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Review Article

A review on pharmacological activity of *Terminalia chebula*

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ABSTRACT

Since the beginning of civilization, people have used medicinal herbs to treat illnesses. Medicinal plants, which are valued as plentiful sources of folk medicine, are the source of many contemporary pharmaceuticals. *T. chebula* is used in several ayurvedic formulations and may have therapeutic benefits. *Terminalia chebula* Retz. (Family Combretaceae) is frequently at the top of the list of "Ayurvedic Materia Medica" and is referred to as the "King of Medicine" in Tibet due to its exceptional healing abilities, popularly referred to as "Harar". The entire plant is very restorative and has historically been used to treat a variety of human illnesses. Folklore claims that this plant was used to heal a variety of ailments, including gout, asthma, sore throats, bleeding piles, ulcers, hiccoughs, diarrhoea, and dysentery. Numerous pharmacological and therapeutic actions of the plant have been identified, including anti-inflammatory, anti-mutagenic, anti-proliferative, radioprotective, cardioprotective, anti-arthritic, and qualities that increase gastrointestinal motility. We have looked into the phyto-pharmacological characteristics of the plant and compiled its varied pharmacological uses in this review in order to comprehend and synthesise the issue of *T. chebula* potential role as a multifunctional therapeutic agent.

1. Introduction

The term "medicinal plants" refers to plants with therapeutic qualities or that have positive pharmacological effects on the human or animal body. Medicinal plants have had a tremendous impact on the development of human civilisation. Almost all tribes and civilizations have turned to medicinal plants for cure. Traditional medicines are said to be abundant in medicinal plants, and many modern medications are made from these plants. Herbal medicines, when administered under the guidance of a skilled and trained practitioner, herbs are generally safe and have minimal adverse effects. They are significant sources of vitamins, minerals, and phytochemicals used in natural medicine, all of which have demonstrated curative effects in the past (Khan et al.,2005).[1] *Terminalia chebula*, also known as Harar, Harra, Hirda, Myrobalan, and Haritaki, is one of the most renowned indigenous multi-purpose tree species (Burkill, 1985).[2] In addition to being used commercially in numerous Ayurvedic medications to treat digestive disorders like dyspepsia, heartburn, and flatulence, as well as asthmatic liver and spleen disorders, the fruits of the species are used locally in a variety of medications and are an essential component of the herbal formulation "Triphala". Nearly 80% of people worldwide rely on plant-based traditional medicine for their basic medical needs, according to the World Health Organization (World Health Organization, 2002).[3] It has been demonstrated that the plant performs a number of pharmacological and therapeutic roles, including wound healing, hepato-protection, antibacterial, antioxidant, and anti-diabetic (Khatak et al.,2020).[4]

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2. *T.Chebula* Retz

2.1. Description of the plant

The tree is between 50 and 80 feet tall. Its top is rounded, and its limbs are widely spaced. The bark has a few longitudinal fissures and is a dark brown colour. The ovate, elliptical leaves have two large glands close to the summit. The terminal spikes or short panicles of monoecious, dull white to yellow blooms are held in the centre and have an offensive, pungent odour. Flowers bloom in May through June, and fruit is visible from July through December. The fruit, sometimes known as a drupe, is one to two inches in size. There are five ribs or lines on the skin's surface. Green fruit is unripe, while yellowish-gray fruit is ripe. Fruit formation started in November, and fruits were gathered between January and April (The Ayurvedic pharmacopoeia of India, 2001).[5]

2.2. Special identity

Taxonomy of *Terminalia chebula* Retz

1. Kingdom: Plantae-Plants;
2. Genus: Terminalia L-tropical almond;
3. Subkingdom: Tracheobionta-Vascularplants;
4. Subclass: Rosidae;
5. Super division: Spermatophyta-seed plants;
6. Order: Myrtales;
7. Division: Magnoliophyta- flowering plants;
8. Genus: Terminalia L-tropical almond;
9. Family: Combretaceae-Indian almond family;
10. Species: *T. chebula*

Names given to *T. chebula* Retz by local:. English: "Chebulic myrobalan"; Assamese: "shilikha"; Bengali: "haritaki"; Gujrati: "hardi, harde"; Hindi: "hara"; Kannada: "alale"; Konkani: "ordo, hardi"; Malayalam: "katukka"; Manipuri: "Manali"; Marathi: "hirda"; Oriya: "karadha Kata-K-Kay in Tamil; Haejarad in Urdu. The Sub-Himalayan pathways leading from the east to West Bengal and Assam contain *T. chebula*, which grows as high as 1,500 m in the Himalayas. This tree can be found in abundance in Madras, Mysore, and the southernmost region of the Bombay presidency. It also grows wild in Bengal, the central provinces of India, and the northern woods of India (Gupta et al.,2003).[6]

Classification based on *T. chebula* fruit size: Survariharade, a 2 inch long, big, dense, and heavy yellowish brown object; Rangariharade: These measure about an inch in length, are less furrowed and wrinkled than Survariharade, and have a yellow epidermis. Balaharade is smaller than the previous two types and has an epidermis that is dark or brown and extremely wrinkled. The smallest of all the characters is called Java harade; the other characters are comparable to Balaharade.

Classification of fruit growth When the size is similar to a cumin seed, it is called zira; Javi: When it is the same size as a grain of barley; Zangi: When it is of a raisin's size; Chini: Fruit that is somewhat firm with a greenish-yellow colour. Asfer - just before full development; Kabul –when it is fully developed (Sukhdev et al.,1999).[7]

2.3. Varieties

Bhavamisra describe seven different varieties of *Terminalia chebula* (Sastry et al.,2005).[8]

Varities of fruits	Uses
Vijaya	All disease
Rohini	Wound healing
Putana	External application
Amrta	Purification procedure
Abhaya	Eye disorders
Jivanti	All disease
Chetaki	All disease

3. Ethnobotanical Applications

The fruit has negligible tonic, alterative, antispasmodic, and laxative effects. It aids in the treatment of oral ulcers, dental caries, bleeding gums, and haemorrhoids. Anti-inflammatory, analgesic, detoxifying, and wound-healing effects have been linked to its paste when combined with water. For mouth ulcers and sore throats, its decoction is gargled. This substance's advantages include gastrointestinal prokinetics, liver stimulation, stomachic effects, and mild laxative effects. Chronic diarrhoea has been treated with *T. chebula* fruit powder. It treats weakness and irritability of the neurological system. Due to its astringent qualities, it is useful for asthma, chorizo, sore throats, and chronic coughs in addition to being an adjuvant in haemorrhages. These plants' bioactive elements, including steroids, terpenoids, carotenoids, flavonoids, alkaloids, tannins, and glycosides, have been investigated for their capacity to inhibit lipid peroxidation and scavenge free radicals (Nigam et al.,2020).[9]

4. Pharmacological activities of *T chebula* Retz

4.1. Antidiabetic activity

Strong intestinal maltase inhibitory activity of *Terminalia chebula* fruit extract in rats did not affect intestinal sucrase or isomaltase activity, but its inhibitory effect on -glucosidase indicates that it may be effective for treating type 2 diabetes (Sabu et al.,2002).[10]

In both short- and long-term experiments, *T. chebula* fruit and seeds reduced blood glucose levels in streptozotocin-induced diabetic rats in a dose-dependent manner. They also displayed reno protective behaviour (kumar et al., 2009 and Kannan et al.,2012).[11,12]

4.2. Anticarcinogenic activity

When the phenolics of *Terminalia chebula* fruit were studied, chebulinic acid, tannic acid, and ellagic acid were shown to have the highest growth-inhibitory effects on cancer cell proliferation (Saleem et al.,2002).[13] Chebulinic acid, tannic acid, and ellagic acid were discovered to be the greatest cancer cell growth-inhibitory phenolics in *T. chebula*, according to a team of researchers that examined the fruit's phenolics' effects on the growth of the disease-causing cells (Saleem et al., 2002).[13] The *T. chebula* fruit's ethanol extract was found to have effects on human (MCF-7) and mouse (S115) breast cancer cell lines, human osteosarcoma cell line (HOS-1), human prostate cancer cell (PC-3) and a non-tumorigenic immortalised human prostate cell (Reddy et al., 2009).[14]

4.3. Antiviral activity

Additionally, it has been noted that T.chebula shows modest effectiveness against HSV-1, HIV-1, and CMV (Yukawa et al.,1996).[15]

The *T. chebula* extract displayed strong anti-HSV-1 efficacy when coupled with acyclovir. It raised the mean survival times of infected mice and decreased the occurrence of skin lesions at doses suitable for human use when compared to acyclovir and mice treated only with the herbal extract (p0.01 and p0.05) (Kurokawa et al.,1995).[16]

Fruits from *Terminalia chebula* contained gallic acid, three galloyglucoses, and four HIV-1 integration inhibitors. Significantly inhibiting the compounds' 3'-processing of HIV-1 integrase is their galloylmoiety. (Ahn et al., 2002).[17]

The fruits of *T. chebula* provided three galloyl glucoses and GA (I), four HIV-1 integrase inhibitors (II-IV). Their galloyl moiety significantly contributes to the compounds' suppression of HIV-1 integrase's 3'-processing (Jeong et al.,2002).[18] The retroviral reverse transcriptase inhibitory activity of *T. chebula* is also present (Lee et al., 2011).[19]

Haritaki (*T. chebula*) in vitro study against SARS-CoV2 may require screening (Dâmaris et al., 2020).[20] Biomolecules from some *Terminalia chebula* plant species have already been shown to have antiviral properties.

Chebulagic and chebulinic acids exhibit superior direct antiviral action against HSV-2 compared to acyclovir and are more successful at preventing virus attachment and penetration to the host cells. In order to prevent sexually transmitted HSV-2 infection, it may therefore be a good candidate for alternative therapy (Kesharwani et al., 2017).[21]

IAV (the influenza A virus) replication can be efficiently stopped by chelating acids chebulinic and chebulagic. These substances exhibit antiviral effectiveness against both oseltamivir-resistant and wild-type IAV strains by acting as neuraminidase inhibitors (Li et al., 2020).[22] In vitro influenza is inhibited by chebulagic acid and/or its hydrolysis products as a novel drug that recovers M2(S31N)-expressing yeast development. Without reference to the M2 (Duncan et al., 2020).[23]

4.4. Cardiotonic & cardioprotective activity

Several extracts made from the *Terminalia chebula* fruit rind have demonstrated cardiotonic action when tested on healthy and hypodynamic isolated frog hearts. Without altering heart rate, the extracts increased cardiac output and force of contraction. (Reddy et al.,1990).[24] Pretreatment with *T. chebula* extract was observed to reduce the impact of the medication on the production of lipid peroxide and maintain the activity of the diagnostic marker enzymes in rats with isoproterenol-induced heart injury (Suchalatha et al., 2004).[25] In an isolated frog heart model, its pericap has also been shown to have cardioprotective effects (Reddy, 1990).[24]

4.5. Anti-bacterial activity

A variety of bacterial species were resistant to *Terminalia chebula* antimicrobial properties (Ahmad et al.,1998).[26] One team of researchers discovered that it is efficient in preventing Helicobactorpyroli (H. pyroli), a common bacteria linked to the emergence of gastritis, ulcers, and stomach malignancies, from producing urease (Malckzadehet al.,2001).[27] Its antimicrobial properties include those against bacteria, fungi, protozoa, anthelmintics, and salmonella (Denis et al.,2021).[28] Sharma et al., 2012[29] evaluated the antimicrobial efficacy of acetone, ethanol, methanol, hot aqueous and cold aqueous extracts of fruits of *T.chebula* against ear pathogens i.e. *S.aureus*, *Acinetobacter sp., P.aeruginosa, P.mirabilis, E.coli* and *C.albicansand* found that all extracts were effective against pathogens causing ear infections.

In another study by Singh et al.(2012)[30], the therapeutic effect of ethyl acetate, acetone, methanol and water extracts of fruits of T.chebula against several human pathogens (*S.auerus, S.mutans, S.pyrogens, S.pneumoniaand S.aeruginosa*) have been known. The aqueous extract of *T.chebula* Retz. Fruit also showed inhibitory effect against *B.subtilis, S.aureus, S.epidermis, E.coli, P.aeruginosa* and Staphylococcus flexineria (Kumar et al.,2009).[11] Agarwal et al. (2010),[31] studied the antibacterial activity of hydro-alcohalic fruit extract of *T.chebula* against microorganisms. *B.subtilis, B.cereus, S.aureus, S.epidermis, E.coli, P.aeruginosa, S.flexineria* and found that extract was effective against all test organisms. It is well known that tannins have antibacterial properties and can stop the growth of many bacterium, yeast, and fungal virus strains. The fruit of the *Terminalia Chebula* has shown antibacterial effectiveness against specific clinical strains of pathogens (Zhang et al.,2019).[32] By combining methanolic, aqueous, and ethyl acetate extracts with a

variety of standard antibiotics, the potential of *T. chebula* fruit extract was examined. The extracts demonstrated significant antibacterial action against the bacterial causes of all autoimmune inflammatory disorders (Mandeville et al.,2018).[33]

4.6. Antifungal activity

Aqueous *Terminalia chebula* extract shown antifungal efficacy against several yeasts and dermatophytes. The alcoholic ethyle acetate extract shows the activity against *Aspergillus niger, aspergillus flavus*, alternate. 70% of methanol ethylacetate, hexane, chloroform extract shows activity against *Fusarium oxysporum, Phytopthoracapsici, Fusarium solanietc* (Dutta et al., 1998 and Mehmood et al., 1999).[34,35]

It is effective against the *Dermatophytes, Epidermophyton floccosum, Microsporum gypseum*, and *Trichophyton rubrum* as well as the pathogenic yeast *Candida albicans* (Barazani et al., 2003).[36]

Additionally, its inhibition of three yeasts (*Candida spp.*) and three dermatophytes (*Trichophyton spp.*) (Mehmood et al., 1999).[35] Three yeasts *(Candida spp.*) and three dermatophytes (*Trichophyton spp.*) were inhibited by an aqueous preparation of *T. chebula* galls (Barazani et al., 2003).[36] *T. chebula* methanol extract demonstrated in vitro anti-candidal action against Candida albicans that were resistant to clotrimazole (Bonjar, 2004).[37] A seed extract was effective against the fungus *Trichophyton glabrata*. (Barazani et al., 2003).[36]

4.7. Antioxidant activity

Antioxidants are substances that stop oxidative chain reactions from spreading, hence preventing the oxidation of vital biomolecules (Kumar et al.,2020).[38]

Rats can benefit from the radioprotective and antioxidant characteristics of *Terminalia chebula* fruits. In cultured rat primary hepatocytes and rat liver, tert-butyl hydroperoxide (t-BHP)-induced oxidative damage has also been shown.It has been demonstrated that a fruit extract from *Terminalia chebula* possesses preventive properties (Naik et al.2004).[39] The fruit of the *Terminalia chebula* showed antioxidant activity in six extracts and four compounds, all to varying degrees (Cheng et al.,2003).[40] Its fruit has anti-inflammatory and radioprotective effects on rats (Naik et al., 2004).[39] Furthermore, the protective effects of the *Terminalia chebula* fruit extract against tert-butyl hydroperoxide (t-BHP)-induced oxidative injury on cultured rat primary hepatocytes and rat liver have been linked (Lee et al.,2005 and Lee et al.,2007).[41,42]

4.8. Cytoprotective activity

On the HEK-N/F cells, the fruit of *Terminalia chebula* ethanolic extract demonstrated a strong cytoprotective effect. Additionally, its extract demonstrated a sizable cytoprotective effect against oxidative damage brought on by UVB. Southern blot examinations of DNA extracted from sub-culture passages showed that *Terminalia chebula* had an inhibitory effect on the age-dependent shortening of the telomere length, which was attributed to these findings (M.Na et al.,2004).[43]

Gallic acid (GA) and caffeic acid (CA) were extracted as the active ingredients that prevented the cytotoxic Tlyphocyte-mediated cytotoxicity from the herbal remedy Kashi (myrobalan, the fruit of *T. chebula*). In addition, GA and CA blocked granule exocytosis in response to anti-CD3 stimulation when used in the same dosages. (Chang et al., 2010).[44]

4.9. Antimutagenic, radioprotective and chemopreventive activity

Aqueous extract and hydrolyzable tannins from *T. chebula* have been shown to have an antimutagenic action on *Salmonella typhimurium* (Grover et al.,1992).[45] Gamma radiation was used to damage the DNA from the plasmid PBR322, however an aqueous extract of *T. chebula* prevented the strand breaks that ensued (Naik et al., 2004).[39] Prior to receiving a whole-body radiation dose, mice that had received an aqueous extract of *T. chebula* displayed decreased radiation-induced DNA damage and lessened hepatic membrane lipid peroxidation. Furthermore, it protected human cells from gamma radiation harm when their DNA was exposed in vitro. (Gandhi et al.,2005).[46]

4.10. Antiprotozoal activity

In experiments on amoebic liver in hamsters and caecalamoebiasis in rats, *Boerhavia diffusa, Berberis aristata, Tinospora cordifolia*, and *Zingiber officinale* were combined with *T. chebula* to produce a maximum cure rate of 73% and 89%, respectively (Sohni et al.,1995; Dwivedi et al., 2008).[47,48] *T. chebula* seeds' acetone extract displayed anti-plasmodial efficacy against *Plasmodium falciparum* (Bagavan et al.,2011).[49]

4.11. Anti-inflammatory and anti-arthritic activity

T. chebula dried fruit extract demonstrated anti-inflammatory properties by preventing the production of inducible nitric oxide (Moeslinger et al.,2000).[50] Animals with arthritis caused by collagen developed much more slowly after being given immature *T. chebula* seeds. (Nair et al.,2010).[51] When included in a polyherbal formulation, *T. chebula* has demonstrated a dose-dependent anti-inflammatory effect to treat Freund's adjuvant-induced arthritis in rats (Aller-7) (Pratibha et al.,2004).[52] Studies suggest that tissue protein denaturation, which generates autoantigens, may be associated with inflammatory and

arthritic diseases (Liu et al., 2019).[53]

4.12. Adaptogenic and antianaphylactic activities

In an research administration of *T. chebula* extract after inducing anaphylactic shock decreased serum histamine levels, demonstrating the plant's potent anti-anaphylactic activity (Shin et al.,2001).[54] Rats' peritoneal mast cells greatly enhanced their production of tumour necrosis factor-alpha when exposed to *T. chebula* water-soluble fraction, confirming the plant's potentially anaphylactic activity (Shin et al.,2001).[54]

4.13. Hypolipidemic and hypocholesterolemic acivity

T. chebula extract has been shown to have established hypolipidemic efficacy against experimentally generated athersclerosis (Maruthappan et al.,2010).[55] Additionally, it had hypocholesterelomic action against rabbit atherosclerosis and hypercholesterolemia brought on by cholesterol (Israni et al.,2010).[56]

4.14. Gastro-intestinal motility improving and antiulcerogenic activity

Although *T. chebula* fruit has a long history of usage as a laxative, studies have shown that it can speed up stomach emptying (Tamhane et al., 1997).[57] As Brunner's gland's secretory state improved, it emerged that this action was counterbalanced by a protective impact on the gastrointestinal mucosa, which plays a role in the prevention of duodenal ulcers (Sharma et al., 2011).[58]

4.15. Anti-spasmodic activity

One of the numerous studies on *T. Chebula*, abnormal blood pressure, and intestinal spasms all decreased, indicating the herb's "anti-vata" or "anti-spasmodic" properties. This proves its continuous effectiveness for digestive issues including spastic colon and others (Seyyed et al., 2011).[59]

5. Conclusions

T. chebula, one of the most adaptive plants, has a variety of pharmacological and therapeutic effects. This adaptable plant is a rare source of a range of chemicals with distinct chemical structures since it is utilised as medicine. Although it contains a number of bioactive compounds that have a variety of pharmacological effects, relatively little study has been done on the plant's potential medical use, particularly against multidrug-resistant bacterial infections. These factors, along with the potentially dangerous adverse effects of these medications, have recently resulted in the proscription of numerous widely used treatments. Additionally, long-term usage of powerful medications is linked to the body's defence mechanisms gradually deteriorating. A thorough review of the literature revealed that *Terminalia chebula* has numerous uses and possesses qualities like antimicrobial and wound healing. Therefore, a greater emphasis should be placed on investigating *Terminalia chebula* as a possible antibacterial agent.

6. Source of Funding

None.

7. Conflict of Interest

None.

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