly increased tissue plasminogen activator activity as compared with placebo. Furthermore, platelet aggregation induced h}, adenosine diphosphate and collagen was significantly inhibited 2 and 4 hours after garlic ingestion and remained lower for 7 to 14 days after treatment. Another randomized, double- blind, placebo-controlled study investigated the effects of garlic on platelet aggregation in 60 subjects with increased risk of juvenile ischaemic attack.Daily ingestion of 800mg of powdered garlic for 4 weeks significantly decreased the percentage of circulating platelet aggregates and spontaneous platelet aggregation as compared with the placebo group.

Oral administration of garlic powder (800mg/day) to 120 patients for 4 weeks in a double- blind, placebo-controlled study decreased the average blood glucose by 11.6%. Another study found no such activity after dosing non- insulin-dependent patients with 700mg/day of a spray-dried garlic preparation for 1 month.

Contraindications
Bulbus Allii Sativi is contraindicated in patients with a known allergy to the drug. The level of safety for Bulbus Allii Sativi is reflected by its worldwide use as a seasoning in food.

Warnings
Consumption of large amounts of garlic may increase the risk of postoperative bleeding.

Precautions
Drug interactions
Patients on warfarin therapy should be warned that garlic supplements may increase bleeding times. Blood clotting times have been reported to double in patients taking warfarin and garlic supplements.

Carcinogenesis, mutagenesis, impairment of fertility
Bulbus Allii Sativi is not mutagenic in vitro (Salmonella microsome reversion assay and Escherichia coli)

Pregnancy: non-teratogenic efects
There are no objections to the use of Bulbus Allii Sativi during pregnancy and lactation.

Nursing Mothers
Excretion of the components of Bulbus Allii Sativi into breast milk and its effect on the newborn has not been established.

Other precautions
No general precautions have been reported, and no precautions have been reported concerning drug and laboratory test interactions, paediatric use, or teratogenic or non-teratogenic effects on pregnancy.

Adverse reactions
Bulbus Allii Sativi has been reported to evoke occasional allergic reactions such as contact dermatitis and asthmatic attacks after inhalation of the powdered drug. Those sensitive to garlic may also have a reaction to onion or tulip. Ingestion of fresh garlic bulbs, extracts, or oil on an empty stomach may occasionally cause heartburn, nausea, vomiting, and diarrhea. Garlic odor from breath and skin may be perceptible. One case of spontaneous spinal epidural haematoma, which was associated with excessive ingestion of fresh garlic cloves, has been reported.

Posology
Unless otherwise prescribed, average daily dose is as follows: fresh garlic, 2-5g; dried powder, O.4-1.2g; oil, 2-5mg; extract, 300-1000mg (as solid material). Other preparations should correspond to 4-12mg of alliin or about 2-5 mg of allicin).

Bulbus Allii Sativi should be taken with food to prevent gastrointestinal upset.

Reference:

1. http://islamset.com/science/medicinalplants/bulbus.html
2. WHO monograph on selected medicinal plants.

Chapter- 2

Rhizoma Curcumae Longae

Definition
Rhizoma Curcumae Longae is the dried rhizome of *Curcuma longa* L. (Zingiberaceae).Dried rhizomes of *Curcuma wenyujin* Y.H. Lee et C. Ling, *C. kwangsiensis* S. Lee et C.F. Liang. and *C. phaeocaulis* Val. are also official sources of Radix Curcumae or Turmeric Root-Tuber in China.

Synonyms
Curcuma domestica Valeton., *C. rotunda* L., *C. xanthorrhiza* Naves, *Amomum curcuma* Jacq.

Selected vernacular names
Acafrao, arqussofar, asabi-e-safr, avea, cago rerega, chiang-huang, commontumeric, curcum, curcuma, dilau, dilaw, Gelbwurzel, gezo, goeratji, haladi,haldi, haldu, haku halu, hardi, haridra, huang chiang, hsanwen, hurid, Indian saffron, jiânghuang, kaha, kakoenji, kalo haledo, khamin chan, khaminchan,kilunga kuku, kitambwe, kiko eea, koening, koenit, koenjet, kondin, kooneit,
kunyit, kurcum, kurkum, Kurkumawurzelstock, luyang dilaw, mandano,manjano, manjal, nghe, nisha, oendre, pasupu, rajani, rame, renga, rhizome de curcuma, saffran vert, safran, safran des indes, skyer-rtsa, tumeric, tumeric root,tumeric rhizome, turmeric, ukon, ul gum, wong keong, wong keung, yellow root, yii-chin, zardchob.

Description
Perennial herb up to 1.0 m in height; stout, fleshy, main rhizome nearly ovoid (about 3 cm in diameter and 4 cm long). Lateral rhizome, slightly bent (1cm -2–6cm), flesh orange in color; large leaves lanceolate, uniformly green, up to 50cm long and 7–25cm wide; apex acute and caudate with tapering base,petiole and sheath sparsely to densely pubescent. Spike, apical, cylindrical, 10–15cm long and 5–7 cm in diameter. Bract white or white with light green upper
half, 5–6 cm long, each subtending flowers, bracteoles up to 3.5 cm long. Pale yellow flowers about 5cm long; calyx tubular, unilaterally split, unequally toothed; corolla white, tube funnel shaped, limb 3-lobed. Stamens lateral, petaloid, widely elliptical, longer than

the anther; filament united to anther about the middle of the pollen sac, spurred at base. Ovary trilocular; style glabrous . Capsule ellipsoid. Rhizomes orange within.

Plant material of interest: dried rhizome

General appearance

The primary rhizome is ovate, oblong or pear-shaped round turmeric, while the secondary rhizome is often short-branched long turmeric; the round form is about half as broad as long; the long form is from 2–5cm long and 1–1.8cm Thick; externally yellowish to yellowish brown, with root scars and annulations, the latter from the scars of leaf bases; fracture horny; internally orange yellow to orange; waxy, showing a cortex separated from a central cylinder by a distinct endodermis.

Organoleptic properties

Odor, aromatic; taste, warmly aromatic and bitter. Drug when chewed colors the saliva yellow.

Microscopic characteristics

The transverse section of the rhizome is characterized by the presence of mostly thin-walled rounded parenchyma cells, scattered vascular bundles, definite endodermis, a few layers of cork developed under the epidermis and scattered oleoresin cells with brownish contents. The cells of the ground tissue are also filled with many starch grains. Epidermis is thin walled, consisting of
cubical cells of various dimensions. The cork cambium is developed from the subepidermal layers and even after the development of the cork, the epidermis is retained. Cork is generally composed of 4–6 layers of thin-walled brick shaped parenchymatous cells. The parenchyma of the pith and cortex contains curcumin and is filled with starch grains. Cortical vascular bundles are scattered and are of collateral type. The vascular bundles in the pith region are mostly scattered and they form discontinuous rings just under the endodermis. The vessels have mainly spiral thickening and only a few have reticulate and annular structure.

Powdered plant material

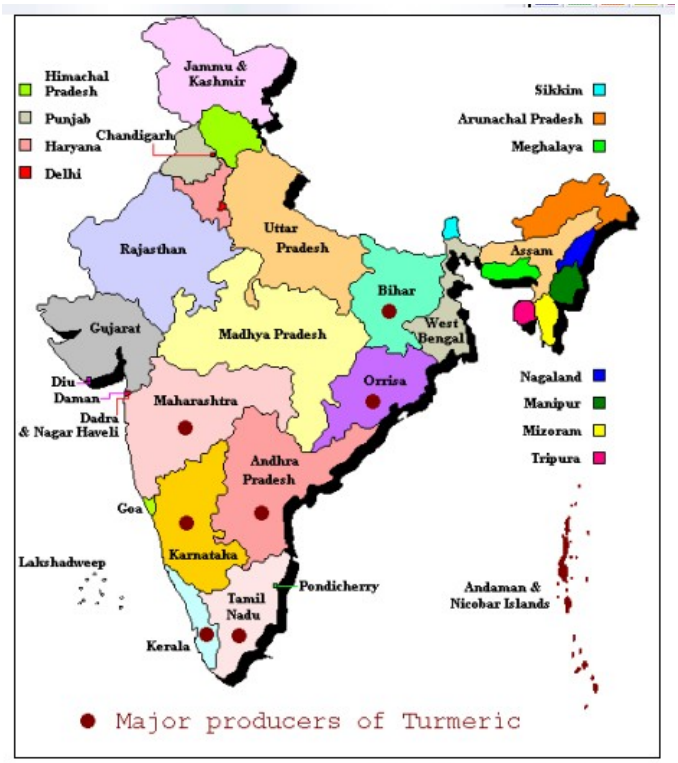
Colored deep yellow. Fragments of parenchymatous cells contain numerous altered, pasty masses of starch grains colored yellow by curcumin, fragments of vessels; cork fragments of cells in sectional view; scattered unicellular trichomes; abundant starch grains; fragments of epidermal and cork cells in surface view; and scattered oil droplets, rarely seen.

Geographical distribution

Cambodia, China, India, Indonesia, Lao People's Democratic Republic, Madagascar, Malaysia, the Philippines, and Viet Nam. It is extend *Rhizoma Curcumae Longae* sively cultivated in China, **India**, Indonesia, Thailand and throughout the tropics, including tropical regions of Africa.

General identity tests

Macroscopic and microscopic examinations*;* test for the presence of curcuminoids by colorimetric and thin-layer chromatographic methods



Purity tests

Microbiology
The test for *Salmonella* spp. in Rhizoma Curcumae Longae products should be negative. The maximum acceptable limits of other microorganisms are as follows. For preparation of decoction: aerobic bacteria—not more than 107/g; fungi—not more than 105/g; *Escherichia coli*—not more than 102/g. Preparations for internal use: aerobic bacteria—not more than 105/g or ml; fungi—not
more than 104/g or ml; enterobacteria and certain Gram-negative bacteria—not more than 103/g or ml; *Escherichia coli*—0/g or ml.

Foreign organic matter
Not more than 2%.

Total ash
Not more than 8.0%.

Acid-insoluble ash
Not more than 1%.

Water-soluble extractive
Not less than 9.0%.

Alcohol-soluble extractive

Not less than 10%.

Moisture
Not more than 10%.

Pesticide residues
To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in Rhizoma Curcumae Longae is not more than 0.05 mg/kg . For other pesticides, see WHO guidelines on quality control methods for medicinal plants and guidelines for predicting dietary intake of pesticide residues.

Heavy metals
Recommended lead and cadmium levels are not more than 10 and 0.3mg/kg,Respectively, in the final dosage form of the plant material.

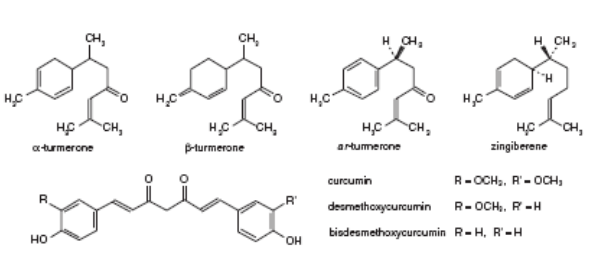
Radioactive residues
For analysis of strontium-90, iodine-131, caesium-134, caesium-137, andplutonium-239, see WHO guidelines on quality control methods for medicinal plants.

Other purity tests
Chemical tests to be established in accordance with national requirements.

Chemical assays
Not less than 4.0% of volatile oil, and not less than 3.0% of curcuminoids. Qualitative analysis by thin-layer and high-performance liquid chromatography and quantitative assay for total curcuminoids by spectrophotometric or by high-performance liquid chromatographic methods.

Major chemical constituents
Pale yellow to orange-yellow volatile oil (6%) composed of a number of monoterpenes and sesquiterpenes, including zingiberene, curcumene, α- and turmerone among others. The coloring principles (5%) are curcuminoids, 50–60% of which are a mixture of curcumin, monodesmethoxycurcumin and bisdesmethoxycurcumin. Representative structures of curcuminoids are presented below.

Dosage forms
Powdered crude plant material, rhizomes, and corresponding preparations. Store in a dry environment protected from light. Air dry the crude drug every 2–3 months.



Medicinal uses

Uses supported by clinical data
The principal use of Rhizoma Curcumae Longae is for the treatment of acid,flatulent, or atonic dyspepsia.

Uses described in pharmacopoeias and in traditional systems of medicine
Treatment of peptic ulcers, and pain and inflammation due to rheumatoid arthritis and of amenorrhoea, dysmenorrhoea, diarrhoea, epilepsy, pain, and skin diseases.

Uses described in folk medicine, not supported by experimental or clinical data
The treatment of asthma, boils, bruises, coughs, dizziness, epilepsy, haemorrhages, insect bites, jaundice, ringworm, urinary calculi, and slow lactation.

Pharmacology

Experimental pharmacology

Anti-inflammatory activity
The anti-inflammatory activity of Rhizoma Curcumae Longae has been demonstrated in animal models. Intraperitoneal administration of the drug in rats effectively reduced both acute and chronic inflammation in carrageenininduced paw oedema, the granuloma pouch test, and the cotton pellet granuloma test.The effectiveness of the drug in rats was reported to be similar to that of hydrocortisone acetate or indometacin in experimentally induced inflammation. Oral administration of turmeric juice or powder did not produce an anti-inflammatory effect; only intraperitoneal injection was effective. The volatile oil has exhibited anti-inflammatory activity in rats against adjuvant-induced arthritis, carrageenin-induced paw oedema, and hyaluronidase-induced inflammation. The anti-inflammatory activity appears to be mediated through the inhibition of the enzymes trypsin and hyaluronidase. Curcumin and its derivatives are the active anti-inflammatory constituents of the drug. After intraperitoneal administration, curcumin and sodium curcuminate exhibited strong anti-inflammatory activity in the carrageenin-induced oedema test in rats and mice. Curcumin was also found to be effective after oral administration in the acute carrageenin-induced oedema test in mice and rats. The anti-inflammatory activity of curcumin may be due to its ability to scavenge oxygen radicals, which have been implicated
in the inflammation process. Furthermore, intraperitoneal injection of a polysaccharide fraction, isolated from the drug, increased phagocytosis capacity in mice in the clearance of colloidal carbon test.

Activity against peptic ulcer and dyspepsia
Oral administration to rabbits of water or methanol extracts of the drug significantly decreased gastric secretion and increased the mucin contents of astric juice. Intragastric administration of an ethanol extract of the drug to rats effectively inhibited gastric secretion and protected the gastroduodenal mucosa against injuries caused by pyloric ligation, hypothermic-restraint stress,

indometacin, reserpine, and mercaptamine administration, and cytodestructive agents such as 80% methanol, 0.6mol/l hydrochloric acid, 0.2mol/l sodium hydroxide and 25% sodium chloride. The drug stimulated the production of gastric wall mucus, and it restored non-protein sulfides in rats . Curcumin, one of the anti-inflammatory constituents of the drug, has been shown to prevent and ameliorate experimentally induced gastric lesions in animal models by stimulation of mucin production. However, there are conflicting reports regarding the protective action of curcumin against histamine-induced gastric ulceration in guinea-pigs. Moreover, both intraperitoneal and oral administration of curcumin (100 mg/kg) have been reported to induce gastric ulceration in rats. Non-specific inhibition of smooth muscle contractions in isolated guinea-pig ileum by sodium curcuminate has been reported. The effect of curcumin on intestinal gas formation has been demonstrated *in vitro* and *in vivo*. Addition of curcumin to *Clostridium perfringens* of intestinal origin *in vitro* and to a chickpea flour diet fed to rats led to a gradual reduction in gas formation. Both the essential oil and sodium curcuminate increase bile secretion after intravenous administration to dogs. In addition, gall-bladder muscles were stimulated.

Clinical pharmacology
Oral administration of the drug to 116 patients with acid dyspepsia, flatulent dyspepsia, or atonic dyspepsia in a randomized, double blind study resulted in a statistically significant response in the patients receiving the drug. The patients received 500 mg of the powdered drug four times daily for 7 days. Two other clinical trials, which measured the effect of the drug on peptic ulcers, showed that oral administration of the drug promoted ulcer healing and decreased the abdominal pain involved. Two clinical studies have shown that curcumin is an effective antiinflammatory drug . A short-term (2 weeks) double-blind, crossover study of 18 patients with rheumatoid arthritis showed that patients receiving either curcumin (1200 mg/day) or phenylbutazone (30 mg/day) had significantimprovement in morning stiffness, walking time and joint swelling. In the second study, the effectiveness of curcumin and phenylbutazone on postoperative inflammation was investigated in a double-blind study. Both drugs produced a better anti-inflammatory response than a placebo, but the degree of inflammation in the patients varied greatly and was not evenly distributed among the three groups.

Contraindications
Obstruction of the biliary tract. In cases of gallstones, use only after consultation with a physician. Hypersensitivity to the drug.

Warnings
No information available.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility
Rhizoma Curcumae Longae is not mutagenic *in vitro*.

Pregnancy: teratogenic effects
Orally administered Rhizoma Curcumae Longae was not tetratogenic in mice or rats.

Pregnancy: non-teratogenic effects
The safety of Rhizoma Curcumae Longae during pregnancy has not been established. As a precautionary measure the drug should not be used during pregnancy except on medical advice.

Nursing mothers
Excretion of the drug into breast milk and its effects on the newborn has not been established. Until such data are available, the drug should not be used during lactation except on medical advice.

Paediatric use
The safety and effectiveness of the drug in children has not been established.

Other precautions
No information on drug interactions or drug and laboratory test interactions was found.
Adverse reactions
Allergic dermatitis has been reported. Reactions to patch testing occurred most commonly in persons who were regularly exposed to the substance or who already had dermatitis of the finger tips. Persons who were not previously exposed to the drug had few allergic reactions.

Posology
Crude plant material, 3–9g daily; powdered plant material, 1.5–3.0 g daily; oral infusion, 0.5–1g three times per day; tincture (1 : 10) 0.5–1ml three
times per day.

References:

1. WHO monographs on selected medicinal plants (Online .pdf version)
2. http://islamset.com/sc/plants/curcumae.html

Chapter- 3

Radix Glycyrrhizae

Definition
Radix Glycyrrhizae consists of the dried roots and rhizomes of *Glycyrrhiza glabra* L. and its varieties or of *Glycyrrhiza uralensis* Fisch.(Fabaceae).1

Synonyms
Liquiritae officinalis Moench is a synonym of *Glycyrrhiza glabra* L.

Selected vernacular names

Glycyrrhiza glabra L. and its varieties
Adimaduram, akarmanis, asloosoos, aslussos, athimaduram, athimaduramu, athimathuram, bekh-e-mahak, bois doux, cha em thet, estamee, gancao, glycyrrhiza, herbe aux tanneurs, hsi-pan-ya-kan-tsao, irk al hiel, irk al hilou, irksos, jakyakgamcho-tang, jashtimadhu, jethimadh, jethimadha, kanpo, kanzo, kan-ts'ao, kum cho, Lakritzenwurzel, licorice, licorice root, liquiritiae radix, liquorice, liquorice root, madhuyashti, madhuyashti rasayama, mulathee, muleti, mulhatti, neekhiyu, Persian licorice, racine de reglisse, racine douce, reglisse, reglisse officinalis, rhizoma glycyrrhizae, Russian licorice, Russian liquorice, Russisches Süssholz, si-pei, sinkiang licorice, Spanish licorice, Spanish liquorice, Spanisches Süssholz, Süssholzwurzel, sweet root, sweetwood, ud al sus, velmi, walmee, welmii, xi-bei, yashti, yashtimadhu, yashtimadhukam,
yashtomadhu.

Glycyrrhiza uralensis Fisch.
Chinese licorice, Chinese liquorice, gancao, kan-ts'ao, kanzo, kanzoh, licorice root, liquiritiae radix, north-eastern Chinese licorice, saihokukanzoh, tohoku kanzo, tongpei licorice, tung-pei-kan-tsao, Ural liquorice, uraru-kanzo.

Description

Glycyrrhiza glabra L. and its varieties
A perennial plant, up to more than 1m in height, erect, with highly developed stoloniferous roots. Leaves compound, 9–17 alternate imparipinnate leaflets, oblong to elliptical-lanceolate, acute or obtuse; racemes loose, shorter than the leaves or a little

longer. Flowers 1 cm long. Flat pods oblong to linear, 1–3cm long by 6 mm wide, more or less densely echinate glandular, many-seeded or abbreviated, 2- or 3-seeded.

Glycyrrhiza uralensis Fisch.
A perennial glandular herb, 30–100cm high. Stem erect, with short whitish hairs and echinate glandular hairs; the lower part of the stem is woody. Leaves alternate, imparipinnate; leaflets 7–17, ovate-elliptical, 2–5.5 cm long by 1–3cm wide; apex obtuse-rounded; base rounded; both surfaces covered with glandular hairs and short hairs. Stipules lanceolate. Inflorescence an axillary cluster. Flowers purplish, papilionaceous; calyx villous. Fruit a flat pod, oblong, sometimes falcate, 6–9mm wide, densely covered with brownish echinate glandular hairs. Seeds 2–8. The root is cylindrical, fibrous, flexible, 20–22cm long and 15mm in diameter, with or without cork, cork reddish, furrowed, light yellow inside.

Plant material of interest: dried root and rhizome

General appearance

***Glycyrrhiza glabra* L. and its varieties**
The commercial variety, *G. glabra* var. *typica* Regel & Herd, known as Spanish liquorices, consists generally of roots and rhizomes in nearly cylindrical pieces, up to 1m long and 5–20mm in diameter; externally, the bark is brownish gray to dark brown, longitudinally wrinkled, occasionally bearing small dark buds in rhizomes or small circular or transverse rootlet-scars in roots. The peeled root is yellow, smooth, fibrous, finely striated; fracture, fibrous in the bark and splintery in the wood; internally, bright yellow. A distinct cambium ring separates the yellowish grey bark from the finely radiate yellow wood; central pith, only in rhizomes. The commercial variety, *G. glabra* var. *glandulifera* (Wald et Kit) Regel & Herd, known as Russian liquorice, consists mainly of roots, in cylindrical pieces somewhat tapering and sometimes longitudinally split; 15–40cm long, 1–5cm in diameter. The enlarged crown of the root may attain up to 10 cm in diameter; externally, the unpeeled root purplish brown, somewhat scaly, with stem scars at the top; the peeled root yellowish, coarsely striated; fracture as for Spanish type; internally, yellow, radiating.

***Glycyrrhiza uralensis* Fisch.**
The roots and rhizomes are cylindrical, fibrous, flexible, 20–100cm long, 0.6– 3.5 cm in diameter, with or without cork. Externally reddish brown or greyish brown, longitudinally wrinkled, furrowed, lenticellate, and with sparse rootlet scars. Texture compact, fracture slightly fibrous, yellowish white, starchy; cambium ring distinct, rays radiate, some with clefts. Rhizomes cylindrical, externally with bud scars, pith present in the centre of fracture.

Organoleptic properties
Odor slight and characteristic; taste, very sweet.

Microscopic characteristics
In transverse section the cork is thick, brown or purplish brown, formed of several layers of flattened polygonal thin-walled cells; cortex of phelloderm in root somewhat narrow,

yellow fibers of parenchyma cells contain isolated prisms of calcium oxalate; phloem, wide, yellow, traversed by numerous wavy parenchymatous medullary rays, 1–8 cells wide and consisting of numerous radial groups of fibres, each surrounded by a crystal sheath of parenchyma cells. Each cell usually contains a prism of calcium oxalate and layers of parenchyma alternating with sieve tissue, the latter occasionally obliterated, appearing as refractive irregular structures; phloem fibres, very long, with very narrow lumen and strongly thickened stratified walls which are cellulosic in the inner part of the phloem and slightly lignified in the outer; xylem, yellow, distinctly radiate; xylem rays, consisting of small pale yellow parenchyma, groups of fibres similar to those of the phloem but more lignified, and surrounded by crystal-sheath, tracheids, and large wide lumen vessels, 80–200 m in diameter, with thick yellow reticulate walls or with numerous oval bordered pits with slit-shaped openings. Other parenchyma cells contain small round or oval starch granules. Pith, only in rhizome, dark yellow, parenchymatous. Root, with 4-arch primary
xylem, no pith and shows 4 broad primary medullary rays, radiating from the centre at right angles to one another. In peeled liquorice, the cork, cortex, and sometimes part of the phloem are absent.

Powdered plant material
Light yellow in the peeled or brownish yellow or purplish brown in the unpeeled root. Characterized by the numerous fragments of the fibers accompanied by crystal-sheath, the fibers 8–25µm, mostly 10–15µm, in diameter; dark yellow fragments of vessels, 80–200µm in diameter, containing solitary prismatic crystals of calcium oxalate, free or in cells 10–35µm (mostly 15–25µm) long; numerous simple oval, round or fusiform starch granules, free or in parenchyma cells, with no striation but occasionally showing hilum, 2– 20µm (mostly about 10µm) in diameter; cork may be present.

Geographical distribution

Glycyrrhiza glabra
Native to central and southwestern Asia and the Mediterranean region. It is cultivated in the Mediterranean basin of Africa, in southern Europe, and in **India**.
.

General identity tests
Macroscopic, microscopic, and microchemical examinations; and thin layer chromatographic analysis for the presence of glycyrrhizin.

Purity tests

Microbiology
The test for *Salmonella* spp. in Radix Glycyrrhizae products should be negative. The maximum acceptable limits of other microorganisms are as follows. For preparation of decoction: aerobic bacteria—not more than 107/g; fungi—not more than 105/g; *Escherichia coli*—not more than 102/g. Preparations for internal use: aerobic bacteria—not more than 105/g or ml; fungi—not more than 104/g or ml; enterobacteria and certain Gram-negative bacteria—not more than 103/g or ml; *Escherichia coli*—0/g or ml.

Total ash

Not more than 7% .

Acid-insoluble ash
Not more than 2% .

Sulfated ash
Not more than 10%.

Water-soluble extractive
Not less than 20%.

Dilute alcohol-soluble extractive
Not less than 25%.

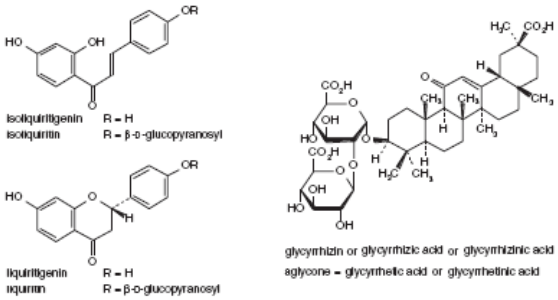
Pesticide residues
To be established in accordance with national requirements. Normally, themaximum residue limit of aldrin and dieldrin for Radix Glycyrrhizae is not more than 0.05 mg/kg. For other pesticides, see WHO guidelines on quality control methods for medicinal plant guidelines for predicting dietary intake of pesticide residues.
Heavy metals
Recommended lead and cadmium levels are no more than 10 and 0.3mg/kg, respectively, in the final dosage form of the plant material.

Radioactive residues
For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants.

Other purity tests
Alcohol-soluble extractive, chemical, and foreign organic matter tests to be established in accordance with national requirements.

Chemical assays
Assay for glycyrrhizin (glycyrrhizic acid, glycyrrhizinic acid) content (at least 4%) by means of spectrophotometric, thin-layer chromatographic– densitometric or high-performance liquid chromatographic methods.

Major chemical constituents
The major constituents are triterpene saponins. Glycyrrhizin (glycyrrhizic acid, glycyrrhizinic acid) is the major component (2–9%); minor components occur in proportions that vary depending on the species and geographical location. Glycyrrhizin occurs as a mixture of potassium and calcium salts . It is a monodesmoside, which on hydrolysis releases two molecules of



D-glucuronic acid and the aglycone glycyrrhetic (glycyrrhetinic) acid (enoxolone). Glycyrrhizin is generally regarded as the active principle of Radix Glycyrrhizae and is responsible for its sweetness, which is 50 times that of sucrose. Flavonoid constituents include liquiritigenin and
isoliquiritigenin.

Dosage forms
Crude plant material, dried extract and liquid extract. Store in a well-closed container, protected from light and moisture.

Medicinal uses

Uses supported by clinical data
None.

Uses described in pharmacopoeias and in traditional systems of medicine
As a demulcent in the treatment of sore throats, and as an expectorant in the treatment of coughs and bronchial catarrh. Also in the prophylaxis and treatment of gastric and duodenal ulcers, and dyspepsia. As an anti-inflammatory agent in the treatment of allergic reactions, rheumatism
and arthritis, to prevent liver toxicity, and to treat tuberculosis and adrenocorticoid insufficiency.

Uses described in folk medicine, not supported by experimental or Clinical data
As a laxative, emmenagogue, contraceptive, galactagogue, antiasthmatic drug, and antiviral agent. In the treatment of dental caries, kidney stones, heart disease, “consumption”, epilepsy, loss of appetite, appendicitis, dizziness, tetanus, diphtheria, snake bite, and haemorrhoids .

Pharmacology

Experimental pharmacology
The demulcent action of the drug is due primarily to glycyrrhizin. The antitussive and expectorant properties of the drug have also been attributed to glycyrrhizin, which accelerates tracheal mucus secretion.The antiulcer activity of Radix Glycyrrhizae has been demonstrated both experimentally and clinically. Intraperitoneal, intraduodenal, or oral administration of aqueous or alcoholic extracts of Radix Glycyrrhizae reduced gastric secretions in rats, and it inhibited the formation of gastric ulcers induced by

pyloric ligation, aspirin, and ibuprofen. Glycyrrhizin and its agly*Radix Glycyrrhizae* cone (glycyrrhetic acid, enoxolone), two of the active constituents of Radix Glycyrrhizae, both have antiphlogistic activity and increase the rate of mucus secretion by the gastric mucosa. Deglycyrrhizinated liquorice (97% of glycyrrhizin is removed) effectively treated stress-induced ulcers in animal models. The mechanism of antiulcer activity involves acceleration of mucin excretion through increasing the synthesis of glycoprotein at the gastric mucosa, prolonging the life of the epithelial cells, and antipepsin activity. The spasmolytic activity of Radix Glycyrrhizae has been demonstrated *in vivo* (guinea-pig, rabbit, and dog, and appears to be due to the flavonoids liquiritigenin and isoliquiritigenin. Glycyrrhizin reduces the toxic action of carbon tetrachloride- and galactosamine-induced cytotoxicity in cultured rat hepatocytes, through its antioxidant activity. Glycyrrhizin inhibited histamine release from rat mast cells and prevented carbon tetrachloride-induced liver lesions and macrophage-mediated cytotoxicity. Intragastric administration of a flavonoid fraction isolated from Radix Glycyrrhizae to mice protected against carbon tetrachloride hepatotoxicity. Glycyrrhizin protected the liver apparently through its membrane stabilization effects. The anti-inflammatory and antiallergic actions of the drug have been attributed to the corticosteroid-like activity of glycyrrhizin and glycyrrhetic acid (enoxolone). These compounds act indirectly by potentiating the activity of corticosteroids. *In vitro*, glycyrrhetic acid inhibits Δ4 _-reductase, an enzyme that competitively inactivates steroid hormones, and 11_-hydroxysteroid dehydrogenase, the enzyme that deactivates cortisol. Glycyrrhizin given intraperitoneally suppressed contact dermatitis in mice, and was more effective than prednisolone, but no effects were observed after oral administration. *In vitro*, the drug inhibits the growth of *Bacillus subtilis*, *Mycobacterium tuberculosis*, *Aspergillus spp*. *Staphylococcus aureus*, *Mycobacterium smegmatis*, and *Candida albicans* .

Clinical pharmacology

Oral administration of Radix Glycyrrhizae to 15 patients with peptic ulcer reduced symptoms and improved healing in 75% of the cases. Glycyrrhetic acid (enoxolone), the active constituent, produced its antiulcer activity by inhibiting 15-hydroxyprostaglandin dehydrogenase and Δ13 prostaglandin reductase. Inhibition of these two enzymes stimulated an increase in the concentration of prostaglandins E and F2α in the stomach, which promoted the healing of peptic ulcers owing to a cytoprotective effect on the gastric mucosa. Carbenoxolone, a derivative of glycyrrhetic acid, has been used clinically for years in the treatment of gastric and duodenal ulcers. Oral administration of deglycyrrhizinated liquorice (380 mg, 3 times daily) to 169 patients with chronic duodenal ulcers was as effective as antacid or cimetidine treatments. These results indicate that, in addition to glycyrrhetic acid, other unidentified constituents of Radix Glycyrrhizae contribute to its antiulcer activity. Reports on the usefulness of liquorice extracts on body fluid homeostasis in patients with Addison disease are contradictory. One study found no positive
effects, while three other studies noted an increase in weight gain and sodium retention.

Contraindications

Radix Glycyrrhizae is contraindicated in patients with hypertension, cholestatic disorders or cirrhosis of the liver, hypokalaemia, or chronic renal insufficiency,and during pregnancy.

Warnings

Prolonged use of large doses (_50g/day) of the drug for extended periods (_6 weeks) may increase water accumulation, causing swelling of the hands and feet. Sodium excretion is reduced and potassium excretion is increased. Blood pressure may rise.

Precautions

General

Radix Glycyrrhizae should not be taken concurrently with corticosteroid treatment. If sore throat or cough persists for more than 3 days, the patient should consult a physician.

Drug interactions

Because it increases potassium loss, Radix Glycyrrhizae should not be administered for prolonged use with thiazide and loop diuretics or cardiac glycosides. Because it reduces sodium and water excretion, the effectiveness of drugs used in the treatment of hypertension may be reduced. Radix Glycyrrhizae should not be administered in conjunction with spironolactone or amiloride.

Carcinogenesis, mutagenesis, impairment of fertility

Radix Glycyrrhizae is not mutagenic *in vitro*.

Pregnancy: teratogenic effects

The drug is not teratogenic in animal models

Pregnancy: non-teratogenic effects

The safety of Radix Glycyrrhizae preparations during pregnancy has not been established. As a precautionary measure the drug should not be used during pregnancy.

Nursing mothers

The safety of Radix Glycyrrhizae preparations during lactation has not been established. As a precautionary measure the drug should not be used during lactation except on medical advice.

Paediatric use

The safety and effectiveness of the drug in children have not been established.

Other precautions

No information available about drug and laboratory test interactions.

Adverse reactions

No adverse reactions have been associated with the drug when used within the recommended dosage and treatment period. Prolonged use (_6 weeks) of excessive doses (_50g/day) can lead to pseudoaldosteronism, which includes potassium depletion, sodium retention, oedema, hypertension, and weight gain. In rare cases, myoglobinuria and myopathy can occur.

Posology

Unless otherwise prescribed, average daily dose of crude plant material, 5–15g, corresponding to 200–800mg of glycyrrhizin. Doses of other preparations should be calculated accordingly. Radix Glycyrrhizae should not be used for longer than 4–6 weeks without medical advice.

References:

1. WHO monographs on selected medicinal plants.
2. http://islamset.com/sc/plants/rrhizae.html

Chapter-4

Herba Ephedrae

Definition
Herba Ephedrae consists of the dried stem or aerial part of *Ephedra sinica* Stapf or other ephedrine-containing *Ephedra* species (Ephedraceae).

Synonyms
None.

Selected vernacular names
Amsania, budshur, chewa, Chinese ephedra, ephédra, horsetail, hum, huma, joint fir, khama, ma hoàng, ma huang, máhuáng, mao, maoh, maou, mao-kon, môc tac ma hoàng, mu-tsei-ma-huang, phok, san-ma-huang, shrubby, soma, song tuê ma hoàng, trung aa hoàng, tsao-ma-huang, tutgantha.

Description
Erect or prostrate, green, almost leafless shrub, 20–90 cm high. Branches erect, short, glaucous green, somewhat flat, 1.0–1.5 mm in diameter, with small sparse longitudinal striae, fasciated at the nodes; nodes reddish brown; internode 2.5– 5.5 cm long _ 2 mm in diameter. Small triangular leaves opposite, reduced to scales, barely 2mm. Flowers in summer, unisexual, dioecious; male flowers pedunculate or nearly sessile, grouped in catkins composed of 4 to 8 pairs of flowers with about 8 anthers; female flowers biflorous, pedunculate with 3 or 4 pairs of bracts, the naked ovule surrounded by an urn-shaped perianth sheath, fruiting with often fleshy red succulent bracts, 2-seeded.

Plant material of interest: stem or aerial part

General appearance
Macroscopically, Herba Ephedrae occurs as thin cylindrical or ellipsoidal cylinder, 1–2 mm in diameter; 3.5–5.5cm in length of internode; light green to yellow-green; numerous parallel vertical furrows on the surface; scaly leaves at the node portion; leaves, 2–4 mm in length, light brown to brown in colour, usually opposite at every node, adhering at the base to form a tubular sheath
around the stem. Under a magnifying glass, the transverse section of the stem appears as circle and ellipse, the outer portion grayish green to yellow-green in color, and the center filled with a red-purple substance or hollow. When fractured at an internode, the outer part is fibrous and easily split vertically.

Organoleptic properties
Odor, slight; taste, slightly bitter and astringent, giving a slight sensation of numbness on the tongue.

Microscopic characteristics
The epidermal cells of the stem are covered with a moderately thick granular cuticle; the cells are polygonal or subrectangular, axially elongated, having straight anticlinal walls. The stomata are few and are of the ranunculaceous type with lignified appendages. The epidermis of the scaly leaf is covered with smooth (upper) or warty (lower) cuticle and consists of subrectangular to polygonal cells, having straight or sometimes slightly beaded anticlinal walls; few stomata are present resembling those of stem. The epidermis of the apical and marginal regions of the scaly leaf shows short papillae-like outgrowths. Chlorenchymatous palisade-like cells form the outer zone of the cortex; rounded ordinary parenchymatous cells form the inner zone of the cortex. Cortical parenchyma and pith cells contain an amorphous reddish brown substance. Non-lignified or lignified hypodermal and pericyclic fibres, which have thick walls, bear slit-like pits and blunt, slightly tapering, occasionally forked ends. The vessels of the secondary xylem of the stem are lignified with bordered pits, having rounded or oval apertures. The vessel segments have much inclined end walls, bearing foraminate perforation plates. The tracheids and fibrous tracheids of secondary xylem of the stem are lignified with bordered pits having oval or slit-like apertures. The fibres of the scaly leaf are lignified, usually irregular or nearly straight, having moderately thick walls and blunt or sometimes forked ends. Few, small, rounded, simple and compound starch granules with indistinct hilum are present in cortical parenchyma, pith, and medullary ray cells. Few, small prisms of calcium oxalate are present in the cortical parenchyma.

Powdered plant material
Powdered Herba Ephedrae is greyish green. Numerous thick fragments of cutinized outer walls of epidermis vary from colourless to varying shades of brown or red; numerous fragments of sclerenchyma fibres with extremely thickened, non-lignified to lignified walls, narrow, frequently indistinct lumina and sharp pointed ends; fragments of vascular tissue showing tracheids with bordered pores and occasional spiral and pitted tracheae; numerous chlorenchyma cells; starch grains simple, spheroidal to occasionally ovate, averaging up to 1.2µm but occasionally up to 20µm; fragments of epidermis with rectangular cells and granular contents, some with sunken elliptical stomata; fragments of lignified or non-lignified pith parenchyma, some of the cells showing mucilage sacs; papillae; granules of calcium oxalate.

Geographical distribution
Ephedra species are found in Afghanistan, Central America, China, **India**, regions of the Mediterranean, Mongolia, and North America.

General identity tests
Macroscopic and microscopic examinations and microchemical tests for the presence of alkaloids with Mayer’s reagent.

Purity tests

Microbiology
The test for *Salmonella* spp. in Herba Ephedrae products should be negative. The maximum acceptable limits for other microorganisms are as follows. For preparation of decoction: aerobic bacteria—not more than 10^7/g; fungi—not more than 10^5/g; *Escherichia coli*—not more than 10^2/g. Preparations for internal use: aerobic bacteria

—not more than 10^5/g or ml; fungi—not more than 10^4/g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^3/g or ml; *Escherichia coli*—0/g or ml.

Foreign organic matter
Woody stems, not more than 5%. Does not contain stems of Equisetaceae or Gramineae plants, nor any other foreign matter.

Total ash
Not more than 9% .

Acid-insoluble ash
Not more than 2%.

Moisture
Not more than 9%.

Pesticide residues
To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin for Herba Ephedrae is not more than 0.05 mg/kg . For other pesticides, see WHO guidelines on quality control methods for medicinal plants and guidelines for predicting dietary intake of pesticide residues.

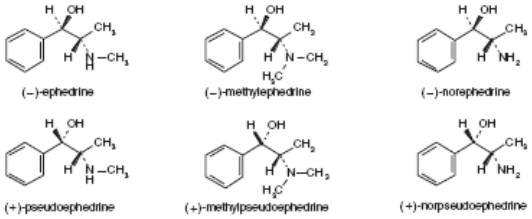
Heavy metals
Recommended lead and cadmium levels are no more than 10 and 0.3mg/kg, respectively, in the final dosage form of the plant material.

Radioactive residues
For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants.

Other purity tests
Chemical, dilute ethanol-soluble extractive, and water-soluble extractive tests to be established in accordance with national requirements.

Chemical assays
Contains not less than 0.7% total alkaloids, calculated as ephedrine by highperformance
liquid chromatography in the Japanese pharmacopoeia; or not less than 0.8% of total alkaloids, calculated as ephedrine in the Chinese pharmacopoeia. Thin-layer, gas–liquid or high-performance liquid chromatographic analysis for ephedrine and related alkaloids are available.

Major chemical constituents
The major active principle found in Herba Ephedrae is (-)-ephedrine in concentrations of 40–90% of the total alkaloid fraction, accompanied by (+)-pseudoephedrine. Other trace alkaloids in the alkaloid complex include (-)-norephedrine, (+)-norpseudoephedrine, (-)-methylephedrine and (+)-methylpseudoephedrine. The total alkaloid content can exceed 2% depending on the species. Not all *Ephedra* species contain ephedrine or alkaloids.



Dosage forms

Powdered plant material; extracts and other galenicals. Store in well closed, light-resistant containers.

Medicinal uses

Uses supported by clinical data

Herba Ephedrae preparations are used in the treatment of nasal congestion due to hay fever, allergic rhinitis, acute coryza, common cold, and sinusitis. The drug is further used as a bronchodilator in the treatment of bronchial asthma.

Uses described in pharmacopoeias and in traditional systems of medicine

Herba Ephedrae has been used for the treatment of urticaria, enuresis, narcolepsy, myasthenia gravis, and chronic postural hypotension.

Uses described in folk medicine, not supported by experimental or clinical data

Other medical uses claimed for Herba Ephedrae preparations include its use as an analgesic, an antiviral agent, an antitussive and expectorant, an antibacterial, and an immune stimulant.

Clinical pharmacology

Two of the main active constituents of Herba Ephedrae, ephedrine and pseudoephedrine, are potent sympathomimetic drugs that stimulate α-, _1- and _2-adrenoceptors. Pseudoephedrine's activity is similar to ephedrine, but its hypertensive effects and stimulation of the central nervous system are somewhat weaker. Part of ephedrine's peripheral action is due to the release of norepinephrine, but the drug also directly affects receptors. Tachyphylaxis develops to its peripheral actions, and rapidly repeated doses become less effective owing to the depletion of norepinephrine stores.

Cardiovascular actions

Like epinephrine (adrenaline), ephedrine excites the sympathetic nervous system, causing vasoconstriction and cardiac stimulation. Ephedrine differs from epinephrine in that it is orally active, has a much longer duration of action, and has more pronounced activity in the central nervous system, but is much less potent. The drug stimulates the heart rate, as well as cardiac output, and increases peripheral resistance, thereby producing a lasting rise in blood pressure. The cardiovascular effects of ephedrine persist up to ten times as long as those of epinephrine. Ephedrine elevates both the systolic and diastolic pressures and pulse pressure. Renal and splanchnic blood flows are decreased, while coronary, cerebral, and muscle blood flows are increased.

Bronchodilator and nasal decongestant

Ephedrine, like epinephrine, relaxes bronchial muscles and is a potent bronchodilator owing to its activation of the _-adrenoceptors in the lungs. Bronchial muscle relaxation is less pronounced but more sustained with ephedrine than with epinephrine. As a consequence, ephedrine should be used only in patients with mild cases of acute asthma and in chronic cases that require maintenance medication. Ephedrine, like other sympathomimetics with α-receptor activity, causes vasoconstriction and blanching when applied topically to nasal and pharyngeal mucosal surfaces Continued, prolonged use of these preparations (_3 days) may cause rebound congestion and chronic rhinitis (*26*). Both ephedrine and pseudoephedrine are useful orally as nasal decongestants in cases of allergic rhinitis, but they may not be very effective for the treatment of nasal congestion due to colds.

Central nervous system

Mydriasis occurs after local application of ephedrine (3–5%) to the eye, but the effect lasts for only a few hours. Ephedrine is of little value as a mydriatic in the presence of inflammation. The activity of the smooth muscles of the uterus is usually reduced by ephedrine; consequently, the drug has been used to relieve the pain of dysmenorrhoea. Ephedrine is a potent stimulator of the central nervous system. The effects of the drug may last for several hours after oral administration. Thus, preparations containing Herba Ephedrae have been promoted for use in weight reduction and thermogenesis (fat burning). The safety and effectiveness of these preparations is currently an issue of debate and requires further investigation Ephedrine stimulates the α-adrenoceptors of the smooth muscle cells of the bladder base, which increases the resistance to the outflow of urine. Thus Herba Ephedrae has been used in the treatment of urinary incontinence and nocturnal enuresis.

Contraindications

Herba Ephedrae should not be administered to patients with coronary thrombosis, diabetes, glaucoma, heart disease, hypertension, thyroid disease, impaired circulation of the cerebrum, phaeochromocytoma, or enlarged prostate.Co-administration of Herba Ephedrae preparations with monoamine oxidase inhibitors is contraindicated as the combination may cause severe, possibly fatal, hypertension.

Warnings

Dosage should be reduced or treatment discontinued if nervousness, tremor, sleeplessness, loss of appetite or nausea occurs. Not for children under 6 years of age. Keep out of the reach of children. Continued, prolonged use may cause dependency.

Precautions

General

Insomnia may occur with continued use of Herba Ephedrae preparations.

Drug interactions

In combination with cardiac glycosides or halothane, may cause heart rhythm disturbances; with guanethidine, may cause an enhancement of sympathomimetic effect; with monoamine oxidase inhibitors, can cause severe, possibly fatal, hypertension; with ergot alkaloid derivatives or oxytocin, may increase risk of high blood pressure.

Carcinogenesis, mutagenesis, impairment of fertility

Extracts of *Ephedra sinica* are not mutagenic in the *Salmonella*/microsome reversion assay.

Pregnancy: teratogenic effects

Ephedra sinica did not have any teratogenic effects *in vivo*.

Pregnancy: nonteratogenic effects
Ephedra sinica is not abortifacient in rats.Clinical studies in humans are not available; therefore, use of the drug during pregnancy is not generally recommended.
Nursing mothers
There are no reliable studies on this subject. Therefore, nursing mothers should not take Herba Ephedrae without consulting a physician.
Paediatric use
Herba Ephedrae should not be administered to children under 6 years of age.

Other precautions
No information available concerning drug and laboratory test interactions.

Adverse reactions
In large doses Herba Ephedrae products can cause nervousness, headaches, insomnia, dizziness, palpitations, skin flushing and tingling, and vomiting. The principal adverse effects of ephedrine and Herba Ephedrae are stimulation of the central nervous system, nausea, tremors, tachycardia, and urine retention. Continued, prolonged use (_3 days) of topical preparations containing Herba Ephedrae, for the treatment of nasal congestion, may cause rebound congestion and chronic rhinitis. Continued prolonged use of oral preparations may cause dependency.

Posology
Crude plant material: 1–6g for decoction daily . Liquid extract (1 :1 in 45% alcohol): 1–3ml daily. Tincture (1 :4 in 45% alcohol): 6–8ml daily.
Reference :

1. WHO monographs on selected medicinal plants
2. http://islamset.com/sc/plants/herba.html

Chapter- 5

Aloe vera

Definition
Aloe is the dried juice of the leaves of *Aloe vera* (L.) Burm. f. or of *A. ferox* Mill. and its hybrids with *A. africana* Mill. and *A. spicata* Baker (Liliaceae).

Synonyms

Aloe vera (L.) Burm. f.

Aloe barbadensis Mill., *Aloe chinensis* Bak., *A. elongata* Murray, *A. indica* Royle, *A. officinalis* Forsk., *A. perfoliata* L., *A. rubescens* DC, *A. vera* L. var. *littoralis* König ex Bak., *A. vera* L. var. *chinensis* Berger, *A. vulgaris* Lam. In most formularies and reference books, *Aloe barbadensis* Mill. is regarded as the correct species name, and *Aloe vera* (L.) Burm. f. is considered a synonym. However, according to the International Rules of Botanical Nomenclature, *Aloe vera* (L.) Burm. f. is the legitimate name for this species. The genus *Aloe* has also been placed taxonomically in a family called Aloeaceae.

Aloe ferox Mill.

Aloe horrida Haw., *A. perfoliata* Thunberg., *A. pseudoferox* Salm. Dyck, *A. socotrina* Masson., *A. supralaevis* Haw., *Pachydendron ferox* Humb. & Bonpl., *P. supralaeve* Haw.

Selected vernacular names

Aloe capensis, aloe curacao, aloe vera, aloes, aloès, aloès du Cape, aloès fèroce, aloes vrai, aloès vulgaire, alovis, Barbadoes aloe, Barbadoes aloes, Barbados aloe, Bergaalwyn, Bitteraalwyn, Cape aloe, chirukattali, Curacao aloe, Curacao aloes, Curacao alos, Echte Aloe, ghai kunwar, ghai kunwrar, gheekuar, ghikanvar, ghikuar, ghikumar, ghikumari, ghikwar, ghiu kumari, ghrita kumari, ghritakumari, grahakanya, gwar-patha, haang takhe, hlaba, Indian aloe, jadam, korphad, kumari, kumaro, kunvar pata, kunwar, laloi, laluwe, lo-hoei, lo-hoi, lou-houey, lu wei, luchuy, manjikattali, Mediterranean aloe, murr sbarr, musabar, rokai, sabbara, saber, sábila, sabilla, sabr, saibr, savila, savilla, semper vivum, shubiri, sibr, siang-tan, star cactus, tuna, umhlaba, waan haang charakhe, wan-hangchorakhe, yaa dam, yadam, zábila, zambila.

Description

Aloe vera (L.) Burm. f.

Succulent, almost sessile perennial herb; leaves 30–50cm long and 10cm broad at the base; colour pea-green (when young spotted with white); bright yellow tubular flowers 25–35cm in length arranged in a slender loose spike; stamens frequently project beyond the perianth tube.

Aloe ferox Mill.

Arborescent perennial shrub with a single stem of 2–3m in height, crowned by a large rosette of numerous leaves which are glaucous, oval-lanceolate, 40– 60cm in length, thorny on the ridge and the edges; inflorescence an erect raceme 60 cm in height; flowers with perianth 2.5 cm in length, red, yellow, or orange.

Plant material of interest: dried juice

Solidified juice originating in the cells of the pericycle and adjacent leaf parenchyma, and flowing spontaneously from the cut leaf, allowed to dry with or without the aid of heat. It is not to be confused with Aloe Vera Gel, which is the colourless mucilaginous gel obtained from the parenchymatous cells in the leaves of *Aloe vera* (L.) Burm. f.

General appearance

Curacao or Barbados Aloe, derived from *Aloe vera* (L.) Burm. f.

The dried juice occurs in dark chocolate-brown usually opaque masses; fracture, dull waxy, uneven, and frequently conchoidal.

Cape Aloe, derived from *A. ferox* Mill. and its hybrids with *A. africana* Mill. and *A. spicata* Baker

The dried juice occurs in dark brown or greenish brown glassy masses, often covered with a yellowish powder; in thin fragments it is transparent and exhibits a yellowish, reddish brown or greenish tinge; fracture, smooth, even, and glassy.

Organoleptic properties

Aloe is marketed as opaque masses that range from reddish black to brownish black to dark brown in colour. Odour, characteristic and disagreeable; taste, somewhat sour, nauseating and very bitter.

Microscopic characteristics

Powdered plant material

Powdered aloes are yellowish brown to dark reddish brown. Microscopically, Cape Aloe appears as transparent brown or greenish brown irregular and angular fragments; Curacao Aloe shows fragments with numerous minute acicular crystals embedded in an amorphous matrix.

Geographical distribution

Native to southern and eastern Africa, and subsequently introduced into northern Africa, the Arabian peninsula, China, Gibraltar, the Mediterranean countries, and the West Indies. It is commercially cultivated in Aruba, Bonaire, Haiti, **India**, South Africa, the United States of America, and Venezuela.

General identity tests

Macroscopic and microscopic examinations; solvent solubility (hot alcohol, boiling water, and ether) determination; chemical reactions; and thin-layer chromatographic analysis employing barbaloin as the reference standard.

Purity tests

Microbiology

The test for *Salmonella* spp. in aloe products should be negative. The maximum acceptable limits of other microorganisms are as follows. For preparation of decoction: aerobic bacteria—not more than 10_7/g; fungi—not more than 10_5/g; *Escherichia coli*—not more than 10_2/g. Preparations for internal use: aerobic bacteria —not more than 10_5/g or ml; fungi—not more than 10_4/g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10_3/g or ml; *Escherichia coli*—0/g or ml.

Foreign organic matter

Adulterants: Aloe in commerce may sometimes be adulterated with black catechu, pieces of iron, and stones. These can be detected by examining alcohol- soluble extracts under ultraviolet light which gives a deep brown colour with aloe and a black colour with catechu.

Total ash

Not more than 2% (*3–5*).

Water-soluble extracts
Not less than 50%

Alcohol-insoluble extracts
Not more than 10%

Moisture
Not more than 10% for Cape Aloe, and not more than 12% for Curacao or Barbados Aloe.

Pesticide residues
To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin for Aloe is not more than 0.05 mg/kg. For other pesticides, see the WHO guidelines on quality control methods for medicinal plants (*16*) and guidelines for predicting dietary intake of pesticide residues.

Heavy metals
Recommended lead and cadmium levels are not more than 10 and 0.3mg/kg, respectively, in the final dosage form of the plant material.

Radioactive residues
For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants.

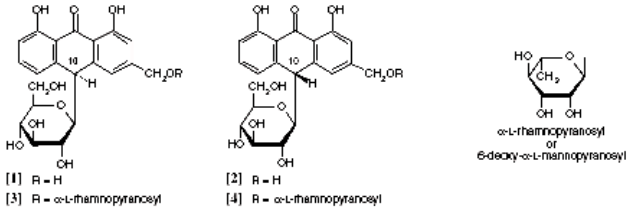
Other tests
Acid-insoluble ash and chemical tests to be established in accordance with national requirements.

Chemical assays
Thin-layer chromatography and microchemical analyses are employed for the qualitative analysis for the presence of anthracene glycosides. Quantitative analysis of total anthracene glycosides, calculated as barbaloin, is performed by spectrophotometry.

Curacao or Barbados Aloe, derived from Aloe vera (L.) Burm. f.
Contains not less than 28% of hydroxyanthracene derivatives, expressed as barbaloin.

Cape Aloe, derived from A. ferox Miller and its hybrids with A. africana Mill. and A. spicata Baker
Contains not less than 18% of hydroxyanthracene derivatives, expressed as barbaloin.

Major chemical constituents
Aloe contains as its major and active principles hydroxyanthrone derivatives, mainly of the aloe-emodin-anthrone 10-*C*-glucoside type. The major constituent is known as barbaloin (aloin) (15–40%) (*8*, *13*). It also contains hydroxyaloin (about 3%). Barbaloin (_aloin) is in fact a mixture of aloin A (10*S*) [**1**] and B (10*R*) [**2**]. *A. ferox* also contains aloinoside A [**3**] and B [**4**]. Aloin A and B
interconvert through the anthranol form as do aloinoside A and B.



Dosage forms

Powdered, dried juice and preparations thereof for oral use.

Medicinal uses

Uses supported by clinical data

Short-term treatment of occasional constipation.

Uses described in pharmacopoeias and in traditional systems of medicine

None.

Uses described in folk medicine, not supported by experimental or clinical data

Treatment of seborrhoeic dermatitis, peptic ulcers, tuberculosis, and fungal infections, and for reduction of blood sugar (glucose) levels.

Pharmacology

Experimental pharmacology

As shown for senna, Aloe's mechanism of action is twofold. It stimulates colonic motility, augmenting propulsion and accelerating colonic transit, which reduces fluid absorption from the faecal mass. It also increases paracellular permeability across the colonic mucosa probably owing to an inhibition of Na_, K_-adenosine triphosphatase or to an inhibition of chloride channels, which results in an increase in the water content in the large intestine.

Clinical pharmacology

The laxative effects of Aloe are due primarily to the 1, 8-dihydroxyanthracene glycosides, aloin A and B (formerly designated barbaloin). After oral administration aloin A and B, which are not absorbed in the upper intestine, are hydrolysed in the colon by intestinal bacteria and then reduced to the active metabolites (the main active metabolite is aloe-emodin-9-anthrone), which like senna acts as a stimulant and irritant to the gastrointestinal tract. The laxative effect of Aloe is not generally observed before 6 hours after oral administration, and sometimes not until 24 or more hours after.

Toxicity

The major symptoms of overdose are griping and severe diarrhoea with consequent losses of fluid and electrolytes. Treatment should be supportive with generous amounts of fluid. Electrolytes, particularly potassium, should be monitored in all recipients, especially in children and the elderly.

Contraindications

As with other stimulant laxatives, products containing Aloe should not be used in patients with intestinal obstruction or stenosis, atony, severe dehydration with electrolyte depletion, or chronic constipation. Aloe should not be administered to patients with inflammatory intestinal diseases, such as appendicitis, Crohn disease, ulcerative colitis, irritable bowel syndrome, or diverticulitis, or to children under 10 years of age. Aloe should not be used during pregnancy or lactation except under medical supervision after evaluating benefits and risks. Aloe is also contraindicated in patients with cramps, colic, haemorrhoids, nephritis, or any undiagnosed abdominal symptoms such as pain, nausea, or vomiting.

Warnings

Aloe-containing products should be used only if no effect can be obtained through a change of diet or use of bulk-forming products. Stimulant laxative products should not be used when abdominal pain, nausea, or vomiting are present. Rectal bleeding or failure to have a bowel movement within 24 hours. after use of a laxative may indicate a serious condition. Chronic use may cause dependence and need for increased dosages, disturbances of water and electrolyte balance (e.g. hypokalaemia), and an atonic colon with impaired function. The use of stimulant laxatives for more than 2 weeks requires medical supervision. Chronic abuse with diarrhoea and consequent fluid and electrolyte losses (mainly hypokalaemia) may cause albuminuria and haematuria, and may result in cardiac and neuromuscular dysfunction, the latter particularly in the case of concomitant use of cardiac glycosides (digoxin), diuretics, corticosteroids or liquorice root.

Precautions

General

Laxatives containing anthraquinone glycosides should not be used continuously for longer than 1–2 weeks, owing to the danger of electrolyte imbalance.

Drug interactions

Decreased intestinal transit time may reduce absorption of orally administered drugs. Existing hypokalaemia resulting from long-term laxative abuse can potentiate the effects of cardiotonic glycosides (digitalis, strophanthus) and antiarrhythmic drugs such as quinidine. The induction of hypokalaemia by drugs such as thiazide diuretics, adrenocorticosteroids, and liquorice root may be enhanced, and electrolyte imbalance may be aggravated.

Drug and laboratory test interactions

Standard methods may not detect anthranoid metabolites, so measurements of faecal excretion may not be reliable. Urinary excretion of certain anthranoid metabolites may discolour the urine, which is not clinically relevant but which may cause false positive results for urinary urobilinogen, and for estrogens when measured by the Kober procedure.

Carcinogenesis, mutagenesis, impairment of fertility

Data on the carcinogenicity of Aloe are not available. While chronic abuse of anthranoid-containing laxatives was hypothesized to play a role in colorectal cancer, no causal relationship between anthranoid laxative abuse and colorectal cancer has been demonstrated. *In vitro* (gene mutation and chromosome aberration tests) and *in vivo* (micronucleus test in murine bone marrow) genotoxicity studies, as well as human and animal pharmacokinetic data, indicate no genotoxic risk from Cape Aloe.

Pregnancy: teratogenic effects

No teratogenic or fetotoxic effects were seen in rats after oral treatment with aloe extract (up to 1000 mg/kg) or aloin A (up to 200 mg/kg).

Pregnancy: non-teratogenic effects
Aloe should not be used during pregnancy except under medical supervision after benefits and risks have been evaluated.

Nursing mothers
Anthranoid metabolites appear in breast milk. *Aloe* should not be used during lactation except under medical supervision, as there are insufficient data available to assess the potential for pharmacological effects in the breast-fed infant.

Paediatric use
Oral use of Aloe in children under 10 years old is contraindicated.

Adverse reactions
Abdominal spasms and pain may occur after even a single dose. Overdose can lead to colicky abdominal spasms and pain, as well as the formation of thin, watery stools. Chronic abuse of anthraquinone stimulant laxatives can lead to hepatitis. Long-term laxative abuse may lead to electrolyte disturbances (hypokalaemia, hypocalcaemia), metabolic acidosis, malabsorption, weight loss, albuminuria, and haematuria. Weakness and orthostatic hypotension may be exacerbated in elderly patients when stimulant laxatives are repeatedly used. Secondary aldosteronism may occur owing to renal tubular damage after aggravated use. Steatorrhoea and protein-losing gastroenteropathy with hypoalbuminaemia have also been observed, as have excessive excretion of calcium in the stools and osteomalacia of the vertebral column. Melanotic pigmentation of the colonic mucosa (pseudomelanosis coli) has been observed in individuals taking anthraquinone laxatives for extended time periods. The pigmentation is clinically harmless and usually reversible within 4 to 12 months after the drug is discontinued. Conflicting data exist on other toxic effects such as intestinal-neuronal damage after long-term use.

Posology
The correct individual dose is the smallest amount required to produce a soft-formed stool (*26*). As a laxative for adults and children over 10 years old, 0.04–0.11 g (Curacao or Barbados Aloe) or 0.06–0.17 g (Cape Aloe) of the dried juice (*6*, *14*), corresponding to 10–30mg hydroxyanthraquinones per day, or 0.1 g as a single dose in the evening.

Reference :

1. WHO monographs on selected medicinal plants.

Chapter- 6

Radix Paioneae

Definition
Radix Paeoniae is the dried root of Paeollia filciflora Pallas (Paeonaceae).

Synonyms
Paeonia alblflora Pallas., P. edulis Salisb., P. officinalis Thunb.

Selected vernacular names
Baishao, bo-baishao, chuan-baishao, hang-baishao, mu-shaoyao, mudan, paeoniae alba, paeony, pai shao yao, pe-shou, peony, peony root, Pfingstrose, shakuyaku, shaoyao, syakuyaku, white peony, white-flowered peony.

Description
Paeollia lactiflora Pallas is a perennial herb, 50-80cm high, with a stout branched root. Leaves alternate and biternately compound, the ultimate segments red- veined, oblong-elliptical. The leaflets are narrow-ovate or elliptical, 8-12 cm long and 2-4cm wide. The petioles are 6-10cm long. Flowers large (5-10cm in diameter), solitary, and red, white, or purple. Sepals 4, herbaceous, persistent. Petals 5-10, larger than sepals. Stamens numerous and anthers yellow; carpels 3-5, many-seeded. Fruit, 3-5 coriaceous few-seeded follicles. Seeds large, subglobose; testa thick.

Plant material of interest: dried root

General appearance

Radix Paeoniae is cylindrical, straight or slightly curved, two ends truncate, 5- 20cm long and 1-2.5cm in diameter; externally light greyish brown to reddish brown, glossy or with longitudinal wrinkles, rootlet scars and occasional remains of brown cork, and with laterally elongated lenticels; texture compact, easily broken, fracture relatively even, internally whitish or pale brownish red. Cambium ring distinct and rays radial.

Organoleptic properties

Odour, slight; taste, slightly sweet at first, followed bya sour or astringent taste and a slight bitterness.

Microscopic characteristics

Literature description not available; to be established in accordance with national requirements.

Powdered plant material

Light greyish brown powder; masses of gelatinized starch granules fairly abundant, 5-25µm in diameter; clusters of calcium oxalate 11-35µm in diameter,packed in parenchyma cells in rows or singly; bordered, pitted, or reticulate vessels 20-65µm in diameter, walls thickened and slightly lignified.

Geographical distribution

China, **India**, and Japan.

General identity tests

Macroscopic, microscopic, and microchemical examinations; thin-layer chromatographic analysis for the presence of the monoterpene glycoside paeoniflorin.

Purity tests

Microbiology

The test for Salmonella spp. in Radix Paeoniae products should be negative. The maximum acceptable limits of other microorganisms are as follows. For preparation of decoctions: aerobic bacteria--not more than 10 7/g; fungi--not more than 10 5/g; Escherichia coli--not more than 10 2/g. Preparations for internal use: aerobic bacteria--not more than 10 5/g or ml; fungi--not more than 10 4/g or ml; enterobacteria and certain Gram-negative bacteria--not more than 10 8/g or ml; Escherichia coli-0/g or ml.

Total Ash

Not more than 6.5%.

Acid-insoluble ash

Not more than 0.5%.

Pesticide residues

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin for Radix Paeoniae is not more than 0.05 mg/kg. For

other pesticides, see WHO guidelines on quality control methods for medicinal plants and guidelines for predicting dietary intake of pesticide residues.

Heavy metals
Recommended lead and cadmium levels are not more than 10 and 0.3 mg/kg. respectively, in the final dosage form of the plant material.

Radioactive residues
For analysis of strontium-90, iodinc-13l, cacsium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants.

Other purity tests
Alcohol-soluble extractive, chemical, foreign organic matter, moisturc and water-soluble extractive tests to be established in accordance with national requirements.

Chemical assays
Contains not less than 2.0% of paeoniflorin, assayed by a combination of thin-layer chromatographic-spectrophotometric methods or by high- performance liquid chromatography.

Major chemical constituents
Paeoniflorin, a mono terpene glycoside that is the major active constituent, is present in the range of 0.05-6.01%.

Dosage forms
Crude plant material, powder, and decoction. Store in a ventilated dry environment protected from light.

Medicinal uses

Uses supported by clinical data
None

Uses described in pharmacopoeias and in traditional systems of medicine
As an analgesic, anti-inflammatory and antispasmodic drug in the treatment of amenorrhoea, dysmenorrhoea, and pain in the chest and abdomen. Radix paeniae is also used to treat dementia, headache, vertigo, spasm of the calf muscles, liver disease, and allergies, and as an anticoagulant.

Used described in folk medicine, not supported by experimental or clinical data
The treatment of atopic eczema, boils, and sores; to reduce fevers, induce sterility, and treat burns.

Pharmacology

Experimental pharmacology
The primary pharmacological effects of Radix Paeoniae are antispasmodic, anti-inflammatory, and analgesic. A decoction of the drug had antispasmodic effects on the

ileum and uterus when administered orally to mice, rabbits, and guinea-pigs. Similar effects were observed with a methanol extract in rat uterus, but an ethanol extract had uterine stimulant activity in rabbits. Radix Paeoniae extracts tested in vitro relaxed smooth muscles in both rat stomach and uterine assays.

Intragastric administration of a hot-water extract of Radix Paeoniae to rats inhibited inflammation in adjuvant-induced arthritis and carrageenin- induced paw oedema. The major active constituent of the drug, paeoniflorin, a monoterpenoid glycoside, has sedative, analgesic, antipyretic, anti-inflammatory and vasodilatory effects in vivo. Hexobarbital-induced hypnosis was potentiated and acetic acid-induced writhing was inhibited in mice after intragastric administration of paeoniflorin.

Intragastric administration of hot-water or ethanol extracts of Radix Paeoniae to rats inhibited ADP-, arachidonic acid- and collagen-induced platelet aggregation, as well as endotoxin-induced disseminated intravascular coagulation. Similar effects were observed in rabbits and mice after intraperitoneal administration of the drug. When tested by the standard fibrin plate method, ethanol and hot-water extracts of the drug had antifibrinolytic activity in vitro. Paeoniflorin had anticoagulant activity both in vitro, and in vivo (in mice).

Intragastric administration of extracts of Radix Paeoniae protected the liver against carbon tetrachloride-induced hepatotoxicity in mice and rats.

Oral administration of water extracts of Radix Paeoniae or its major constituent, paeoniflorin, attenuated the scopolamine-induced impairment of radial maze performance in rats. Paeoniflorin prevented the scopolamine- induced decrease in acetylcholine content in the striatum, but not in the hippocampus or cortex. Oral administration of paeoniflorin further attenuated learning impairment of aged rats in operant brightness discrimination tasks. The results of this study suggest that further research to explore the therapeutic potential of paeoniflorin in cognitive disorders such as senile dementia may be promising.

Contraindications
Reports of traditional use indicate that Radix Paeoniae may have abortifacient activity; therefore, the use of Radix Paeoniae in pregnancy is contraindicated.

Warnings
No information available.

Precautions

Drug interactions
Radix Paeoniae should not be combined with Fritillaria vericillata, Cuscuta japonica, and Rheum officinale.

Carcinogenesis, mutagenesis, impairment of fertility
Hot-water or methanol extracts of Radix Paeoniae are not mutagenic in vitro.

Pregnancy: non-teratogenic effects

Reports of traditional use indicate that Radix Paeoniae may have abortifacient activity; therefore, the use of Radix Paeoniae in pregnancy is contraindicated.

Nursing mothers

Excretion of the drug into breast milk an dits effects on the newborn have not been established; therefore, use of the drug during lactation is not recommended.

Paediatric use

No information available about general precautions, drug and laboratory test interactions, or teratogenic effects on pregnancy.

Adverse reactions

No information available.

Posology

Maximum daily oral dose of crude plant material, 6-15g, standardized for paeoniflorin.

Refrence :

1. European pharmacopoeia, 3rd ed. Strasbourg, Council of Europe, 1997.
2. Guidelines for predicting dietary intake of pesticide residues, 2nd rev. ed. Geneva, World Health Organization, 1997 (unpublished document WHO/FSF/FOS/97.7; available from Food Safety, WHO, 1211 Geneva 27, Switzerland).
3. Quality control methods for medicinal plant materials. Geneva, World Health Organization,1998.

Chapter – 7

Radix Rauwolfiae

Definition

Radix Rauwolfiae is the dried root of *Rauvolfia serpentina* (L.) Benth. ex Kurz (Apocynaceae)

Synonyms

Ophioxylon obversum Miq., *O. sautiferum* Salisb., *O. serpentinum* L., *Rauvolfia obversa* (Miq.) Baill., *R. trifoliata* (Gaertn.) Baill.

Selected vernacular names

Most commonly called “rauwolfia”. Acawerya, aika-wairey, akar-tikos, arsol, bhudra, bongmaiza, chandmaruwa, chandra, chandrika, chotachand, chotachard, chundrika, chundrooshoora, churmuhuntree, chuvannayilpuri, covanamilpori, covannamipori, dhanbarua, dhannerna, dogrikme, eiya-kunda, ekaweriya, garudpathal, hadki, harkai, harkaya, ichneumon plant, Indian snakeroot, indojaboku, karai, karavi, karuvee, makeshwar chadrika, makeshwar churna, matavi-aloos, nogliever, nundunee, pagla-ka-dawa, palalganni, patalaagandhi, poelé pandak, poeleh pandak, pushoomehnunkarika, ra-yom, radix mungo, radix mustelae, raiz de mongo alba, rametul, ratekaweriya, rayom noi, rauvolfia, rauwalfia, rauwolfia, Rauwolfiawurzel, sanochado, sapasan, sarpagandha, sarpgandha, serpentina, sjouanna-amelpodi, snakeroot, sung, suvapaval-amepodi, talona, vasoopooshpa, vasura.

Description

Small, erect, glabrous shrub, 30–60 cm high. Leaves whorled, 7.5–17.5 cm long, lanceolate or oblanceolate, acute or acuminate, tapering gradually into the petiole, thin. Flowers white or pinkish; peduncles 5.0–7.5 cm long; pedicels and calyx red. Calyx lobes 2.5 mm long, lanceolate. Corolla about 1–1.3cm long; tube slender; inflated slightly above middle; lobes much shorter than tube, obtuse. Drupes about 6 mm (diameter), single or didymous and more or less
connate, purplish black when ripe.

Plant material of interest: root

General appearance

The root occurs as segments 5–15cm in length and 3–20mm in diameter, subcylindrical to tapering, tortuous or curved, rarely branched, occasionally bearing twisted rootlets, which are larger, more abundant, and more rigid and woody on the thicker parts of the roots. Externally light brown to greyish yellow to greyish brown, dull, rough or slightly wrinkled longitudinally, yet smooth to the touch, occasionally showing rootlet scars on the larger pieces, with some exfoliation of the bark in small areas that reveals the paler wood beneath. Bark separates easily from the wood on scraping. Fracture short but irregular, the longer pieces readily breaking with a snap, slightly fibrous marginally. The freshly fractured surfaces show a rather thin layer of greyish yellow bark, and the pale yellowish white wood constitutes about 80% of the radius. The smooth transverse surface of larger pieces shows a finely radiate stele with three or more clearly marked growth rings; a small knob-like protuberance isfrequently noticeable in the centre. The wood is hard and of relatively low density.

Organoleptic properties

Root odour is indistinct, earthy, reminiscent of stored white potatoes, and the taste is bitter.

Microscopic characteristics

A transverse section of the root shows externally 2–8 alternating strata of cork cells, the strata with larger cells alternating with strata made up of markedly smaller cells. Each stratum composed of smaller cells includes 3–5 tangentially arranged cell layers. In cross-sectional view, the largest cells of the larger cell group measure 40–90µm radially and up to 75µm tangentially, while the cells of the smaller group measure 5–20µm radially and up to 75µm tangentially. The walls are thin and suberized. The secondary cortex consists of several rows of tangentially elongated to isodiametric parenchyma cells, most densely filled with starch grains; others (short latex cells) occur singly or in short series and contain brown resin masses. The secondary phloem is relatively narrow and is made up of phloem parenchyma (bearing starch grains and less commonly tabular to angular calcium oxalate crystals up to 20µm in length; also, occasionally, with some brown resin masses in outer cells and phloem rays) interlaid with scattered sieve tissue and traversed by phloem rays 2–4 cells in width. Sclerenchyma cells are absent in root (a distinction from other *Rauvolfia* species). Cambium is indistinct, narrow, dark, and wavering. The secondary xylem represents the large bulk of the root and shows one or more prominent annual rings with a dense core of wood about 500µm across at the centre. The xylem is composed of many wood wedges separated by xylem rays, and on closer examination reveals vessels in interrupted radial rows, much xylem parenchyma,

many large-celled xylem rays, few wood fibres, and tracheids, all with lignified walls. The xylem fibres occur in both tangential and radial rows. The xylem rays are 1–12, occasionally up to 16 cells in width.

Powdered plant material

Powdered Radix Rauwolfiae is brownish to reddish grey. Numerous starch grains (simple, 2- to 3-compound, occasionally 4-compound) present; simple grains spheroid, ovate, plano- to angular-convex, or irregular; hilum simple, Yshaped, stellate, or irregularly cleft; unaltered grains 6–34µm in diameter; altered grains up to about 50µm; large unaltered grains clearly show polarization cross; calcium oxalate prisms and cluster crystals scattered, about 10–15µm in size; brown resin masses and yellowish granular secretion masses occur occasionally; isolated cork cells elongated, up to 90µm in length; phelloderm and phloem parenchyma cells similar in appearance; vessels subcylindrical, up to 360µm in length and about 20–57µm in diameter, the vessel end walls oblique to transverse, generally with openings in the end walls, some vessels showing tyloses; tracheids pitted, with moderately thick, tapering, beaded walls, with relatively broad lumina, polygonal in cross-section; xylem parenchyma cells with moderately thick walls with simple circular pits, cells polygonal in crosssection, bearing much starch, sometimes with brown resin masses; xylem fibres with thick heavily lignified walls showing small transverse and oblique linear pits and pointed simple to bifurcate ends, measuring about 200–750µm in length. No phloem fibres or sclereids are present in root (colourless non-lignified pericycle or primary phloem fibres, single or in small groups, may be present from rhizome or stem tissues).

Geographical distribution

The plant is found growing wild in the sub-Himalayan tracts in **India** and is alsofound in Indonesia, Myanmar, and Thailand.Overcollection of Radix Rauwolfiae in India has significantly diminishedsupply and since 1997 there has been an embargo on export of this drug from India. Reserpine is currently either extracted from the roots of *Rauvolfia vomitoria* of African origin or produced by total synthesis.

General identity tests

Macroscopic and microscopic examinations and thin-layer chromatographic analysis for the presence of characteristic indole alkaloids.

Purity tests

Microbiology

The test for *Salmonella* spp. in Radix Rauwolfiae products should be negative. The maximum acceptable limits of other microorganisms are as follows.
For preparation of decoction: aerobic bacteria—not more than 107/g; moulds and yeast not more than 104/g; *Escherichia coli*—not more than 102/g; other enterobacteria— not more than 104/g. Preparations for internal use: aerobic bacteria— not more than 105/g; moulds and yeast—not more than 103/g; *Escherichia coli*—not more than 101/g; other enterobacteria—not more than 103/g.

Foreign organic matter

Not more than 2.0% of stems, and not more than 3.0% of other foreign organic matter.

Total ash
Not more than 10%

Acid-insoluble ash
Not more than 2.0%

Moisture
Not more than 12%

Pesticide residues
To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in Radix Rauwolfiae is not more than 0.05 mg/kg . For other pesticides, see WHO guidelines on quality control methods for medicinal plants and guidelines for predicting dietary intake of pesticide residues.

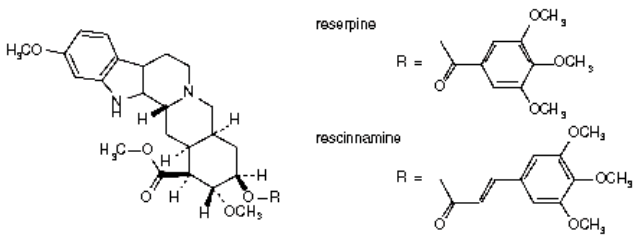
Heavy metals
Recommended lead and cadmium levels are no more than 10 and 0.3mg/kg, respectively, in the final dosage form of the plant material.

Radioactive residues
For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants.

Other purity tests
Chemical, alcohol-soluble extractive and water-soluble extractive tests to be established in accordance with national requirements.

Chemical assays
Contains not less than 1% total alkaloids; and a minimum of 0.1% alkaloids of the reserpine–rescinnamine group Thin-layer chromatography to detect the presence of the reserpine– rescinnamine group of alkaloids. Quantitative analysis of total and reserpine–rescinnamine group of alkaloids can be performed by spectrophotometric analysis or by high-performance liquid chromatography.

Major chemical constituents
Radix Rauwolfiae contains more than 60 indole alkaloids; the principal hypotensive alkaloids are identified as reserpine and rescinnamine.



Dosage forms

Crude drug and powder. Package in well-closed containers and store at 15–25°C in a dry place, secure against insect attack.

Medicinal uses

Uses supported by clinical data

The principal use today is in the treatment of mild essential hypertension.Treatment is usually administered in combination with a diuretic agent to support the drug's antihypertensive activity, and to prevent fluid retention which may develop if Radix Rauwolfiae is given alone.

Uses described in pharmacopoeias and in traditional systems of medicine

As a tranquillizer for nervous and mental disorders.

Uses described in folk medicine, not supported by experimental or clinical data

As a tonic in states of asthenia, a cardiotonic and antipyretic; against snake and insect bites; and for constipation, liver diseases, flatulence, insomnia, and rheumatism.

Pharmacology

Experimental pharmacology

It is well accepted that the pharmacological effects of Radix Rauwolfiae are due to its alkaloids, especially the reserpine–rescinnamine group. The experimental pharmacology of reserpine and related compounds has been well documented. Powdered Radix Rauwolfiae, as well as various forms of extracts (ethanolic, dried), has been reported to lower the blood pressure of experimental animals (dogs or cats) by various routes of administration.

Clinical pharmacology

Radix Rauwolfiae and its major alkaloids probably lower high blood pressure by depleting tissue stores of catecholamines (epinephrine and norepinephrine) from peripheral sites. By contrast, their sedative and tranquillizing properties are thought to be related to depletion of catecholamines and serotonin (5- hydroxytryptamine) from the brain. Following absorption from the gastrointestinal tract the active alkaloids concentrate in tissues with high lipid content. They pass the blood–brain barrier and the placenta. Radix Rauwolfiae products are characterized by slow onset of action and sustained effect. Both the cardiovascular and central nervous system effects may persist following withdrawal of the drug. The active alkaloids are metabolized in the liver to inactive compounds that are excreted primarily in the urine. Unchanged alkaloids are excreted primarily in the faeces.

Contraindications

Radix Rauwolfiae products are contraindicated in patients who have previously demonstrated hypersensitivity to the plant or its alkaloids. They are also contraindicated in patients with a history of mental depression (especially those with suicidal tendencies) during or shortly after therapy with monoamine oxidase inhibitors; active peptic ulcer,

sinus node disorders, ulcerative colitis; epilepsy; or decreased renal function; and in patients receiving electroconvulsive therapy.

Warnings

Radix Rauwolfiae products may cause mental depression (*24*). Recognition of depression may be difficult because this condition may often be disguised by somatic complaints (masked depression). The products should be discontinued at first signs of depression such as despondency, early morning insomnia, loss of appetite, impotence, or self-deprecation. Drug-induced depression may persist for several months after drug withdrawal and may be severe enough to result in suicide. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. The use of Radix Rauwolfiae products may impair alertness and make it inadvisable to drive or operate heavy machinery.

Precautions

General

Because Radix Rauwolfiae preparations increase gastrointestinal motility and secretion, they should be used cautiously in persons with a history of peptic ulcer, ulcerative colitis, or gallstones where biliary colic may be precipitated. Persons on high doses should be observed carefully at regular intervals to detect possible reactivation of peptic ulcer. Caution should be exercised when treating hypertensive patients with renal insufficiency since they adjust poorly to lowered blood-pressure levels.

Drug interactions

When administered concurrently, the following drugs may interact with or potentiate Radix Rauwolfiae and its alkaloids: alcohol or other central nervous system depressants, other antihypertensives or diuretics, digitalis glycosides or quinidine, levodopa, levomepromazine, monoamine oxidase inhibitors, sympathomimetics (direct-acting) and tricyclic antidepressants. Concomitant use of Radix Rauwolfiae products and anaesthetics may provoke a fall in blood pressure and add to the _ adrenoceptor–blocking activity of propranolol.

Drug and laboratory test interactions

Chronic administration of Radix Rauwolfiae preparations may increase serum prolactin levels and decrease excretion of urinary catecholamines and vanilmandelic acid. Therefore, any diagnostic tests performed for these determinations should be interpreted with caution. Radix Rauwolfiae preparations slightly decrease absorbance readings obtained on urinary steroid colorimetric determinations (e.g. modified Glenn– Nelson technique or Holtorff Koch modification of Zimmermann reaction), and thus false low results may be reported. Preoperative withdrawal of Radix Rauwolfiae products does not necessarily ensure circulatory stability during the procedure, and the anaesthetist must be informed of the patient's drug history. Caution is indicated in elderly patients and also in those suffering from coronary and cerebral arteriosclerosis. Administration of products including Radix Rauwolfiae preparations at doses that might precipitate a sharp decrease in blood pressure should be avoided.

Carcinogenesis, mutagenesis, impairment of fertility

Animal carcinogenicity studies using reserpine at doses 50 times as high as the average human dose have been conducted with rats and mice. Carcinogenic effects associated with the administration of reserpine include an increased incidence of adrenal medullary phaeochromocytomas in male rats, unidentified carcinomas of the seminal vesicles in male mice, and mammary cancer in female mice; carcinogenic effects were not seen in female rats. Bacteriological studies to determine mutagenicity using reserpine showed negative results. The extent of risk to humans is uncertain.

Pregnancy: teratogenic effects

Reserpine, the major active alkaloid in Radix Rauwolfiae, administered parenterally has been shown to be teratogenic in rats at doses up to 2mg/kg and to have an embryocidal effect in guinea-pigs at 0.5 mg daily. There are no adequate and well-controlled studies in pregnant women.

Pregnancy: non-teratogenic effects

Increased respiratory secretions, nasal congestion, cyanosis, hypothermia, and anorexia have occurred in neonates of mothers treated with Radix Rauwolfiae. Therefore, the use of Radix Rauwolfiae is not recommended during pregnancy.

Nursing mothers

Rauwolfia alkaloids are excreted in human milk. Because of the potential for serious adverse reactions in nursing infants, use of Radix Rauwolfiae during lactation is not recommended.

Paediatric use

Safety and effectiveness in children have not been established.

Adverse reactions

The following adverse reactions have been observed, but there are insufficient data to support an estimate of their frequency. The reactions are usually reversible and disappear when the Radix Rauwolfiae preparations are discontinued. Cardiovascular system: bradycardia, arrhythmias, particularly when used concurrently with digitalis or quinidine, angina-like symptoms. Water retention with oedema in persons with hypertensive vascular disease may occur rarely, but the condition generally clears with cessation of therapy, or the administration of a diuretic agent. Vasodilation produced by rauwolfia alkaloids may result in nasal congestion, flushing, a feeling of warmth, and conjunctival congestion. Central nervous system: sensitization of the central nervous system manifested by optic atrophy, glaucoma, uveitis, deafness, and dull sensorium. Other reactions include depression, paradoxical anxiety, nightmares, nervousness, headache, dizziness, drowsiness. Large doses have produced parkinsonian syndrome, other extrapyramidal reactions, and convulsions. Gastrointestinal system: hypersecretion and increased intestinal motility, diarrhoea, vomiting, nausea, anorexia, and dryness of mouth. Gastrointestinal bleeding has occurred in isolated cases. Respiratory system: dyspnoea, epistaxis, nasal congestion. Hypersensitivity: purpura, pruritus, rash. Other: dysuria, muscular aches, weight gain, breast engorgement, pseudolactation, impotence or decreased libido, gynaecomastia.

Posology

Powder, 200 mg daily in divided doses for 1–3 weeks; maintenance 50–300mg daily. Doses of other preparations should be calculated accordingly. Doses of Radix Rauwolfiae should be based on the recommended dosage of rauwolfia alkaloids, which must be adjusted according to the patient's requirements and tolerance in small increments at intervals of at least 10 days. Debilitated and geriatric patients may require lower dosages of rauwolfia alkaloids than do other adults. Rauwolfia alkaloids may be administered orally in a single daily dose or divided into two daily doses.

Reference:

1. WHO monographs on selected medicinal plants.

Chapter – 8

Withania sumnifera

Description:

Common name: Ashwagandha
Family: Solanaceae
Author: (L.) Dunal.

Botanical references:

Synonyms: Physalis somnifera
Known Hazards: The plant is toxic if eaten.
Range: Australia, E. Asia, Africa
Habitat: Open places, disturbed areas etc. An undershrub in stony places.
Plants For A Future Rating (1-5): 3
Other Possible Synonyms : From various places across the web, may not be correct.
Physalis somnifera[G]

Other Common Names: Ajagandha [E], Ashwagandha [H], Clustered Wintercherry [H], Kanaje Hindi [E], Orovale [E], Samm Al Ferakh [E], Strychnos [E], Withania [P]
Epithets: somnifer = sleep inducing; somnifera = sleep inducing
Other Range Info: Afghanistan; Africa; Asia; Ethiopia; Greece; India; India(Ayurvedic); India(Punjab); India(Rajasthan); Iraq; Lesotho; Pakistan; South Africa(Kaffir); Spain; Sudan; Yemen.
Plant Passport required for Trade in UK/EU: Plant Passport Required for commercial growers in the UK/Europe.

History :
Robin Lane Fox, in his biography of Alexander the Great, claims *Withania somnifera* has been used in wine in ancient times. According to Anne Van Arsdall, *Withania somnifera* was called *apollinaris* and also *glofwyrt* in *The Old English Herbarium*, and had a legend that Apollo found it first and gave it to the healer Aesculapius.

Physical Characteristics
An evergreen shrub growing to 1m by 0.5m . It is hardy to zone 9 and is frost tender. It is in leaf all year. The flowers are hermaphrodite (have both male and female organs). We rate it 3 out of 5 for usefulness. The plant prefers light (sandy), medium (loamy) and heavy (clay) soils and requires well-drained soil. The plant prefers acid, neutral and basic (alkaline) soils. It cannot grow in the shade. It requires moist soil.

Habitats and Possible Locations
Woodland, Cultivated Beds, Sunny Edge, Dappled Shade, By Walls, By South Wall, By West Wall.

Edible Uses
Curdling agent. The seeds are used to curdle plant milks in order to make vegetarian cheeses.

Medicinal Uses
Disclaimer *Abortifacient; Adaptogen; Antibiotic; Aphrodisiac; Astringent; Deobstruent; Diuretic; Narcotic; Sedative; Tonic.* Ashwagandha is one of the most widespread tranquillisers used in India, where it holds a position of importance similar to ginseng in China. It acts mainly on the reproductive and nervous systems, having a rejuvenative effect on the body, and is used to improve vitality and aid recovery after chronic illness. The plant is little known in the West.

The whole plant, but especially the leaves and the root bark, are abortifacient, adaptogen, antibiotic, aphrodisiac, deobstruent, diuretic, narcotic, strongly sedative and tonic. Internally, it is used to tone the uterus after a miscarriage and also in treating post-partum difficulties. It is also used to treat nervous exhaustion, debility, insomnia, wasting diseases, failure to thrive in children, impotence, infertility, multiple sclerosis etc. Externally it has been applied as a poultice to boils, swellings and other painful parts. The root is harvested in the autumn and dried for later use. Some caution is advised in the use of this plant since it is toxic[K].

The fruit is diuretic. The seed is diuretic and hypnotic.

All parts of the plant are used in herbal medicine. In Ayurveda, the fresh roots are sometimes boiled in milk, prior to drying, in order to leach out undesirable constituents. The berries are used as a substitute for rennet, to coagulate milk in cheese making

Ashwagandha in Sanskrit means "horse's smell", probably originating from the odor of its root which somewhat resembles that of a sweaty horse. The species name *somnifera* means "sleep-bearing" in Latin, indicating it was considered a sedative, but it has been also used for sexual vitality and as an adaptogen. Some herbalists refer to ashwagandha as Indian ginseng, since it is used in ayurvedic medicine in a similar way that ginseng is used in traditional Chinese medicine. The product called "ashwagandha oil" is a combination of ashwagandha with almond oil and rose water designed to be used as a facial toner, therefore should not be consumed.

Other Uses

Repellent; Soap. The fruit is rich in saponins and can be used as a soap substitute. The leaves are an insect repellent.

Cultivation details

A fairly easily grown plant, it requires a warm sheltered position in full sun and a well-drained moderately fertile soil. Prefers a dry stony soil. This species is not hardy in temperate climates but it can be grown as an annual, flowering and fruiting in its first year from seed.

Propagation

Seed - sow early spring in a greenhouse. There is usually a high germination rate within 2 weeks. Prick out the seedlings into individual pots once they are large enough to handle and plant them out after the last expected frost. Consider giving the plants some protection, such as a cloche, until they are established and growing away well.

Other Species and Parts of the Herb that are Used

So far, all discussion is about the use of the root which possesses the most valued tonic properties. However, the bitter leaves are used as a hypnotic in the treatment of alcoholism and to relax the spasms of the lungs for the treatment of asthma and emphysema. They can also be made into an anti-inflammatory poultice and topically applied for boils and carbuncles. Internally, as with so many other strongly bitter herbs, they are anthelmintic (clearing worms). The seeds of the fruits are diuretic and can be used as a substitute for rennet to curdle milk.

Ashwagandha Coagulans, a related species and occasional adulterant, primarily uses the inside kernel of the seed capsule containing “withanin” which is similar to rennet to curdle milk. “About a tablespoon of the mixture of seeds with a little milk (1 in 40) is enough to coagulate a gallon of milk in approximately a half an hour.” [1][12] Alcohol will destroy the coagulating principle but the dried capsules can be used. A. coagulans is also therapeutically used as an alterative and emetic.

1

History, Description and Pharmacology

The use of ashwagandha in Ayurvedic medicine extends back over 3000 to 4000 years to the teachings of an esteemed rishi (sage) Punarvasu Atriya [2][13] . It has been described in the sacred texts of Ayurveda, including the Charaka and Sushruta Samhitas where it is widely extolled as a tonic especially for emaciation in people of all ages including babies, enhancing the reproductive function of both men and women. It has also been used for inflammations especially for arthritic and rheumatic conditions and as a major tonic to counteract the ravages of aging and promote youthful longevity. Some of its other traditional uses have been as a mild purgative for chronic constipation and for the treatment of swollen glands.

Ashwagandha is a small woody shrub or herb in the Solanaceae family that grows usually about 2 feet in height and is naturally found in diverse areas ranging from Africa, the Mediterranean and East into India. Because of its wide range, there is considerable morphological and chemotypical variations in terms of local species. Considering its powerful healing properties, except for the bright red fruit, it is a fairly plain, nondescript plant. The fruit is harvested in the late fall and the bright yellow seeds are dried for planting in the following spring. The cultivated Nagori species of Ashwagandha seems to be significantly larger, one source describing it as a shrub growing from 5 to 7 feet tall. However, the primary alkaloids of both the wild as well as the cultivated species are the same.

The commercial supplies of ashwagandha are obtained from both wild and commercial sources. The fresh root of one year old plants are harvested from January to March. It is either dried whole or cut in short transverse pieces and dried directly in the sun. Quality is determined by the size of the main tap root as well as its color, odor and flavor.

The major biochemical constituents of ashwagandha from which its primary medicinal properties emanate, are based upon the actions of certain steroidal alkaloids and steroidal lactones in a class of constituents called withanolides[3] [14] . These serve as important hormone precursors which the body is then able, as needed, to convert into human physiological hormones. If there is an excess of a certain hormone, the plant based hormone precursors occupy the so-called hormone receptor sites, without converting to human hormones, to block absorption. In this way, ashwagandha, like other adaptogenic tonic herbs, is amphoteric and can serve to regulate important physiological processes, increasing or decreasing as needed.

The term adaptogen was first defined by the Russians[4] [15] as a result of their extensive research on the tonic, Siberian Ginseng (Eleutherococcus senticosus). The definition of adaptogen is based on the following, according to Brekhman: 1). Safety of the adaptogen's action on the organism; 2). A wide range of regulatory activity, but manifesting its action only against the actual challenge to the system; 3). Act through a nonspecific mechanism to increase the nonspecific resistance (NSR) to harmful influences of an extremely wide spectrum of physical, chemical and biological factors causing stress; 4). Has a normalizing action irrespective of the direction of foregoing pathological changes.

2

3

4

An adaptogenic herb of which ashwagandha would be a first rate example[5] [16], allows one to adapt to a variety of is a class of herbs that allows one to adapt to a variety of heightened stressful circumstances. This will result in heightened stamina and endurance for athletic competition, the workplace and conditions of inclement environment and weather conditions.

With its ease of cultivation, there is hardly a reason that most people and certainly old age nursing homes does not have its own garden patch of ashwagandha as a hedge, so to speak, against the ravages of aging decrepitude. Given the fact that for better or worse, more people are living longer in the world than any other time in its history, trying to save enough money in long term retirement accounts for a comfortable old age and at the same time sensing real concerns at the thought of dwindling governmental entitlement benefits, it seems imperative that everyone grow their personal supply of ashwagandha and learn how to prepare and take it.

Besides over 3000 years of empirical experience, numerous studies on both animals and humans have attested to the anti-arthritis and mind calming properties of crude preparations of the herb. The combined alkaloids seem to exhibit calming, anti-convulsant and antispasmodic properties against many spasmogenic agents on the intestinal, uterine, bronchial, tracheal and blood-vascular muscles. It is described as similar but considerably weaker that papaverine and phenobarbitone[6] [17] . Other constituents, namely the sitoindosides enhance pathogenic devouring phagocytes. Even anti-tumor properties have been found based on the use of the crude extract on mice both in living specimens as well as against cancer cells in the petri dish.

PREPARATIONS:

Ashwagandha is used in Ayurvedic medicine as a powder, decoction, medicated wine, mixed with clarified butter, combined with honey or sugar syrup or as a medicated oil. The most common form is as an alcoholic extract or capsules, of the powdered root.

Dosage is as follows:

Powder:	3-6 grams daily or up to 5 to 10 grams as an occasional tonic
Decoction:	16 to 31 grams added to heated cow's milk
Alcoholic Extract:	2 Tblsp., 2-4 times daily.
Mixed with ghee or honey:	1 tsp. 2 times daily
Narayana Taila Oil:	Internally, 3-10 drops; or freely applied externally to painful, arthritic joints.

Contraindications and Toxicity:

Large doses of ashwagandha may possess abortifacient properties so that it should not be taken drink pregnancy unless under the direction of an experienced health professional. It is also contraindicated in conjunction with sedatives or anxioletics (a substance that reduces anxiety) or if one is suffering from stomach ulcers. Traditionally, like other tonics

5

6

such as ginseng, ashwagandha should not be taken when there are signs of inflammation or advanced arterial congestion. For this reason is may be best to precede or accompany taking it with a general detoxifying herb or formula such as Yogaraj guggul.

Ashwagandha is relatively safe when taken in the prescribed range of dosage. [7][18] Large doses, however, have been shown to cause gastrointestinal upset, diarrhea and vomiting. Finally, because ashwagandha has been found to potentiate the effects of barbituates, it is generally recommended that it be not taken under such conditions.

Ashwagandha according to the TCM model:

Because of its actions and flavors, ashwagandha would be classified as a Yang tonic with particular affinity for the Kidneys, because of its hormonal action, and the Heart, because of its ability to calm the mind and relieve anxiety and insomnia. As an anti-arthritis and antispasmodic, it has wind dispelling properties. Ashwaganda is used by herbalist Alan Tillotson and his Chinese herbalist wife, Naixin, for cases where ginseng is too stimulating or hot and the patient appears nervous and fragile. For fatigue caused by overwork without nervousness, he prefers to use Siberian ginseng.

Some Traditional and Non-Traditional Ayurvedic Combinations Using Ashwagandha are as Follows:

General Use: The root is taken in 30 gram dosage for general debility, consumption, mal-nourishment in children, senile debility, rheumatic and arthritic conditions, nervous exhaustion, fatigue, brain-gag, memory weakness, senile dementia, muscular weakness, spermatorrhea and leucorrhea. Normally this can be taken as a powder 10 grams three times daily mixed with warm milk or water, or as a one to 5 alcoholic extract, one or two tablespoonsful three times daily.

For insomnia, ashwagandha can be mixed with valerian root and oyster shell.

As a general nerve tonic, especially for hypoglycemia or low blood pressure, ashwagandha is combined with Goksura.

For chronic fatigue ashwagandha is combined with another great Ayurvedic tonic herb, shatavari (Asparagus racemosa), licorice, amla (emblica myrobalan) and multi-minerals, especially calcium and magnesium. If there is mild inflammation or low grade fevers Dr. Mana, a prominent Nepalese Ayurvedic doctor gives a separate formula to reduce inflammation along with the ashwagandha preparation.

For impotence it can be used alone or combined with fried Cow-hage seeds. The method is to remove the inside of the seeds and mix this with ashwagandha and ginger.

7

For weak lungs, ashwagandha is combined with Sida cordifolia (Bala).

Milk, to stimulate production: combine with equal parts Dioscorea batatas (also available as Shan Yao, a Chinese herb) and licorice and make a decoction of 30 grams of the mixture. Take three times daily.

Nerve tonic

combine with Goksura (Hygrophila spinosa) equal parts. This is especially good for hypoglycemia and low blood pressure.

Nutrition

of malnourished children, Improving: Make a paste of the root with ghee and milk. Administer three times daily.

Skin diseases

Make a salve of ashwagandha or mix the powder with sesame oil and apply topically.

Sterility, Female: Boil a decoction of 30 grams in water down to half a cup, add mild and one tablespoon of ghee (clarified butter) and a teaspoon of honey. Take three times daily for two weeks after menstruation.

Ashwagandha is available from Planetary Formulas Online Store. For further information about Michael Tierra's East West School of Herbology please visit our website: www.planetherbs.com

References

American Herbal Pharmacopoeia and Therapeutic Compendium, Ashwagandha Root Monograph, coordinated by herbalist Upton, Roy, President of the American Herbalist Guild, et al. 1996 (pending publication).

PFAF Web Pages

This plant is mentioned in the following web pages

- PFAF Catalogue: Checklist of plants

  PFAF Plant Catalogue (T-W)

Web References

-
- [H] Details of Scandanavian and European Common names in Henriette's names database

- [E] Ethnobotany Data (common names, uses, countries) from the Ethnobotany Database (sadly ftp only. The searchable web pages have been pulled).
- http://www.planetherbs.com/articles/ashwagandha.htm

  http://www.planetherbs.com/showcase/

Chapter- 9

Bulbus Allii Cepae

Definition

Bulbus Allii Cepae is the fresh or dried bulbs of *Allium cepa* L. (Liliaceae) or its varieties and cultivars.

Synonyms

Allium esculentum Salisb., *Allium porrum cepa* Rehb.

Selected vernacular names

It is most commonly known as “onion”. Basal, basl, cebolla, cebolla morada, cepa bulb, cepolla, cipolla, common onion, cu hanh, hom hua yai, hom khaao, hom yai, hu-t’sung, hu t’sung t’song, hua phak bhu, i-i-bsel, kesounni, khtim, Küchenzwiebel, l’oignon, loyon, Madras oignon, oignon, palandu, piyaj, piyaz, pyaz, pyaaz, ralu lunu, red globe onion, sibuyas, Spanish onion, tamanegi, umbi bawang merah, vengayan, yellow Bermuda onion, white globe onion, Zwiebel.

Description

A perennial herb, strong smelling when crushed; bulbs vary in size and shape from cultivar to cultivar, often depressed-globose and up to 20 cm in diameter; outer tunics membranous. Stem up to 100cm tall and 30 mm in diameter, tapering from inflated lower part. Leaves up to 40 cm in height and 20mm in diameter, usually almost semicircular in section and slightly flattened on upper side; basal in first year, in second year their bases sheathing the lower sixth of the stem. Spathe often 3-valved, persistent, shorter than the umbel. Umbel 4–9cm in diameter, subglobose or hemispherical, dense, many-flowered; pedicels up to 40mm, almost equal. Perianth stellate; segments 3–4.5 _ 2–2.5mm, white, with green stripe, slightly unequal, the outer ovate, the inner oblong, obtuse or acute. Stamens exserted; filaments 4–5mm, the outer subulate, the inner with an expanded base up to 2 mm wide and bearing short teeth on each side. Ovary whitish. Capsule about 5mm, 2*n* _ 16.

Plant material of interest: fresh or dried bulbs

General appearance

Macroscopically, Bulbus Allii Cepae varies in size and shape from cultivar to cultivar, 2-20cm in diameter; flattened, spherical or pear-shaped; white or coloured.

Organoleptic properties

Odour strong, characteristic alliaceous; taste strong; crushing or cutting the bulb stimulates lachrymation.

Microscopic characteristics

The external dried leaf scales of the bulbs show a large-celled epidermis with lightly spotted cell walls; the cells are elongated longitudinally. The underlying hypodermis runs perpendicular to the epidermis and contains large calcium oxalate crystals bordering the cell walls. The epidermis of the fleshy leaf scales resembles that of the dried leaf scales, and the epidermal cells on the dorsal side are distinctly longer and more elongated than the epidermal cells on the ventral side. Large calcium oxalate crystals are found in the hypodermis; stomata rare; large cell nuclei conspicuous; and spiral vessel elements occur in the leaf mesophyll.

Powdered plant material

Contains mainly thin-walled cells of the mesophyll with broken pieces of spiral vessel elements; cells containing calcium oxalate crystals are scarce.

Geographical distribution

Bulbus Allii Cepae (“onion”) is probably indigenous to western Asia, but it is commercially cultivated worldwide, especially in regions of moderate climate.

General identity tests

Macroscopic inspection, microscopic characteristics and microchemical examination for organic sulfur compounds; and thin-layer chromatographic analysis for the presence of cysteine sulfoxides.

Purity tests

Microbiology
The test for *Salmonella* spp. in Bulbus Allii Cepae products should be negative. The maximum acceptable limits of other microorganisms are as follows (*12– 14*).
Preparations for oral use: aerobic bacteria—not more than 105/g or ml; fungi—not more than 104/g or ml; enterobacteria and certain Gram-negative bacteria—not more than 103/g or ml; *Escherichia coli*—0/g or ml.

Total ash
Not more than 6%

Acid-insoluble ash
Not more than 1.0%

Water-soluble extractive
Not more than 5.0%

Alcohol-soluble extractive
Not more than 4.0%

Pesticide residues
To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin for Bulbus Allii Cepae is not more than 0.05 mg/kg. For other pesticides, see WHO guidelines on quality control methods for medicinal plants and guidelines for predicting dietary intake of pesticide residues.

Heavy metals
Recommended lead and cadmium levels are no more than 10 and 0.3mg/kg, respectively, in the final dosage form of the plant material.

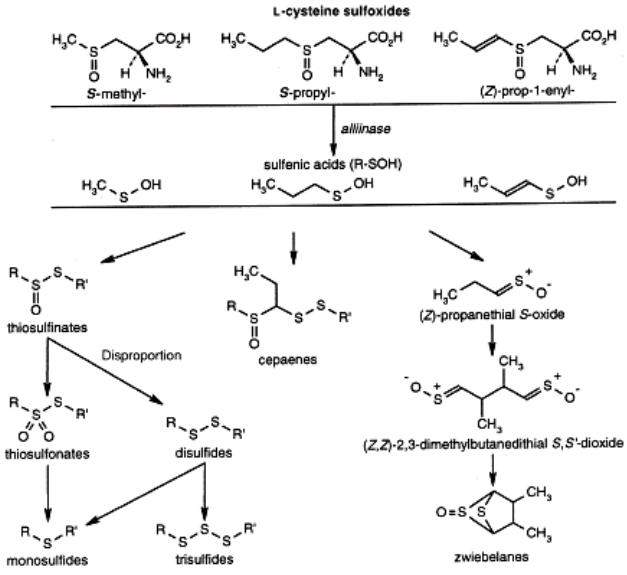
Radioactive residues
For analysis of strontium-90, iodine-131, caesium-134, caesium-137 and plutonium-239, see WHO guidelines on quality control methods for medicinal plants.

Other purity tests
Chemical, foreign organic matter, and moisture tests to be established in accordance with national requirements.

Chemical assays
Assay for organic sulfur constituents, cysteine sulfoxides and sulfides by means of high-performance liquid chromatographic or gas–liquid chromatographic methods, respectively. Quantitative levels to be established by appropriate national authority.

Major chemical constituents
Sulfur- and non-sulfur-containing chemical constituents have been isolatedfrom Bulbus Allii Cepae; the sulfur compounds are the most characteristic.
The organic sulfur compounds of Bulbus Allii Cepae, including the thiosulfinates, thiosulfonates, cepaenes, *S*-oxides, *S*,*S*_-dioxides, monosulfides, disulfides, trisulfides, and zwiebelanes occur only as degradation products of the naturally occurring cysteine

sulfoxides (e.g. (-)-*S*-propyl-L-cysteine sulfoxide). When the onion bulb is crushed, minced, or otherwise processed, the cysteine sulfoxides are released from compartments and contact the enzyme alliinase in adjacent vacuoles. Hydrolysis and immediate condensation of the reactive intermediate (sulfenic acids) form the compounds as indicated below (*1*). The odorous thiosulphonates occur (in low concentrations) only in freshly chopped onions, whereas the sulfides accumulate in stored extracts or steamdistilled oils. Approximately 90% of the soluble organic-bound sulfur is present as γ-glutamylcysteine peptides, which are not acted on by alliinase. They function as storage reserve and contribute to the germination of seeds. However, on prolonged storage or during germination, these peptides are acted on by γ-glutamyl transpeptidase to form alk(en)yl-cysteine sulfoxides, which in turn give rise to other volatile sulfur compounds.



Dosage forms

Fresh juice and 5% and 50% ethanol extracts have been used in clinical studies. A "soft" extract is marketed in France but is not recognized as a drug by French authorities (*7*). Dried Bulbus Allii Cepae products should be stored in well-closed containers, protected from light, moisture, and elevated temperature. Fresh bulbs and juice should be refrigerated (2–10°C).

Medicinal uses

Uses supported by clinical data

The principal use of Bulbus Allii Cepae today is to prevent age-dependent changes in the blood vessels, and loss of appetite.

Uses described in pharmacopoeias and in traditional systems of medicine

Treatment of bacterial infections such as dysentery, and as a diuretic. The drug has also been used to treat ulcers, wounds, scars, keloids, and asthma . Bulbus Allii Cepae has also been used as an adjuvant therapy for diabetes.

Uses described in folk medicine, not supported by experimental or clinical data

As an anthelminthic, aphrodisiac, carminative, emmenagogue, expectorant, and tonic,and for the treatment of bruises, bronchitis, cholera, colic, earache, fevers, high blood pressure, jaundice, pimples, and sores.

Pharmacology

Experimental pharmacology

An aqueous extract or the juice of Bulbus Allii Cepae inhibited the *in vitro* growth of *Escherichia coli, Serratia marcescens, Streptococcus* species, *Lactobacillus odontolyticus, Pseudomonas aeruginosa*, and *Salmonella typhosa*. A petroleum ether extract of Bulbus Allii Cepae inhibited the *in vitro* growth of *Clostridium paraputrificum* and *Staphylococcus aureus*. The essential oil has activity against a variety of fungi including *Aspergillus niger*, *Cladosporium werneckii*, *Candida albicans*, *Fusarium oxysporium*, *Saccharomyces cerevisiae*, *Geotrichum candidum*, *Brettanomyces anomalus*, and *Candida lipolytica*. The hypoglycaemic effects of Bulbus Allii Cepae have been demonstrated *in vivo* Intragastric administration of the juice, a chloroform, ethanol, petroleum ether (0.25 g/kg) or water extract (0.5 ml), suppressed alloxan-, glucose- and epinephrine-induced hyperglycaemia in rabbits and mice . Inhibition of platelet aggregation by Bulbus Allii Cepae has been demonstrated both *in vitro* and *in vivo*. An aqueous extract inhibited adenosine diphosphate-, collagen-, epinephrine- and arachidonic acid-induced platelet.

aggregation *in vitro*. Platelet aggregation was inhibited in rabbits after administration of the essential oil, or a butanol or chloroform extract of the drug . An ethanol, butanol or chloroform extract or the essential oil (10–60µg/ml) of the drug inhibited aggregation of human platelets *in vitro* by decreasing thromboxane synthesis. Both raw onions and the essential oil increased fibrinolysis in *ex vivo* studies on rabbits and humans. An increase in coagulation time was also observed in rabbits. Intragastric administration of the juice or an ether extract (100 mg/kg) of the drug inhibited allergen- and platelet activating factor-induced allergic reactions, but not histamine- or acetylcholine-induced allergenic responses in guinea-pigs. A water extract of the drug was not active. A chloroform extract of Bulbus Allii Cepae (20–80mg/kg) inhibited allergen- and platelet aggregation factor-induced bronchial obstruction in guinea-pigs. The thiosulphinates and cepaenes appear to be the active constituents of Bulbus Allii Cepae. Both ethanol and methanol extracts of Bulbus Allii Cepae demonstrated diuretic activity in dogs and rats after intragastric administration. Antihyperlipidaemic and anticholesterolaemic activities of the drug were observed after oral administration of minced bulbs, a water extract, the essential oil (100 mg/kg), or the fixed oil to rabbits or rats. However, one study reported no significant changes in cholesterol or lipid levels of the eye in rabbits, after treatment of the animals for 6 months with an aqueous extract (20% of diet).

Oral administration of an ethanol extract of the drug to guinea-pigs inhibited smooth muscle contractions in the trachea induced by carbachol and inhibited histamine-, barium chloride-, serotonin-, and acetylcholine-induced contractions in the ileum.

Topical application of an aqueous extract of Bulbus Allii Cepae (10% in a gel preparation) inhibited mouse ear oedema induced by arachidonic acid. The active

antiallergic and anti-inflammatory constituents of onion are the flavonoids (quercetin and kaempferol). The flavonoids act as antiinflammatory agents because they inhibit the action of protein kinase, phospholipase A2, cyclooxygenase, and lipoxygenase, as well as the release of mediators of inflammation (e.g. histamine) from leukocytes.
In vitro, an aqueous extract of Bulbus Allii Cepae inhibited fibroblast proliferation. A 0.5% aqueous extract of onion inhibited the growth of human fibroblasts and of keloidal fibroblasts (enzymically isolated from keloidal tissue). In a comparative study, an aqueous extract of Bulbus Allii Cepae (1– 3%) inhibited the proliferation of fibroblasts of varying origin (scar, keloid, embryonic tissue). The strongest inhibition was observed with keloid fibroblasts (65–73%) as compared with the inhibition of scar and embryonic fibroblasts (up to 50%). In human skin fibroblasts, both aqueous and chloroform onion extracts, as well as thiosulfinates, inhibited the plateletderived growth factor-stimulated chemotaxis and proliferation of these cells. In addition, a protein fraction isolated from an onion extract exhibited antimitotic activity.

Clinical pharmacology

Oral administration of a butanol extract of Bulbus Allii Cepae (200mg) to subjects given a high-fat meal prior to testing suppressed platelet aggregation associated with a high-fat diet.

Administration of a butanol extract to patients with alimentary lipaemia prevented an increase in the total serum cholesterol, _-lipoprotein cholesterol, and _-lipoprotein and serum triglycerides. A saponin fraction (50 mg) or the bulb (100 mg) also decreased serum cholesterol and plasma fibrinogen levels. However, fresh onion extract (50 g) did not produce any significant effects on serum cholesterol, fibrinogen, or fibrinolytic activity in normal subjects.

Antihyperglycaemic activity of Bulbus Allii Cepae has been demonstrated in clinical studies. Administration of an aqueous extract (100 mg) decreased glucose- induced hyperglycaemia in human adults. The juice of the drug (50 mg) administered orally to diabetic patients reduced blood glucose levels. Addition of raw onion to the diet of non-insulin-dependent diabetic subjects decreased the dose of antidiabetic medication required to control the disease. However, an aqueous extract of Bulbus Allii Cepae (200mg) was not active.

The immediate and late cutaneous reactions induced by injection of rabbit anti-human IgE-antibodies into the volar side of the forearms of 12 healthy volunteers were reduced after pretreatment of the skin with a 50% ethanol onion extract. Immediate and late bronchial obstruction owing to allergen inhalation was markedly reduced after oral administration of a 5% ethanol onion extract 1 hour before exposure to the allergen.

In one clinical trial in 12 adult subjects, topical application of a 45% ethanolic onion extract inhibited the allergic skin reactions induced by anti-IgE.

Contraindications

Allergies to the plant. The level of safety of Bulbus Allii Cepae is reflected by its worldwide use as a vegetable.

Warnings
No warnings have been reported.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility
Bulbus Allii Cepae is not mutagenic *in vitro*.

Other precautions
No general precautions have been reported, and no precautions have been reported concerning drug interactions, drug and laboratory test interactions, nursing mothers, paediatric use, or teratogenic or non-teratogenic effects on pregnancy.

Adverse reactions
Allergic reactions such as rhinoconjunctivitis and contact dermatitis have been reported.

Posology
Unless otherwise prescribed: a daily dosage is 50 g of fresh onion or 20 g of the dried drug; doses of preparations should be calculated accordingly.

Reference :
1. WHO monographs on selected medicinal plants.

Chapter- 10

Rhizoma Zingiberis

Definition

Rhizoma Zingiberis is the dried rhizome of *Zingiber officinale* Roscoe (*Zingiberaceae*)

Synonyms

Amomum zingiber L., *Zingiber blancoi* Massk.

Selected vernacular names

Ada, adrak, adu, African ginger, ajenjibre, ale, alea, allam, allamu, ardak, ardraka, ardrakam, ardrakamu, asunglasemtong, ata-le jinja, baojiang, beuing, chiang, citaraho, cochin ginger, common ginger, djae, gember, gengibre, gingembre, ginger, ginger root, gnji, gung, halia bara, halia, halija, hli, inchi, Ingberwurgel, inguere, inguru, Ingwer, jahe, Jamaica ginger, janzabeil, kallamu, kan chiang, kanga, kerati, khenseing, khiang, khing, khing-daeng, khing klaeng, khing phueak, khuong, kintoki, jion, konga, lahja, lei, luya, mangawizi, ngesnges, niamaku, oshoga, palana, palu, rimpang jahe, sa-e, sakanjabir, sge ugser, shengiang, shenjing, shoga, shonkyoh, shokyo, shouhkyoh, tangawizi, wai, zanjabeel, zangabil ee-e-tar, zingabil urratab, zingibil, zingiberis rhizoma, zinjabil, zingiber, zinam

Description

A perennial herb with a subterranean, digitately branched rhizome producing stems up to 1.50 m in height with linear lanceolate sheathing leaves (5–30cm 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 one side; an orange yellow corolla composed of a tube divided above into 3 linearoblong, blunt lobes; 6 staminodes in 2 rows, the outer row of 3 inserted at mouth of corolla; the posterior 2, small, horn-like; the anterior petaloid, purple and spotted and divided into 3 rounded lobes; an inferior, 3-celled ovary with tufted stigma. Fruit a capsule with small arillate seeds

Plant material of interest: dried rhizome

General appearance

Ginger occurs in horizontal, laterally flattened, irregularly branching pieces; 3–16cm long, 3–4cm 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 1–3cm 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 (*1–5*); 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 50µm long and 25µm wide and 7µm thick, and showing 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 thinwalled 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 parenchyma cells containing starch granules; 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– 60µm usually 15–30µm long, 5–40µm (usually 18–25µm) wide, 6–12µm (usually 8–10µm) thick with somewhat marked fine transverse striations.

Geographical distribution

The plant is probably native to south-east Asia and is cultivated in the tropical regions in both the eastern and western hemispheres. It is commercially grown in Africa, China, **India**, and Jamaica; India is the world's largest producer.

General identity tests

Rhizoma Zingiberis is identified by its macroscopic and organoleptic characteristics, including its characteristic form, colour, pungent taste, and volatile oil content; and by microchemical tests.

Purity tests

Microbiology

The test for *Salmonella* spp. in Rhizoma Zingiberis products should be negative. The maximum acceptable limits of other microorganisms are as follows (*15– 17*). For preparation of decoction: aerobic bacteria—not more than 107/g; fungi—not more than 105/g; *Escherichia coli*—not more than 102/g. Preparations for internal use: aerobic bacteria—not more than 105/g or ml; fungi—not more than 104/g or ml; enterobacteria and certain Gram-negative bacteria—not more than 103/g or ml; *Escherichia coli*—0/g or ml.

Foreign organic matter

Not more than 2.0% (*1*). Powdered ginger is frequently adulterated with exhausted ginger

Total ash

Not more than 6.0%

Acid-insoluble ash

Not more than 2.0%

Water-soluble extractive

Not less than 10%

Alcohol-soluble extractive

Not less than 4.5%

Pesticide residues

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in Rhizoma Zingiberis is not more than 0.05 mg/kg. For other pesticides, see WHO guidelines on quality control methods for medicinal plants and guidelines for predicting dietary intake of pesticide residue

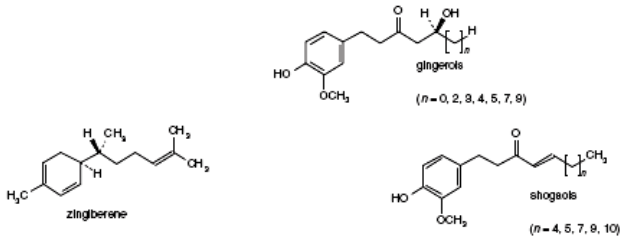
Heavy metals
Recommended lead and cadmium levels are not more than 10 and 0.3mg/kg, respectively, in the final dosage form of the plant material

Radioactive residues
For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants.

Other purity tests
Chemical and moisture tests to be established in accordance with national requirements.

Chemical assays
Contains not less than 2% v/w of volatile oil (*1*), as determined by the method described in WHO guidelines (*15*). Qualitative analysis by thin-layer chromatography (*1*); qualitative and quantitative gas chromatography and highperformance liquid chromatography analyses of ginger oils for gingerols, shogaols, α-zingiberene, _-bisabolene, _-sesquiphellandrene, and *ar*-curcumene.

Major chemical constituents
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, (-)-_- sesquiphellandrene, and _-bisabolene. Monoterpene 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. Representative structures of zingiberene, gingerols and shogaols are presented below.



Dosage forms
Dried root powder, extract, tablets and tincture. Powdered ginger should be stored in well-closed containers (not plastic) which prevent access of moisture. Store protected from light in a cool, dry place.

Medicinal uses

Uses supported by clinical data
The prophylaxis of nausea and vomiting associated with motion sickness, postoperative nausea (*24*), pernicious vomiting in pregnancy, and seasickness

Uses described in pharmacopoeias and in traditional systems of medicine

The treatment of dyspepsia, flatulence, colic, vomiting, diarrhoea, spasms, and other stomach complaints. Powdered ginger is further employed in the treatment of colds and flu, to stimulate the appetite, as a narcotic antagonist, and as an anti-inflammatory agent in the treatment of migraine headache and rheumatic and muscular disorders.

Uses described in folk medicine, not supported by experimental or clinical data

To treat cataracts, toothache, insomnia, baldness, and haemorrhoids, and to increase longevity.

Pharmacology

Experimental pharmacology

Cholagogic activity

Intraduodenal administration of an acetone extract (mainly essential oils) of ginger root to rats increased bile secretion for 3 hours after dosing, while the aqueous extract was not active. The active constituents of the essential oil were identified as [6]- and [10]-gingerol.Oral administration of an acetone extract of ginger (75 mg/kg), [6]-shogaol (2.5 mg/kg), or [6]-, [8]-, or [10]-gingerol enhanced gastrointestinal motility in mice, and the activity was comparable to or slightly weaker than that of metoclopramide (10mg/kg) and domperidone. The [6]-, [8]-, or [10]- gingerols are reported to have antiserotoninergic activity, and it has been suggested that the effects of ginger on gastrointestinal motility may be due to this activity. The mode of administration appears to play a critical role in studies on gastrointestinal motility. For example, both [6]-gingerol and [6]-shogaol inhibited intestinal motility when administered intravenously but accentuated gastrointestinal motility after oral administration

Antiemetic activity

The emetic action of the peripherally acting agent copper sulfate was inhibited in dogs given an intragastric dose of ginger extract, but emesis in pigeons treated with centrally acting emetics such as apomorphine and digitalis could not be inhibited by a ginger extract. These results suggest that ginger's antiemetic activity is peripheral and does not involve the central nervous system. The antiemetic action of ginger has been attributed to the combined action of zingerones and shogaols

Anti-inflammatory activity

One of the mechanisms of inflammation is increased oxygenation of arachidonic acid, which is metabolized by cyclooxygenase and 5-lipoxygenase, leading to prostaglandin E2 and leukotriene B4, two potent mediators of inflammation. *In vitro* studies have demonstrated that a hot-water extract of ginger inhibited the activities of cyclooxygenase and lipoxygenase in the arachidonic acid cascade; thus its anti-inflammatory effects may be due to a decrease in the formation of prostaglandins and leukotrienes. The drug was also a potent inhibitor of thromboxane synthase, and raised prostacyclin levels without a concomitant rise in prostaglandins E2 or F2α. *In vivo* studies have shown that oral administration of ginger extracts decreased rat paw oedema. The potency of the extracts was comparable to that of acetylsalicylic acid. [6]- Shogaol inhibited carrageenin-induced

paw oedema in rats by inhibiting cyclooxygenase activity. Recently, two labdane-type diterpene dialdehydes isolated from ginger extracts have been shown to be inhibitors of human 5- lipoxygenase *in vitro*.

Clinical pharmacology

Antinausea and antiemetic activities

Clinical studies have demonstrated that oral administration of powdered ginger root (940 mg) was more effective than dimenhydrinate (100 mg) in preventing the gastrointestinal symptoms of kinetosis (motion sickness). The results of this study further suggested that ginger did not act centrally on the vomiting centre, but had a direct effect on the gastrointestinal tract through its aromatic, carminative, and absorbent properties, by increasing gastric motility and adsorption of toxins and acids.

In clinical double-blind randomized studies, the effect of powdered ginger root was tested as a prophylactic treatment for seasickness. The results of one study demonstrated that orally administered ginger was statistically better than a placebo in decreasing the incidence of vomiting and cold sweating 4 hours after ingestion. The other investigation compared the effects of seven over-the-counter and prescription antiemetic drugs on prevention of seasickness in 1489 subjects. This study concluded that ginger was as effective as the other antiemetic drugs tested.

At least eight clinical studies have assessed the effects of ginger root on the symptoms of motion sickness. Four of these investigations showed that orally administered ginger root was effective for prophylactic therapy of nausea and vomiting. The other three studies showed that ginger was no more effective than a placebo in treating motion sickness. The conflicting results appear to be a function of the focus of these studies. Clinical studies that focused on the gastrointestinal reactions involved in motion sickness recorded better responses than those studies that concentrated primarily on responses involving the central nervous system. The hypothesis that an increase in gastric emptying may be involved in the antiemetic effects of ginger has recently come under scrutiny. Two clinical studies demonstrated that oral doses of ginger did not affect the gastric emptying rate, as measured by sequential gastric scintigraphy or the paracetamol absorption technique. In a double-blind, randomized, cross-over trial, oral administration of powdered ginger (250 mg, 4 times daily) effectively treated pernicious vomiting in pregnancy. Both the degree of nausea and the number of vomiting attacks were significantly reduced. Furthermore, in a prospective, randomized, double-blind study, there were statistically significantly fewer cases of postoperative nausea and vomiting in 60 patients receiving ginger compared to a placebo. The effect of ginger on postoperative nausea and vomiting was reported to be as good as or better than that of metoclopramide.

In contrast, another double-blind randomized study concluded that orally administered ginger BP (prepared according to the British Pharmacopoeia) was ineffective in reducing the incidence of postoperative nausea and vomiting.

Anti-inflammatory activity

One study in China reported that 113 patients with rheumatic pain and chronic lower back pain, injected with a 5–10% ginger extract into the painful points or reaction

nodules, experienced full or partial relief of pain, decrease in joint swelling, and improvement or recovery in joint function. Oral administration of powdered ginger to patients with rheumatism and musculoskeletal disorders has been reported to provide varying degrees of relief from pain and swelling.

Contraindications
No information available.

Warnings
No information available.

Precautions

General
Patients taking anticoagulant drugs or those with blood coagulation disorders should consult their physician prior to self-medication with ginger. Patients with gallstones should consult their physician before using ginger preparations.

Drug interactions
Ginger may affect bleeding times and immunological parameters owing to its ability to inhibit thromboxane synthase and to act as a prostacyclin agonist. However, a randomized, double-blind study of the effects of dried ginger (2 g daily, orally for 14 days) on platelet function showed no differences in bleeding times in patients receiving ginger or a placebo (*49*, *50*). Large doses (12–14g) of ginger may enhance the hypothrombinaemic effects of anticoagulant therapy, but the clinical significance has yet to be evaluated.

Carcinogenesis, mutagenesis, impairment of fertility
The mutagenicity of ginger extracts is a controversial subject. A hot-water extract of ginger was reported to be mutagenic in B291I cells and *Salmonella typhimurium* strain TA 100, but not in strain TA 98. A number of constituents of fresh ginger have been identified as mutagens. Both [6]-gingerol and shogaols have been determined to be mutagenic in a *Salmonella*/microsome assay , and increased mutagenesis was observed in an Hs30 strain of *Escherichia coli* treated with [6]-gingerol. However, the mutagenicity of [6]- gingerol and shogaols was suppressed in the presence of various concentrations of zingerone, an antimutagenic constituent of ginger. Furthermore, ginger juice was reported to be antimutagenic and suppressed the spontaneous mutations induced by [6]-gingerol, except in cases where the mutagenic chemicals 2-(2-furyl)-3-(5 nitro-2-furyl)acryl amide and *N*-methyl-*N*_-nitro-*N*-nitrosoguanidine were added to [6] gingerol. Other investigators have also reported that ginger juice is antimutagenic.

Pregnancy: teratogenic effects
In a double-blind randomized cross-over clinical trial, ginger (250mg by mouth, 4 times daily) effectively treated pernicious vomiting in pregnancy. No teratogenic aberrations were observed in infants born during this study, and all newborn babies had Apgar scores of 9 or 10 after 5 minutes.

Paediatric use

Not recommended for children less than 6 years of age.

Other precautions

No information available concerning drug and laboratory test interactions, or non-teratogenic effects on pregnancy or nursing mothers.

Other precautions

No information available concerning drug and laboratory test interactions, or non-teratogenic effects on pregnancy or nursing mothers.

Posology

For motion sickness in adults and children more than 6 years: 0.5 g, 2–4 times daily. Dyspepsia, 2–4g daily, as powdered plant material or extracts.

Reference:

1. WHO monographs on selected medicinal plants.