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Phyto Pharmacology and Ethnomedical Approach of *Terminalia chebula* (Kadukkaai): A Review

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Review Article

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Abstract: Traditional medicine can take part a significant task in achieving the goal of 'Health for All' and is offered to assisting the integration of traditional medicine with Western medicine all over the world (WHO). As a part of policy to reduce financial trouble on developing countries which spend 40 – 50 % of their total health budget on drugs, WHO currently supports, suggests and endorses the inclusion of herbal drugs in national health care programmes. Herbal drugs are simply available at a price within the reach of an ordinary man and as such are time tested and thus believed to be much safer than modern synthetic drugs. This review highlights the updated information of phyto chemistry, pharmacology, ethno medicine, safety studies and clinical studies on *Terminalia chebula*.
Keywords: Kadukkai, *Terminalia chebula* , Ethno medicine, Pharmacology, Traditional Medicine.

INTRODUCTION

The traditional medicine all over the world is now days revalue by a widespread activity of research on different plant species and their therapeutic principle. Past 10 to 20 years, there has been raise of scientific information concerning plants, crude plant extracts, and various materials from plants as therapeutic agents. Plants still play a major role in modern pharmacy. In universal, herbal formulations are thought to have three major advantages. They are lower cost, fewer side effects and medicinal effects which tend to control physiological function. Herbs and their preparations can play important role in increasing the efficacy of developed drug, reducing suffering of the patients and to certain extent, increasing the longevity of life. Herbal medicine will definitely play a major role in the medicine of 21st century.

Terminalia chebula Retz. Is a medicinal plant widely distributed throughout India, Burma and Sri lanka. The Terminalia consists of 250 species and widely distributed in topical areas of the world. *Terminalia chebula* is one of the plants assessed as threatened plant under IUCN Red List categories [2] not only for Chitrakoot but also for Madhya Pradesh and Chatisgarh [1]. Terminalia is known as the mother of medicine as it has a biodiversity of both nutritional as well as medicinal components. It consists of nutrients such as vitamin C, protein, amino acids and minerals. *Terminalia chebula* also known as black myrobalan has traditionally been used in the treatment of asthma, sore throat, vomiting, hiccough, diarrhoea, bleeding piles, and gout, heart and bladder diseases.

In Charaka, this drug has been classified as anti-ageing and in Sushruta, it has been recognized as a tonic and restorative. Dutt (Hindu Materia Medica) informs us that chebulic myrobalans, in Sanskrit Haritaki, Abaya and Pathya were highly extolled by the ancient Hindus as a powerful alterative and tonic. Indian writers describe seven varieties of Haritaki, which however are nothing more than the same fruit in different stages of maturity. Very large fruits are considered particularly valuable. Chebulic myrobalans are considered to be laxative, stomachic, tonic, blood purifier and alterative. They are prescribed alone or in combination with Emblic and Beleric myrobalans in a vast number of diseases, chiefly those affecting the chest and abdomen. The three myrobalans together are called tripala, a very popular traditional medicine for the treatment of chronic disorders.

Synonym

Myrobalanus chebula (Retz) Gaertn

Trade name

Chebulic Myrobalan, Ink tree.

Plant parts used

The fruits (immature and mature), bark, gum, leaves and galls are used.

Actions

Bark: Diuretic, cardio tonic
Fruits: Astringent, laxative, alterative
Gum: Tonic
Galls: Astringent

CHEMICAL CONSTITUENTS

Fruits contain about 30% of an astringent substance. Astringency is due to the Charecteristic principle of chebulinic acid. T.chebula are a rich source of gallic acid based on secondary metabolites (20 - 36%). Major constituents are chebulagic acid and chebulic acid. Other compounds are tannic acid, gallic acid (~1.2%), ethyl gallate, ellagic acid, chebulinic acid, chebulanin, corilagin, terflavin A, punicalagin, terchebulin, casuarinin, 2,4-chebulyl-β-D-glucose, and glucose esterified with gallic acid to various degrees (eg.,1,6-O-galloyl-β-D-glucopyranose), Hydroxy anthraquinones glycosides. Fruit; also contain tannic acid (20-40%) gallic acid, resin etc and some purgative principle of the nature of anthraquinone (IPC 155, USD 1529). Other classes of compounds identified in the fruits are;shikimic acid and related compounds (quinic acid, dihydroshikimic acid, 5- dihydroshikimic acid) sugars (arabinose,fructose, sucrose), triterpenoids (chebupentol, termioic acid, Arjunolic acid, arjungenin)and steroids (β – sitosterol, daucosterol).It is also reported to have 18 amini acids and a small quantity of phosphoric, succinic, syringic and quinic acids. In *Terminalia chebula* 33% of the total phytoconstituents are hydrolysable tannins (which may vary from 20-50%) and are responsible for pharmacological activity.

Therapeutic actions of phytoconstituents

Tannins

Activate the liver.

Corilagin

Corilagin (β-1-O-galloyl-3, 6-(R)-hexahydroxydiphenoyl-d-glucose) is an ellagitannin had chemotherapeutic activity on some tumour cells and virus. It is water soluble tannin beneficial for cardio vascular diseases. In traditional Chinese medicine corilagin or its analogues were being utilized in cardio vascular diseases. The extraction (by acetic acid and acetic ether, n-butanol, or water) from T. chebula was able to promote myocardial contractibility and also showed strong anti-oxidant.

Fruit

Fruit used externally as a local application to chronic ulcers and wounds and as a gargle in stomatitis. Finely powdered fruit used as a dentifrice and considered useful in carious teeth, bleeding and ulcerations of the gums. The ripe fruit is chiefly used as purgative and is considered to remove bile, phlegm and adjust bile. The unripe fruit is most valued in account of its astringent and aperient properties, and is a useful medicine in dysentery and diarrhoea. Twining (Diseases of Bengal, vol. I, P.407) speak very favourably of the immature fruit, as it is a tonic an aperient in enlargements of the abdominal viscera. We have found them a useful medicine in diarrhoea and dysentery given in doses of a drachm twice a day.

Kaducaipu

Kaducaipu (Fl. Ind. II, 435) is a valuable astringent in diarrhoea (pharmacopoeia – Rev. J. K Earns of Tirunelveli).

HABITAT

Abundant in North India from kangra and kumaon to Bengal and southwards to the Deccan tablelands at 1,000 – 3,000 ft and up to 6,000 ft in Travancore higher forests of the Bombay Ghats, Satpuras, Belgaum and kanara. Occasional in deciduous forests of Himachal Pradesh, Karnataka, Kerala, Tamilnadu, Andrapradesh, Uttar Pradesh and West Bengal.

MORPHOLOGY

A moderate sized deciduous tree, up to 20m tall. Leaves are subbed opposite, ovate, with 2 glands near base. Flowers are dull white in simple spikes, fragrant. The mature myrobalan is of an ovoid form, from 1 - 1½ inches long, sometimes tapering towards the lower extremity, obscurely 5 or 6 sided, more or less furrowed longitudinally, covered with a smooth yellowish brown epidermis, within which is an astringent pulp, enclosing a large rough bony one – called endocarp. The unripe fruits are shrivelled, black, ovoid, brittle bodies from ¼ to ¾ of an inch in length having a shining fracture and an astringent taste. The nuts are hard and with a rough grooved surface.

Flower& fruits

March – December

Propagation

By seeds

Types

There are 4 varieties

- Suvari harade: which are large, dense and heavy about 2 inches long, yellowish brown, when cut it contains yellowish or darkish brown, pulp and stone. Suvari harade is a valuable purgative.
- Rangari harade: These are smaller, less wrinkled and less furrowed than the above variety; in length about an inch; the epidermis is yellow; when cut it presents a yellow dried pulp and a stone. Rangari harade are alterative, stomachic, laxative and tonic. The pulp is less astringent than that of suvari harade.

- Bala harade: are smaller than the above two varieties. Their colour is deep brown or black, highly wrinkled, dark or brown epidermis. Their pulp is dark and homogeneous; there is no stone. Bala harade is a mild and safe aperients and antibilious, though astringent. Ripe fruit is considered as purgative removing bile and phlegm and to adjust bile. It is highly useful in chronic diarrhoea and dysentery, flatulence, vomiting, hiccup, colic and enlarged spleen and liver.
- Java harade: These are the smallest of all. Other characters are similar to those of Bala harade.

Ethno medicine

Terminalia chebula is used as laxative, astringent in Vietnam, South East Asia. The Himalayan tribes eat the kernels of this myrobalan, and use the fruit as a remedy for sore throat under the name of Khoki. A paste of its fruits is taken orally for abortion by the tribal women in Arunachal Pradesh. Stem bark made into paste is applied fresh on cuts and wounds in Orissa [34]. Its root paste issued for conjunctivitis by the tribals in Moghalay. The bark extract is advised as a drink for cooling the brain in Bachumburu of Chhotanagpur. Local people in Netarhat plateau use the fruit as tonic, laxative, astringent and for ulcers and oral diseases. Tribal people in Ranchi district eat green fruit to relieve from cough andpowdered fruits taken after meal for proper digestion. Decoction and paste of fresh fruit are applied on boils. Fresh fruit is crushed with leaf of Aegle marmelos (Bel) and the paste is taken orally for blood dysentery in Tribes of Tripura. H.S.Gupta stated that in cases of bronchitis and whooping cough Caesalpinia bonduc (L.) Roxb seeds are mixed with fruits of T.chebula Retz. in equal quantities and ground to make a fine powder. Kowra tribes of Bihar in India, taken 10 g of this powder with lukewarm water twice daily till the cure is obtained. The bark of the plant is used by Kheri Distric forests (Uttar Pradesh), India to check premature graying of hair. 10 g of fruit powder is taken orally once daily in the early morning for one month. Tribe of Gandhamardhan Hills of Orissa has taken equal quantity of fruit powder of T.chebula, T.bellirica and Phyllanthus emblica 20 day for spermatorrhoea [35]. A hand full of leaves made in to paste with water is applied on eczematous patches. Stem bark is used as a remedy for eczema in Uttarpradesh.

Traditional uses

A cold infusion of its fruits is used as a gargle in stomatitis and in chronic ulcers, carious teeth, in cough, asthma and urinary diseases. Finely powdered fruits are used in bleeding and ulceration of the gums. Internally, these are efficacious in chronic diarrhoea, dysentery, flatulence and spleen disorders. Roasted fruit powder is used in stomach ache. Gum is used in colitis. Cold infusion of it is used as a gargle in sore mouth and stomatitis, spongy and ulcerated gums. As alterative tonic for promoting strength and preventing the effects of age, chebulic myrobalan is taken every morning with salt in the rainy season, with sugar in autumn, with ginger in the 1st half of winter, with long pepper in the 2nd half, with honey in spring and with treacle in the 2 hot months. These adjuncts agree best with the humours that are liable to be deranged in the different seasons [36]. 15 g stem bark powder mixed with 50 ml ferula seed soaked water, the mixture taken orally 2 times a day for 2 days against dysentery. 10 g fruits crushed with water and made as paste and given orally 2 times a day for 3 days against children's stomach ailments. 15 g seeds crushed in 25 ml water and made into paste and then taken orally once a day before a week against leucoderma.

External uses

A fruit extract issued as wash in watering eyes and fruit paste in burns. Fruit powder is soaked in water overnight in an earthen pot and eyes are washed with this water in the morning for eye problems [3]. Fruit paste with turmeric powder is applied for inflammation of eyes used by Tharus of Nainital district in Uttar Pradesh. Ashes of Triphala mixed with Sindhu salt (Saindhava, i.e Potassium Nitras or Nitricum) are dusted over syphilitic ulcers for washing away the exudation from the ulcers. A decoction of chebulic myrobalan is a good astringent wash useful in bleeding piles and some vaginal discharges. Finely powdered chebulic myrobalan is used as a dentifrice useful in carious teeth, bleeding and ulcerations of gums. Coarsely powdered and smoked in a pine it affords relief in a fit of asthma.

Simple home remedies

Diabetes mellitus

Two spoons full of dried powder with water are administered once a day for 20 days.
One fruit per day is eaten for 30 days.
One teaspoon full of leaf juice is administered daily once for 2 months.

Sore throat

A fruit is roasted a little on burning charcoal and chewed slowly.

Cough

Fruit powder is mixed with the water or cow's or goat's milk and taken internally twice a day for 7 days.

One roasted fruit is given to chew for instant relief.

Asthma, bronchitis and other respiratory ailments

Equal quantities of fruits of T.chebula, T.bellirica and phyllanthus emblica are ground into powder. One teaspoon of the powder is mixed with ½ teaspoon of honey and taken orally twice a day till cure.nFruit is coarsely powdered and smoked in a pipe.

Tuberculosis

5 g of fresh bark is crushed with 1 g of piper nigrum and taken orally at noon.

Obesity

Haritaki taken orally over extended periods (a few months) has been claimed to counter obesity and bestow bodily strength.

For black hair

Fruits bark is mixed with equal quantity of Shorea robusta (stem bark), Terminalia bellirica(Fruits bark) and stem bark of Syzygium cumini and crushed and applied on hair for 2 -3 hours before hair wash.

Ethno vetenary uses

Fruit is used in dullness of the cattle.

PHARMACOLOGICAL ACTIVITY

Anti-oxidant effect

Bajpai *et al.* [4] investigated the high phenolic content and anti-oxidant activity of leaves, fruits and bark of T.chebula. The TPC of fruits, leaves and bark of T. chebula were 144.7, 162.1 and 150.7 mg/g GAE, respectively. The anti-oxidant activity of T. chebula assayed by auto – oxidation of β – carotene and linoleic acid and expressed as the percent of inhibition relative to the control were 79.8%, 80.1% and 85.2% for fruits, leaves and bark, respectively. Lee *et al.* [5] investigated anti-oxidant activity and DPPH free radical scavenging activities of aqueous extract of fruits of T.chebula. Jain & Agrawal [6] reported anti-oxidant activity of methanolic extract of T.chebula. Naik *et al.* [7] evaluated the aqueous extract of T.chebula for potential anti-oxidant activity by examining its ability to inhibit gamma- radiation-induced lipid peroxidation in rat liver microsomes and damage to superoxide dismutase enzyme in rat liver mitochondria. The extract inhibited xanthine/xanthine oxidase activity and is also an excellent scavenger of DPPH radicals. Jayajothi *et al.* [8] evaluated the methanolic extract of 5 commercial Triphala and all the extracts exhibited significant anti-oxidant effect. A clear correlation between IC50 and neither a content of GAE nor the total phenolic content could be observed. Consumption of Triphala has been suggested to exert several beneficial effects by virtue of its anti-oxidant activity. The estimated TEAC values and total phenolic content by Cai *et al.* [9] for methanolic extract of fruit of T.chebula were 4403.0µmol Trolox equivalent / 100g drug weight (DW), and 13.16g of gallic acid equivalent / 100g drug weight (DW) respectively. Major types of phenolic compounds in T.chebula include tannins (ellagi tannins), phenolic acids (gallic acid). Saleem *et al.* [10] reported that the fruit extract of T.chebula was stronger anti-oxidant than α – tocopherol. HPLC analysis with diode array detection at 280nm of the extract indicated the presence of hydroxibenzoic acid derivatives, hydroxycinnamic acid derivatives, flavonol aglycones and their glycosides as main phenolic compounds. Kim *et al.* [11] showed the free radical scavenging activity in methanol aqueous extract of T.chebula. Vaibhav aher,*et al.* [12] studied the immunomodulatory activity of alcohol extracts of *Terminalia chebula* .

Hepato protective

Fruits are rich source of chebulic acid, tannin and elagic acid that have important role of an astringent and hepato protective. It was considered important since the ancient times to regulate the liver physiology in haemorrhoidal conditions and now it is very well known that portal hypertension can be an important etiological factor in the development of haemorrhoids. Tasduq SS reported that Ethanol extract of T. *chebula* was found to prevent the hepatotoxiocity caused by the administration of rifampicin, isoniazid and pyrazinamide (combination) in sub-chronic model (12 weeks). Lee HS *et al.* in their study, a mixture of chebulic acid (CA) and its minor isomer, neochebulic acid with a ratio of 2:1 isolated from ethanolic extract of *T. chebula* fruits showed strong hepatoprotective activity.

Cyto protective

Na M *et al.* studied the ethanolic extract of *T. chebula* fruit exhibited a notable cytoprotective effect on the HEK-N/F cells and also significant cytoprotective effect against UV-induced oxidative damage.

Nephroprotective

Nalamolu Koteswara Rao *et al.* [13] evaluated the chloroform extract of *T. Chebula exhibited s*ignificant renoprotective activity and also more effectively inhibited the incidence of diabetic nephropathy.

Laxative

Anthraquinone derivatives exhibit laxative action by stimulating the mucous membrane lead to increase in secretion of mucus i.e stimulating peristalsis. Nalini sofia et.al stated that Tender fruits of *Terminalia chebula* remove constipation and rectal spasm. It is safe and effective i.e. gentle laxative. The laxative principle in the pericarp of the fruit has been found to be a glycoside Anthraquione that may be similar to sennoside.

Anti-viral

Aqueous extract of T. Chebula inhibited HIV Protease at the concentration 0.2 mg/ml [37]. Water extract of T.chebula inhibited the DNA polymerase activity of Hepatitis B virus [14]. Methanolic extract of fruit showed significant inhibitory effects on human immune deficiency virus - I reverse transcriptase [15].

Anti-diabetic

Kannan VR *et al.* showed that *T. chebula* fruit and seeds exhibited dose dependent reduction in blood glucose of streptozotocin induced diabetic rats both in

short term and long term study. Sabu M.C *et al*. [16], and Senthilkumar GP *et al*.[17] reported that Tripala extract has reduced the blood sugar level in normal and alloxan (120mg/kg) induced diabetic rats significantly.

Wound healing

Healing is much faster as indicated by improved rates of contraction and decreased period of epithelialisation. Because of significant increase in total protein, DNA and collagen contents in the granulation tissues of treated wounds, tensile strength increased by about 40% [18].

Anti- inflammatory

Feng-Lin H *et al*. reported that Gallic acid (3, 4, and 5- trihydrobenzoic acid) is one of the main endogenous phenolic acids found in *Terminalia chebula* which possess the Anti- inflammatory activity.

Anti-spasmodic

M P. Singh et al in their research showed that T.chebula exhibited anti-spasmodic action on smooth muscle similar to that of papaverin.

Anti urolithiatic

Anil. T. Pawar *et al*. [19] in their study, the aqueous extract of the fruit of *Terminalia chebula* in wistar albino rats decreased the elevated levels of oxalate and phosphate in urine as well as kidney tissue homogenate. The extract supplementation also prevented the elevation of serum levels ie, Blood urea nitrogen, Creatinie and Uric acid.

Anti-bacterial

T. chebula exhibited antibacterial activity against a number of both Gram-positive and Gram-negative human pathogenic bacteria such as, *Clostridium perfingens* and *Escherichia coli* [20] *Helicobactor pyroli* [21] *Staphylococcus aureus [*22] *Streptococcus mutans*, salivary bacteria [24] *Salmonella typhi [*23] *Klebsiella [*25] *Shigella [*26].

Antifungal

Methanolic extract of *T. chebula* exhibited antifungal activity against *Candida albicans* [27], *Trichophyton rubrum* [28]. Seed extract exhibited antifungal activity against *Trichophyton glabrata*.

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Anti caries agent

T.chebula is an anti-plaque forming drug which can be of great help for dental caries [29] Triphala showed bacteriostatic or bacteriocidal effect on gram-positive and gram negative pathogens [25]. Triphala's fruit is rich in citric acid, showed the property of chelation and helps in the removal of smear layer from the walls of the root canal. [30].

Anti-hsv-2

Ajay Kesharwani *et al*. [38]. In their study, 50% ethanolic extract from the fruits of *T. chebula* or compounds chebulagic acid and chebulinic acid, their effect on the viability of Vero cells was determined by MTT assay. The extract of *T. chebula* revealed 409.71 ± 47.70 µg/ml CC_{50} value. The chebulagic and chebulinic acids showed > 95% cell viability when tested up to 200 µg/ml. The extract from *T. chebula* ($IC_{50} = 0.01 \pm 0.0002$ µg/ml), chebulagic ($IC_{50} = 1.41 \pm 0.51$ µg/ml) and chebulinic acids ($IC_{50} = 0.06 \pm 0.002$ µg/ml) showed dose dependent potent in vitro direct anti-viral activity against HSV-2. Oyuntsetseg N *et al*. evaluated the direct anti-viral activity of the aqueous extract from the seeds of *T. chebula* on influenza A (H3N8) virus.

Anti-cancer

Kagawa K.S *et al*. observed cytotoxic activity with the tannin fraction of hatadae fruits. The tannins of T.chebula, especially chebulanin were patented in Japan for its anti-cancer activity. Reddy DB *et al*. evaluated Ethanol extract of *T. chebula* fruit inhibited cell proliferation and induced cell death in a dose dependent manner in several malignant cell lines including human (MCF-7) and mouse (S115) breast cancer cell line, human osteosarcoma cell line (HOS-1), human prostate cancer cell (PC-3) and a non-tumorigenic immortalized human prostate cell line (PNT1A). Chebulagic acid, a COX-LOX dual inhibitor isolated from the fruits of *Terminalia chebula* Retz. Induces apoptosis in COLO-205 cell line

Radio protective

Gandhi NM *et al*.[39] evaluated the aqueous extract of *T. chebula* prior to whole body irradiation of mice resulted in a reduction of peroxidation of membrane lipids in the mice liver as well as a decrease in radiation induced damage to DNA. It also protected the human lymphocytes from undergoing the gamma radiation-induced damage to DNA exposed *in vitro.*

Chemo preventive

Prasad L *et al*. [40] showed *T. chebula* had chemopreventive effect on nickel chloride -induced renal oxidative stress, toxicity and cell proliferation response in male Wistar rats.

Anti-anaphylactic

Water soluble fraction of *T. chebula* had a significant increasing effect on anti-dinitrophenyl IgE-induced tumor necrosis factor-alpha production from rat peritoneal mast cells indicating its strong antianaphylactic action [31].

Hypocholesterolaemic

Ahirwar B *et al*. [41]reported that the ethanolic extract and ethyl acetate fractions of fruits were found to possess significant hypo lipidemic activity. The most active extract was the ethyl acetate fraction of immature fruits, which was able to bring high serum lipids to normal level.

Melanin inhibitory effect

Jin Yin-Z *et al.*[42] in their study, extract of *Terminalia chebula* have great potential as safe effective de pigmenting agent. The methanolic extract of *Terminalia chebula* showed a Melanin inhibitory effect higher than 90% at 100 ppm. Khanna A.K *et al.*[43] showed that chronic feeding of ethyl acetate soluble fraction of the alcoholic extract of T.chebula stem for 30 days to normal rats lowered the levels of LDL-C and increased the levels of HDL-C.

Clinical study

Sood R *et al.*[44] in their clinical study, T.chebula powder given to 15 subjects for 6 weeks showed statistically significant reduction in the level of serum cholesterol, TG, TL, LDL and VLDL. There was a statistically significant increase in the level of HDL. Amirthaveni M *et al.* found that supplementation of T.chebula powder lowered the serum TL, TG, LDL-C and VLDL-C in heart patients [32]. In their clinical study, oral rinsing with extract of *T. chebula* was found to significantly reduce both total bacterial counts and streptococcal counts in saliva samples. The protective effect lasted for about 3 h after rinsing, demonstrating a potential role of *T. chebula* in the prevention of dental caries.

Substitutes/adulterants

Adulteration of the drug is not common. However, occasion adulteration with fruit rind of Terminalia bellerica is found which can be detected by even external surface with greenish colour of latter. It is also Substituted/Adulterated with immature fruits of T.chebula which is used in Indian System of Medicine as a separate drug known as Bal Hareetaki.

Dosage

2 – 4 g in single dose as laxative
3- 6 g of powder

Toxicity

T. chebula is considered as generally safe. LD 50 of chebulin was 550mg/kg [33]. Various safety studied revealed that it has potent hepato protective, nephro protective, cardio protective, and cyto protective.

CONCLUSION

Plants remain a good source for drug discovery. The active ingredients of *Terminalia chebula* are potentially useful for the development of therapeutic agents. An Ethno medicinal use, traditional uses, pharmacological actions and toxicity study of *Terminalia chebula* was useful for the therapeutic use of this single herb to various diseases. Further the herbal drug can be subjected to clinical trials in various ailments.

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