Fructus Chebulae

Definition

Fructus Chebulae consists of the dried fruits of *Terminalia chebula* Retz. or *T. chebula* Retz. var. *tomentella* Kurt. (Combretaceae) (*1–3*).

Selected vernacular names

Abhaya, ahlilaj kâbuli, alalekai, alayla, amagola, arabi, aralu, areyra, aridadi, badamier chebule, bal har, black myrobalan, bush kaduka, chebulic myrobalan, Chebulische Myrobalane, divya, Ga ja, Habra, hacha, halela, halela kabuli, halela zard, halileh, halileh kaboli, halilehsiyâh, halileh zard, hallilaj, harad, harar, harda, hardo, harir, haritaki, harra, harro, harroh, haser, helikha, hezi, himaja, hirda, hirdo, hireda, hlilej khel, hlijej sfer, hokikha, ihlilaj kabuli, inknut tree, jivathi, kabuli-harda, hora, kadukka, kadukkai, kale har, karaka, karakkaya, kashi, katukka, kãyasthã, kot-pung-pla, kurka, medicine terminalia, mirobalan de caboul, mirobalano, myrobalan, myrobalano nero, myrobalans, myrobaran, pathyã, pile har, pilo-harde, post-e-haleela kabli, post-e-haleela siyah, post-e-haleela zard, pulo-harda, rispiger Myrobalanenbaum, rong mao he zi, silikha, sa-mo-thai, samo-thai, shajar shiir hindi, sirri hindi, silikha, sivã, sringitiga, suddha, terminaalia, vayastha, vijayã, yellow myrobalan, yellow myrobalan plum, zama, zangli har (*2–11*).

Geographical distribution

Native to Cambodia, China, India, Lao People's Democratic Republic, Malaysia, Myanmar, Philippines, Thailand and Viet Nam and cultivated elsewhere (*4*, *9*, *10*, *12*).

Description

A tropical shade tree, usually 15–20 m high, but can be up to 30 m in height, and up to 1.3 m in girth; bark rough, scaly; shoots and young leaves usually rusty villous. Leaves simple, opposite, coriaceous, broadly ovate to ovate-elliptic, 7–15 cm in width by 8–25 cm in length, glabrescent; veins obscure above, slightly raised and usually brownish pubescent beneath;

apex acute or abruptly acuminate; base cuneate, slightly cordate or rounded; petiole 1–3 cm long, glabrous or sparsely pubescent with a pair of nodular glands near leaf base. Inflorescences axillary or terminal panicles, usually with 3–6 spikes (each 3–6 cm long); rachis pubescent; flowers 2 mm long, 3–4 mm in diameter; bracts nearly glabrous, 1.5–2.0 mm long; calyx outside glabrous, inside densely villous, calyx-segments triangular; stamens 3–4 mm long; ovary glabrous, ovoid, 1 mm long; style glabrous, 2.5–3.0 mm long; disc lobed, densely villous. Fruit a drupe, glabrous, subglobose to ellipsoid, 2.5–5.0 cm by 1.5–2.5 cm, usually smooth or frequently 5-angulate, ridged, wrinkled, turning blackish when dry. Seed: one, rough, ellipsoid, 1.0–2.0 cm by 0.2–0.7 cm, and without ridges (*9*).

Plant material of interest: dried fruits

General appearance

Oblong or ovoid, 2.5–5.0 cm in length, 1.5–2.5 cm in diameter. Externally yellowish-brown or dark brown, somewhat lustrous, marked with 5 or 6 longitudinal ribs and irregular wrinkles, base with a rounded fruit stalk scar. Texture compact. Sarcocarp 2–5 mm thick, yellowish-brown or dark yellowish-brown; kernels 1.5–2.5 cm long, 1.0–1.5 cm in diameter, pale yellow, rough and hard. One seed, narrowly fusiform, 1.0–2.0 cm by 0.2–0.7 cm; testa yellowish-brown, cotyledons 2, white, overlapping and convolute (*1*, *2*, *8*).

Organoleptic properties

Odour: slight and characteristic (*8*); taste: bitter, sour, astringent, then sweet (*1*, *8*).

Microscopic characteristics

Transverse section of the fruit shows epicarp composed of a layer of epidermal cells, the outer tangential wall and upper portion of the thick radial walls. Mesocarp, 2 or 3 layers of collenchyma followed by a broad zone of parenchyma with fibres and sclereids in groups, and vascular bundles, scattered; fibres, simple-pitted walls; porous parenchyma; sclereids, various shapes and sizes, mostly elongated; tannins and aggregate crystals of calcium oxalate in parenchyma; starch grains simple rounded or oval in shape, measuring 2–7 µm in diameter. Endocarp consists of thick-walled sclereids of various shapes and sizes, mostly elongated. Fibres, sclereids and vessels, lignified. Testa, one layer of large cubical cells, followed by a zone of reticulate parenchyma and vessels; tegmen consists of collapsed parenchyma. Cotyledon folded and containing aleurone grains, oil globules and some rosette aggregate crystals (*2*).

Powdered plant material
Brownish in colour and shows the diagnostic characteristics of the unground drug (*2*).

General identity tests
Macroscopic (*1*, *2*, *8*) and microscopic examinations (*2*), microchemical test (*8*), and thin-layer chromatography (*1*) and high-performance capillary electrophoresis for the presence of the marker tannins chebulinic and chebulagic acids (*13*).

Purity tests
Microbiological
Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*14*).

Foreign organic matter
Not more than 1% (*2*).

Total ash
Not more than 5% (*1*).

Acid-insoluble ash
Not more than 1% (*1*).

Water-soluble extractive
Not less than 30% (*1*).

Alcohol-soluble extractive
Not less than 30–40% (*2*, *8*).

Loss on drying
Not more than 14% (*8*).

Pesticide residues
The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*15*). For other pesticides, see the *European Pharmacopoeia* (*15*) and the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*14*) and pesticide residues (*16*).

Heavy metals
For maximum limits and analysis of heavy metals, consult the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*14*).

Radioactive residues

Where applicable, consult the WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues (*14*).

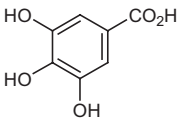
Chemical assays

To be established in accordance with national requirements.

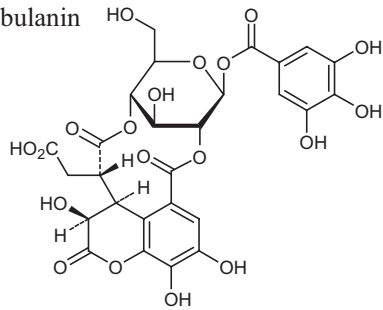
Major chemical constituents

Major constituents of the fruit are hydrolysable tannins and components thereof, including chebulagic acid, chebulinic acid, chebulanin, corilagin, gallic acid, gallic acid methyl ester, punicalagin, terchebulin and terminalic acid. Flavonols of interest include quercetin, isoquercitrin and rutin (*6*). Structures of chebulagic acid, chebulinic acid, chebulanin and gallic acid are presented below.

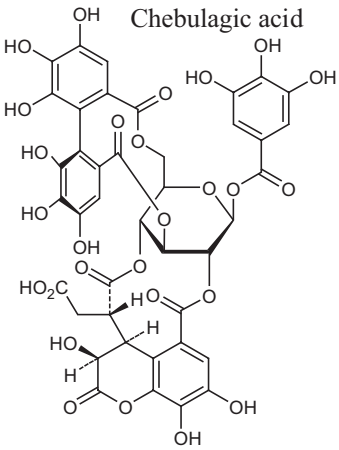
Gallic acid



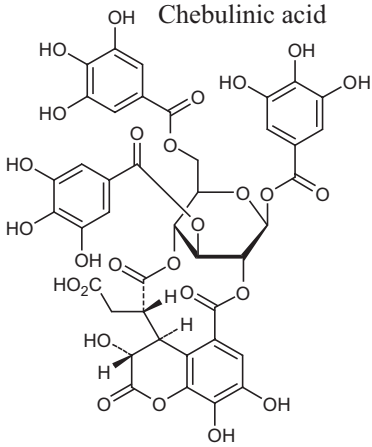
Chebulanin



Chebulagic acid



Chebulinic acid



Medicinal uses

Uses supported by clinical data

None.

Uses described in pharmacopoeias and well established documents

Used orally to treat cough with sore throat, as well as diarrhoea (*1*).

Uses described in traditional medicine

Used orally as an anthelminthic, astringent, cardiotonic, dentifrice, diuretic and laxative. Also used to treat bleeding gums, diabetes, gastrointestinal disorders, ulcers and urinary disorders (*6*).

Pharmacology

Experimental pharmacology

Antiallergic activity

An aqueous ethanol (1:1) extract of the fruit exhibited antihistamine and antispasmodic activities at a concentration of 10 mg/ml in guinea-pig ileum (*17*). The effect of an aqueous soluble fraction of a fruit extract (AF) was investigated in models of systemic and local anaphylaxis (*18*, *19*). Oral administration of AF 1 hour before injection of compound 48/80, inhibited compound 48/80-induced anaphylactic shock by 100% when AF was administered at doses of 0.01–1.0 g/kg body weight (bw). When the extract was administered 5 or 10 min after injection of compound 48/80, the mortality also decreased in a dose-dependent manner. In addition, passive cutaneous anaphylaxis was inhibited by 63.5 ± 7.8% after oral administration of the aqueous extract at a dose of 1.0 g/kg bw. In vitro, AF, in a concentration range of 0.01–1.0 mg/ml also significantly suppressed compound 48/80-induced histamine release from rat peritoneal mast cells ($p < 0.01$), and significantly increased production of tumour necrosis factor-alpha induced by anti-dinitrophenyl IgE (*19*).

Antimicrobial activity

An aqueous extract of the fruit (concentration not stated) was active against six dermatophytes, namely *Trichophyton mentagrophytes*, *T. rubrum*, *T. soudanense*, *Candida albicans*, *Torulopsis glabrata* and *C. krusei* in vitro (*20*). The in vitro antibacterial activity of an extract of the crude drug was assessed in the disc diffusion assay. The extract was active (concentration range 30–500 µg/disc) against human pathogenic Gram-positive and Gram-negative bacteria, including *Shigella dysenteriae*, *S. flexneri*, *S. boydii*, *Proteus mirabilis*, *P. vulgaris*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella* species (*21*). A 50% ethanol ex-

tract of the fruit inhibited the growth of methicillin-resistant *Staphylococcus aureus* (MRSA), with a minimum inhibitory concentration of 31.3 µg/ml (*22*).

The effect of ether, alcohol and aqueous extracts of the fruit on *Helicobacter pylori* was assessed using the agar diffusion method. An aqueous extract of the fruit inhibited the growth of the bacterium with a minimum inhibitory concentration of 125 mg/l and a minimum bactericidal concentration of 150 mg/l. Aqueous extracts, at a concentration of 1–2.5 mg/ml, also weakly inhibited urease activity of *H. pylori* (*23*).

Treatment with the powdered fruit significantly suppressed murine cytomegalovirus load in the lungs of treated mice compared with mice that received water treatment. Intragastric administration of 750 mg/kg bw per day of the dried fruit increased the body weight of infected mice and reduced the virus yield in the lungs (*24*).

The fruit showed stronger anti-herpes simplex virus type 1 activity when used in combination with acyclovir (*25*). When acyclovir and/or the extract were administered to mice by gavage at doses corresponding to those used in humans, the combinations significantly limited the development of skin lesions and/or prolonged the mean survival times of infected animals as compared with that of animals that received either acyclovir or the extract alone ($p < 0.01$ or 0.05). The combinations were not toxic to mice. The extract reduced virus yields in the brain and skin more than acyclovir alone and exhibited stronger anti-herpes simplex virus type 1 activity in the brain than in the skin, in contrast to treatment with acyclovir alone (*25*).

A hot aqueous extract of the fruit was active against anti-herpes simplex virus and was also examined for anti-cytomegalovirus activity in vitro and in vivo. The extract inhibited the replication of human cytomegalovirus and murine cytomegalovirus in vitro and inhibited plaque formation of human cytomegalovirus at a median effective concentration of 2.3 µg/ml. The anti-cytomegalovirus activities of the extract were also examined, in immunosuppressed mice. Mice were treated with various doses of cyclosporin, and immunosuppression and murine cytomegalovirus infection were monitored by measuring suppression of antibody production and virus load in the lung. The extract (15 mg/day) was administered intragastrically to mice which had been treated with 50 mg/kg bw of cyclosporin from one day before intraperitoneal infection. Concomitant administration of the extract reduced the viral load in the lung (*26*).

The effect of a methanol extract of the fruit on HIV-1 reverse transcriptase was assessed. The extracts showed significant inhibitory activity with a median inhibitory concentration (IC_{50}) ≤ 6 µg/ml (*27*).

The inhibitory activity of a hot aqueous extract of the fruit against HIV-1 protease was assessed in vitro (*28*). The extract inhibited the activity of HIV protease at a concentration of 25 µg/ml (*28*).

Antihyperlipidaemic activity

The effect of intragastric administration of an extract of the fruit (500.0 mg/kg bw for 45 days) was investigated in a model of experimental atherosclerosis in rabbits fed a cholesterol-rich diet (*29*). Atherosclerotic lesions of the aorta were examined histologically and hyperlipidaemia was assessed. Treatment of the rabbits with the extract significantly reduced cholesterol, phospholipids and triglyceride levels as compared with those in control animals ($p < 0.05$), and reduced atherosclerotic lesions.

The effect of an extract of the fruit on cholesterol-induced hypercholesterolaemia and atherosclerosis was investigated in rabbits (*30*). The control group was fed a high-cholesterol diet alone whereas the treatment group was fed both the extract and a high-cholesterol diet. Hypercholesterolaemia was significantly less ($p < 0.001$) in the treated group (166 mg/dl) than in the control group (630 mg/dl). Aortic sudanophilia was significantly less after treatment (6%), than in the control group (38%) ($p < 0.001$). The cholesterol contents of the liver and aorta were significantly less in the treatment group (46 mg/100 g and 28 mg/100 g, respectively), than in the control group (604 mg/100 g and 116 mg/100 g) (*30*).

Antioxidant activity

Various extracts (butanol, chloroform, ethyl acetate and methanol) and the isolated pure compounds: casuarinin, chebulanin, chebulinic acid and 1,6-di-*O*-galloyl-β-D-glucose from the crude drug were investigated for anti-lipid peroxidation, anti-superoxide radical formation and free radical scavenging activities in vitro. The results showed that all tested extracts and isolated pure compounds of the crude drug exhibited active to weakly active antioxidant activity at different potencies. Median inhibitory concentrations ranged from 0.005–5.39 mg/ml for the extracts and 0.031–7.27 mg/ml for the pure compounds (*31*).

The antioxidant activity of an aqueous extract of the crude drug, as estimated by thiobarbituric acid reactive substances, was tested by studying the inhibition of radiation-induced lipid peroxidation in rat liver microsomes at different doses in the range of 100–600 µg/ml. The IC_{50} in this assay was 14.5 µg/ml. The extract was also found to restore the antioxidant enzyme superoxide dismutase following radiation-induced damage. The median inhibitory activity of the extract was 11.5 µg/ml in the 1,1-diphenyl-2-picrylhydrazyl radical scavenging assay (*32*).

Cardiovascular effects
A 90% ethanol extract of the fruit increased cardiac output and had positive inotropic effects in isolated frog hearts, when added to the bath media at concentrations of 0.3 to 3.0 mg/ml (*33*).

Gastrointestinal activity
The effect of the dried powdered fruits on gastrointestinal motility in rats was assessed. The animals were divided into four groups as follows: group 1 (n = 15), normal animals; group 2 (n = 6), rats administered metoclopramide (1.35 mg/kg bw); group 3 (n = 8), rats given atropine (0.45 mg/kg bw). These agents were injected intramuscularly, 30 minutes before the experiment. Rats in group 4 (n = 8) were administered the dried fruits by gavage at a dose of 100 mg/kg/day for 15 days before the experiment. All rats were then given a test meal of methyl cellulose (1.5%) mixed with phenol red (50 mg/100 ml) orally, and gastric emptying was measured 20 minutes later. Gastric emptying of normal rats (group 1) was found to be 51.6 ± 7.79%. Treatment with metoclopramide (group 2) significantly increased the gastric emptying (76.33 ± 12.37%; $p < 0.01$) and treatment with atropine (group 3) inhibited the motility (gastric emptying 7.26 ± 19.76%; $p < 0.01$). Administration of the powdered crude drug (group 4) increased the gastric emptying (86.57 ± 6.65%; $p < 0.01$) (*34*).

Intragastric administration of the crude drug to rats, at a dose of 1.5 g/l for 15 days, reduced the number of gastric ulcerations induced by pentagastrin and carbachol (*35*).

Immunosuppressive effects
Gallic acid and chebulagic acid were isolated from a fruit extract as active chemical constituents that block cytotoxic T lymphocyte (CTL)-mediated cytotoxicity. Gallic acid and chebulagic acid weakly inhibited the killing activity of a CD8+ CTL clone with an IC_{50} of 30 µM and 50 µM, respectively. Granule exocytosis in response to anti-CD3 stimulation was also blocked by gallic acid and chebulagic acid at equivalent concentrations (*36*).

Toxicology
Dietary administration of the fruit to rats, as 25% of the diet, produced hepatic lesions which included centrilobular vein abnormalities and centrilobular sinusoidal congestion. Marked renal lesions were also observed, and included marked tubular degeneration, tubular casts and intertubular congestion. A brown pigmentation of the tail and limbs was also observed after 10 days (*37*). The median lethal dose of a 50% ethanol extract of the fruit was 175.0 mg/kg bw after intraperitoneal administration (*38*).

Clinical pharmacology
No information was found.

Adverse reactions
No information was found.

Contraindications
Hypersensitivity or allergy to the plant material.

Warnings
No information was found.

Precautions
General
No information was found.

Carcinogenesis, mutagenesis, impairment of fertility
Extracts of the fruit are not mutagenic, but have antimutagenic activities in various experimental systems. Aqueous, chloroform and acetone extracts were tested in the Ames histidine reversion assay using TA98 and TA100 tester strains of *Salmonella typhimurium* against the direct-acting mutagens, 4-nitro-*o*-phenylenediamine and sodium azide, and the indirect-acting promutagen, 2-aminofluorene, in the presence of phenobarbitone-induced rat hepatic S9 enzymes. The chloroform and acetone extracts inhibited mutagenicity induced by both direct-acting mutagens and by S9-dependent mutagens. A significant inhibition of 98.7% was observed with the acetone extract against the revertants induced by the S9-dependent mutagen, 2-aminofluorene, in a co-incubation mode of treatment (*39*).

The antimutagenic activity of a tannin fraction (TC-E) from the dried fruit pulp of the crude drug was evaluated against two direct-acting mutagens, 4-nitro-*o*-phenylenediamine and 4-nitroquinoline-*N*-oxide, and S9-dependent mutagen, 2-aminofluorene, in TA98 and TA100 strains of *Salmonella typhimurium*. The results showed that the extract (TC-E) and its fractions were antimutagenic against the S9-dependent mutagen, 2-aminofluorene. The effective concentrations ranged from 8.9–320 µg/ml (*40*).

The antimutagenicity of aqueous and chloroform extracts of the fruit were determined against two direct-acting mutagens: sodium azide in strains TA100 and TA1535, and 4-nitro-*o*-phenylenediamine in TA97a

and TA98 strains of *Salmonella typhimurium*, and the S9-dependent mutagen 2-aminofluorene in the TA97a, TA98 and TA100 strains. The aqueous extract reduced 4-nitro-*o*-phenylenediamine- as well as 2-aminofluorene-induced his^+ revertants, but had no perceptible effect against sodium azide-induced his^+ revertants in TA100 and TA1535 strains of *S. typhimurium* (*41*).

Pregnancy: non-teratogenic effects
Due to a lack of safety data, the use of the crude drug during pregnancy is not recommended.

Nursing mothers
Due to a lack of safety data, the use of the crude drug during breastfeeding is not recommended.

Paediatric use
Due to a lack of safety data, the use of the crude drug in children under the age of 12 years is not recommended.

Dosage forms
Crude drug and extracts.

Posology
(Unless otherwise indicated)
Daily dosage: 3–9 g of crude drug for decoction in divided doses (*1*). Store in an airtight container in a dry place (*1*).

References
1. *Pharmacopoeia of the People's Republic of China.* Beijing, Chemical Industry Press, 2005.
2. *The Ayurvedic pharmacopoeia of India*, *Part I, Vol. I*, 1st ed. New Delhi, Government of India Ministry of Health and Family Welfare, Department of Indian Systems of Medicine and Homeopathy, 1990 (reprinted 2001).
3. *Unani pharmacopoeia of India*, *Part I, Vol. I*. New Delhi, Ministry of Health and Family Welfare, Department of Indian System of Medicine and Homeopathy, 1999.
4. Bensky D, Gamble A. *Chinese herbal medicine. Materia medica*, revised ed. Seattle, Washington, Eastland Press, 1993.
5. Bedevian AK. *Illustrated polyglottic dictionary of plant names*. Cairo, Medbouly Library, 1994.
6. Farnsworth NR, ed. *NAPRALERT database.* Chicago, University of Illinois at Chicago, IL (an online database available directly through the University

of Illinois at Chicago or through the Scientific and Technical Network [STN] of Chemical Abstracts Services), 30 June 2005.
7. Hooper D, Field H. Useful plants and drugs of Iran and Iraq. *Field Museum of Natural History, Botanical Series*, 1937, 9:177.
8. *The Japanese standards for herbal medicines*. Tokyo, Yakuji Nippo, 1993.
9. *Medicinal plants in China*. Manila, World Health Organization Regional Office for the Western Pacific, 1989 (WHO Regional Publications, Western Pacific Series, No. 2).
10. Nadkarni AK, ed. *Dr. K.M. Nadkarni's Indian materia medica*. *Vol. 1*. Bombay, Popular Prakshan, 1976.
11. Schlimmer JL. *Terminologie medico-pharmaceutic et Francaise – Persane*. Tehran, University of Tehran, 1970 [in French].
12. Perry LM, Metzger J. *Medicinal plants of east and southeast Asia: Attributed properties and uses*. Cambridge, MA, MIT Press, 1980.
13. Ding G, et al. Analysis of tannins in Fructus Chebulae and its confusion varieties by HPCE. *Acta Pharmaceutica Sinica,* 2001, 36:292–295.
14. *WHO guidelines on assessing quality of herbal medicines with reference to contaminants and residues.* Geneva, World Health Organization, 2007.
15. *European Pharmacopoeia*, 5th ed. Strasbourg, Directorate for the Quality of Medicines of the Council of Europe (EDQM), 2005.
16. *Guidelines for predicting dietary intake of pesticide residues*, 2nd rev. ed. Geneva, World Health Organization, 1997 (WHO/FSF/FOS/97.7).
17. Mokkhasmit M et al. Pharmacological evaluation of Thai medicinal plants. *Journal of the Medical Association of Thailand*, 1971, 54:490–504.
18. Aeom YD et al. Anaphylactic reaction inhibitory effect of Fructus Chebula. *Korean Journal of Herbology,* 2000, 15:123–128.
19. Shin TY et al. Inhibitory action of water soluble fraction of *Terminalia chebula* on systemic and local anaphylaxis. *Journal of Ethnopharmacology*, 2001, 74:133–140.
20. Vonshak A et al. Screening South Indian medicinal plants for antifungal activity against cutaneous pathogens. *Phytotherapy Research*, 2003, 17:1123–1125.
21. Phadke SA, Kulkarni SD. Screening of in vitro antibacterial activity of *Terminalia chebula, Eclapta alba* and *Ocimum sanctum. Indian Journal of Medical Science*, 1989, 43:113–117.
22. Sato Y et al. Extraction and purification of effective antimicrobial constituents of *Terminalia chebula* Rets. against methicillin-resistant *Staphylococcus aureus. Biological and Pharmaceutical Bulletin*, 1997, 20:401–404.
23. Malekzadeh F et al. Antibacterial activity of black myrobalan (*Terminalia chebula* Retz) against *Helicobacter pylori*. *International Journal of Antimicrobial Agents*, 2001, 18:85–88.
24. Shiraki K et al. [Cytomegalovirus infection and its possible treatment with herbal medicines]. *Nippon Rinsho*, 1998, 56:156–160 [in Japanese].
25. Kurokawa M et al. Efficacy of traditional herbal medicines in combination with acyclovir against herpes simplex virus type 1 infection in vitro and in vivo. *Antiviral Research*, 1995, 27:19–37.

26. Yukawa TA et al. Prophylactic treatment of cytomegalovirus infection with traditional herbs. *Antiviral Research*, 1996, 32:63–70.
27. El-Mekkawy S et al. Inhibitory effects of Egyptian folk medicines on human immunodeficiency virus (HIV) reverse transcriptase. *Chemical and Pharmaceutical Bulletin*, 1995, 43:641–648.
28. Xu HX et al. Screening of traditional medicines for their inhibitory activity against HIV-1 protease. *Phytotherapy Research*, 1996, 10:207–210.
29. Shaila HP, Udupa SL, Udupa AL. Hypolipidemic activity of three indigenous drugs in experimentally induced atherosclerosis. *International Journal of Cardiology*, 1998, 67:119–124.
30. Thakur CP et al. The Ayurvedic medicines Haritaki, Amla and Bahira reduce cholesterol-induced atherosclerosis in rabbits. *International Journal of Cardiology,* 1988, 21:167–175.
31. Cheng HY et al. Antioxidant and free radical scavenging activities of *Terminalia chebula. Biological and Pharmaceutical Bulletin*, 2003, 26:1331–1335.
32. Naik GH et al. Comparative antioxidant activity of individual herbal components used in Ayurvedic medicine. *Phytochemistry*, 2003, 63:97–104.
33. Reddy VRC et al. Cardiotonic activity of the fruits of *Terminalia chebula. Fitoterapia*, 1990, 61:517–525.
34. Tamhane MD et al. Effect of oral administration of *Terminalia chebula* on gastric emptying: an experimental study. *Journal of Postgraduate Medicine*, 1997, 43:12–13.
35. Dahanukar SA, Date SG, Karandikar SM. Cytoprotective effect of *Terminalia chebula* and *Asparagus racemosus* on gastric mucosa. *Indian Drugs*, 1983, 20:442–445.
36. Hamada S et al. Immunosuppressive effects of gallic acid and chebulagic acid on CTL-mediated cytotoxicity. *Biological and Pharmaceutical Bulletin*, 1997, 20:1017–1019.
37. Arseculeratne SN, Gunatilaka AAL, Panabokke RG. Studies on medicinal plants of Sri Lanka. Part 14: Toxicity of some traditional medicinal herbs. *Journal of Ethnopharmacology*, 1985, 13:323–335.
38. Abraham Z et al. Screening of Indian plants for biological activity. Part XII. *Indian Journal of Experimental Biology*, 1986, 24:48–68.
39. Kaur S et al. The in vitro antimutagenic activity of Triphala – an Indian herbal drug. *Food and Chemical Toxicology*, 2002, 40:527–534.
40. Kaur S et al. Antimutagenicity of hydrolyzable tannins from *Terminalia chebula* in *Salmonella typhimurium. Mutation Research*, 1998, 419:169–179.
41. Grover IS, Bala S. Antimutagenic activity of *Terminalia chebula* (myroblan) in *Salmonella typhimurium. Indian Journal of Experimental Biology,* 1992, 30:339–341.