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ABSTRACT

Medicinal plants have long been valued as affordable sources of a variety of phytochemical constituents that are frequently used in synthesis of medicines to treat various disorders. *Terminalia chebula* is known as the "king of medicines" and have extensive medicinal potential to explore. It is ranked first in the Ayurvedic materia medica due to the exceptional curative properties. Also, it has a large number of medical applications and high nutrient content and is widely used to treat a lot of health problems. Numerous phytochemical components, including tannins, flavonoids, gallic acid, chebulinic acid and ellagic acid have been reportedly related with this drug. Moreover, it has been well reported that *Terminalia chebula* has antibacterial, antiviral, antioxidant, antidiabetic, antifungal, antiulcer, anticancerous, antimutagenic and wound healing properties. The goal of this review is to compile all the accessible information on phytochemical and pharmacological evaluation of the plant extracts and some isolated constituents along with the significance of this underexploited treasure in the combat over illnesses.

KEYWORDS: Terminalia chebula, phytochemistry, pharmacological activity, plant extract.

INTRODUCTION

Herbal medicines are most widely used among all the authorized health institutions worldwide and have been considered as affordable and reliable sources of various bioactive constituents. It is well known that plants provide a supplementary source of both shelter and energy for humans. World Health Organization (WHO) estimated that almost 80% of all established products are derived from plants either using plant extracts or their chemically active components. The evaluation of drugs, specifically obtained by phytochemical activities, has once again established a significant area for development and research ^[1].

Terminalia chebula used as folk medicine, belongs to the family combretaceae. It is also known as chebulic myrobalan, black myrobalan and ink tree. Iranian traditional medicine (ITM) named this tree as halilaj or halileh, as well as its fruit is used to prepare remedies ^[2]. There seem to be 250 species of *terminalia* throughout the world ^[3].

Tibetans refer it as the "King of Medicines" because it has exceptional medicinal benefits to mend with a variety of biological activity ^[4]. Moreover, it has a history of being frequently used in

Ayurveda, Unani and Homoeopathic medicine based on the plant's large variety of pharmacological properties related to its biologically active compounds ^[5-6].

Additionally, the plant has been very useful in the treatment of conditions like gout, arthritis, ulcers, cancer, paralysis, and cardiovascular diseases. Now, it is recognized as an abundant resource of large number of organic things to treat different illnesses as well as to produce industrial goods. Despite major advancements in modern medicine, it is still seen as important to develop new drugs from natural sources ^{[7].}

Plant Profile:

- **Biological source:** It consists of plant's root, bark and matured dried fruit.
- Family: Combretaceae
- Common Name: Haritaki
- Synonyms:
 - Hindi: Harre, Harad, Harar
 - Punjabi: Hakeka, Harar
 - ➢ Urdu: Halela
 - ➢ China: Hezi, Zhang-Qin-Ge,
 - ➢ Germany: Myrobalane
 - > Tamil: Aritaki, Amutam, Varikkai, Ammai, Pethiyam
 - Malayalam: Katukka
 - Bengali: Haritaki
 - Felugu: Karakkaya
 - Marathi: Hirda, Harda, Haritaki, Hireda









Figure 1. Terminalia chebula: A. Leaves B. Unripe fruit C. Dried fruit D. Seed powder

TAXONOMY AND NOMENCLATURE- TERMINALIA CHEBULA RETZ.

- **Kingdom:** Plantae
- Subkingdom: Vascular plants Tracheobionta
- Class: Magnoliospida dicotyledons
- **Order:** Myrtales
- **Division:** Magnoliophyte (flowering plant)
- Super division: Spermatophyta (seed plant)
- Genus: Terminalia
- **Species:** *Terminalia chebula*

Botanical Description

- *Terminalia chebula* is a large size evergreen tree with crowded branches and an umbrellashaped crown, grow to a height of 25 m. It usually grows in clayey and shaded soils between 1500 and 2000m of altitude.
- The leaves of *T. chebula* are 10-20 cm long, simple, sub-opposite, exstipulate; petiolate; rarely oval; broad elliptic to elliptic-oblong laminae with acute or acuminate tips.
- The flowers vary in colour from white to yellow, mono-tonous autoicous and have a strong, pungent smell, born in short prickles or terminating panicles.
- Fruit: The fruits are elongate, ovate drupes, colour vary from yellow to orange-brown and are glabrous.
- Seed: The seeds of the plant are ellipsoid, single, rough, and 1.0–2.0 cm by 0.2–0.7 cm in size without ridges ^[9].

T. chebula have three different stages, each with a different phase of fruit development:

- (a) large Myrobalan completely developed stage of fruit
- (b) small Myrobalan immature fruit;
- (c) yellow Myrobalan after seed growth, the fruit's mature stage [8].

TRADITIONAL USES:

T. chebula is most widely used plant in the typical remedies in India as well as in other countries. It is a key component in the Ayurvedic remedy Triphala, that is used to treat liver and kidney disease.

- The dried ripe fruits of *Terminalia chebula* are valued as excellent herb often employed in our traditional healthcare system for its laxative, homeostatic, diuretic, cardiotonic and antitussive properties.
- Fruit is often used to treat conjunctivitis due to its anti inflammatory properties.
- The Haritaki fruits are used as both externally and internally for medical purpose. Externally, its water mixed paste proven to be analgesic and anti inflammatory with the ability to heal and cleanse the wounds and ulcers ^[10].
- Used to treat a various infectious disorders including pneumonia, tuberculosis, fever and cough.
- > Useful as digestive aid to increase the appetite.

- > The Haritaki oil helps in faster healing of wounds, especially burns.
- ➢ Used as anti-astringent ^[11].
- ➤ Used as herbal laxative and colon cleaner.
- > It reduces the chances of acquiring typhoid fever ^[12].
- > It has been found to improve mental abilities and used as an anti-aging agent.
- > The plant functions as an adrenergic and helps in stress relief $^{[13]}$.

Also, it has extensive variety of pharmacological and biological uses including antiviral, antifungal, antibacterial, adaptogenic, anti-anaphylactic properties, hypolipidemic, anti – ulcerogenic and gastrointestinal motility-improving, antidiabetic and retinoprotective, hepatoprotective, cardioprotective, purgative, wound healing, antispasmodic, chemo preventive and immunomodulatory ^[8].

Phytochemistry:

Terminalia chebula contains several constituents including high levels of phenolic compound including hydrolysable tannins, anthraquinone, flavanol, carbohydrates, glucose, and sorbitol ^[11]. Tannic acid is present in its fruit ^[14].

The main major constituents of tannic acid are chebulagic acid, chebulic acid, gallic acid and corilagin ^[15-16]. The pyrogallol type of tannic acid present in *Terminalia chebula* is hydrolyzable. Regional differences affect the tannic acid concentration of *Terminalia chebula* ^[17]. Tri-terpenoids, coumarins conjugated with gallic acid, and flavonol glycosides, known as chebulin and phenolic compounds are identified ^[18-19]. Besides, succinic acid, amino acid, fructose, resin and purgative action of anthraquinone. Some ellagitannins have been associated to the plant, including chebulanin, neochebulinic acid, terchebulin, casurarinin, and punicalagin and others like chebulinic acid, chebulagic acid, and chebulic acid ^[20-22].

S. No	Chemical Constituent	Plant Part	Pharmacological activity	References
110.			activity	
1.	Chebulic Acid	Fruit	Hepatoprotective	[34,35]
2.	β Sitosterol	Fruit		[34]
3.	Corilagin			[34]
4.	Chebulagic Acid	Fruit	Immune- suppressive	[33]
			effect	
5.	Ethyl Gallate	Fruit	Anticancer	[38]
6.	Gallic Acid	Fruit	Anticancer	[34,38]
7.	Chebulinic acid	Fruit	Anticancer	[34,36,37]
8.	Punicalagin			[34]
9.	Linoleic Acid	Fruit		[39]
10.	Tannic Acid	Fruit	Anticancer,	[38]
			Antioxidant	
11.	Ellagic Acid	Fruit	Anticancer,	[40,41]

 Table 1: Pharmacological Activity of some isolated Phytochemical Constituents from

 Terminalia

			Anti-HIV	
12.	Galloyl Glucose		Anti-HIV	[40]
13.	Neo chebulic acid		Hepatoprotective	[35]
14.	Chebulanin	Fruit		[36]
15.	Luteolin		Anticancer	[38]
16.	Ascorbic Acid	Fruit		[42]
17.	Saponin	Fruit		[43]
18.	Terflavin B	Leaves		[44]
19.	Terflavin C	Leaves		[44]
20.	Terflavin D	Leaves		[44]

PHARMACOLOGICAL ACTIONS:

Anti-bacterial activity

The plant *Terminalia chebula* has strong antibacterial properties. Leaves of *T. chebula* are very efficient at producing antibacterial action over the agent that cause gastritis in gram-negative bacteria ^[23]. With creation of an inhibitory barrier against S. epidermis, S. aureus, B. bronchiseptica, B. pumilis, B. cereus, Pseudomonas aeruginosa and P. fluorescens, *Terminalia* proves its potency as an antibacterial agent ^[24]. *T. chebula* ether extract has been the most efficient with minimum Bacteriocidal and Inhibitory content among alcohol, ether and water extract ^[25]. Also, the herb *Terminalia chebula* is super-efficient against the stomach cancer-causing bacteria Helicobacter pylori ^[26].

Anti-fungal activity

The herb *Terminalia chebula* is found extremely effective in fighting against fungal diseases. The plant's aqueous extract has anti-fungal action against several yeast and dermatophytes. It acts well against the dermatophytes *Floccosum, Epidermophyton, Microsporum gypseum, Trichophyton rubrum* and pathogenic yeast *Candida albicans*^[27].

Anti-viral activity

Human immune deficiency virus-1 reverse transcriptase demonstrated inhibitory action when exposed to fruit extract of *T. chebula* ^[21]. In an experiment, Terminalia chebula hot water extract indicated both in-vivo and in-vitro anti-herpes simplex virus (HSV) and anti-cytomegalovirus (CMV) action ^[28]. Herpes simplex virus is a prominent human pathogen which affects sensory neurons latently and for lifetime. Moreover, it is helpful with AIDS and sexually transmitted diseases ^[29].

When used with acyclovir combination, *T. chebula* extract showed strong anti- HSV-1 action. Chebulagic and chebulinic acids are more effective at preventing virus adherence and passage of host tissues than acyclovir and have stronger active antiviral action towards Human Simplex Virus-2. As a result, it could be a suitable option for alternative therapies to prevent Herpes Simplex Virus-2 that sexually spreads ^[30].

Anti-anaphylactic activity

Water extract of *T. chebula* have an inhibitory effect on both local anaphylaxis and systemic anaphylaxis. This evaluation resulted as decrease in the overall occurrence of anaphylaxis and supporting the hypothesis that it could have effective anti- anaphylactic characteristics. The plant also helps in stress resistance in numerous ways along with a variety of other plant extracts. When administered after anaphylactic shock, *Terminalia chebula* showed a strong anti-anaphylactic effect lowering serum histamine concentration when given after anaphylactic shock ^[31-33].

Gastrointestinal activity

In Ayurveda, the herb *Terminalia chebula* is usually recommended for enhancing gastrointestinal motility. Its fruit of has also been observed to improve stomach emptying ^[47]. This activity seems to be countered by a preventive impact on the gastric mucosa as a result of an increase in the secretory state of Brunner's gland, implicated in duodenal ulcer prevention ^[48].

T. chebula contains ellagic acid, which has a strong inhibitory effect on bacteria like E. coli and C perfringens. It is usually recommended to increase gastrointestinal motility in order to reduce gastroparesis symptoms and improve the micronutrient's bioavailability and speed up absorption. The purgative effect is caused by the presence of anthraquinone and sennoside ^[45]. A study on rats revealed that this herb can be a great substitute for prokinetic medicines presently available in market ^[46].

Anti-oxidant activity

T. chebula is known for highly effective anti-oxidant. In a research, 4 pure plant components and 6 plant extracts showed In-vitro antioxidant activity in anti - superoxide radical generation, DPPH activity and anti -lipid peroxidation ^[49]. DPPH radical content (IC50 14 g/mL), nitric oxide radical content (IC50 30.51 g/mL) and hydrogen peroxide scavenge activity (IC50 265.53 g/mL) concentrations were measured by in vitro experiments to evaluate polyphenolic extract for antioxidant activity of *T. chebula* fruit.

The highest maximum triterpenoid concentration was found in the *Terminalia chebula* methanol extract, which exhibited strong anti-oxidant effect in the HRP-luminol H2O2 assay. The pyrogallol-luminol tests showed that the 95% ethanolic extracts has great antioxidant properties. Also, the water extract showed good anti-oxidant properties in the both, CuSO4-Phen-Vc-H2O2 and appears to have highest tannin and phenolic content. Because the four system of ROS chemiluminescence have different mechanisms and the efficiency to scavenge ROS varies for three extracts. Moreover, the extract's phytochemical analysis was measured by figuring out the entire tannin, phenolic, ascorbic acid and flavonoid content.

Additionally, it eliminates radicals produced by hydrogen-peroxide. The overall number of polyphenols present in extract might be the cause of its activity. The extract has antioxidant activity which concentration-dependent and is much higher than that of ascorbic acid. Results conclude that *T. chebula* fruits contain a polyphenolic-rich fraction that is a promising natural antioxidant source ^[50].

Wound healing activity

Using dead space wound models and excision, hydroalcoholic extract of the *T. chebula* fruit was investigated to improve wound healing in alloxan - treated diabetic rats. Animals treated with the extract reduced the wound surface by 82% in comparison with standards, that showed 40% reduction. There was a considerable increase in the weight content of wet and dry granular tissues when

compared to the standard. The extract significantly helps to fasten wound healing process in diabetic rats ^[32].

Dermal wounds of rats treated topically with an alcoholic plant leaf extract indicated that treated wound areas healed more faster, shown by increased contraction rate and shorter duration for tissue repair ^[51].

Anti – diabetic activity

In rats with moderate diabetes produced by Streptozotocin (STZ), *T. chebula* fruit's aqueous extract was examined for its anti-diabetic properties and its efficacy was compared with tolbutamide. When pancreatic islets were employed in in vitro experiments, the results revealed that insulin level was almost twice as high in comparison to the diabetic rats left untreated ^[52].

Decreased level of blood sugar was reported in both alloxan and normal diabetic rats, after 4 hours after oral ingestion of 75% methanolic *T. chebula* extract (100 milligram per kilogram b.w). In both long and short-term tests (300 milligram per kilogram b. w for 8 weeks), chloroform extract of decreased blood sugar levels within 4 hours was reported in the both alloxan and normal diabetic rats during oral ingestion of 75% methanolic *T. chebula* extract (100 milligram per kilogram b.w). In a dose-dependent way, *T. chebula* seeds lowered blood sugar levels in diabetic rats (100, 200 and 300 100 milligram per kilogram b.w).

An investigation was done to determine whether the *Terminalia chebula Retz* species fruit may have anti-diabetic effects. For 30 days, alloxan-monohydrate was administered in Wistar albino rats to control diabetes. This extract's (200 milligram per kilogram b. w) and compared with glibenclamide's effects (600 mg kg-1 b. wt.). The toxicity of extract was zero to 500 milligram per kilogram b.w. The samples were examined for biochemical and antioxidant enzymes related to diabetes at the end of the study. The drug's pharmacological impact on the diabetic condition has been demonstrated by the analysis of this study, despite the fact that mechanism of action is unknown ^{[53].}

CONCLUSION

Terminalia chebula is one among several highly adaptable plants with diverse range of medical applications. In addition to the plant's chemistry, the medical interventions and biological activities have made major advances. The key bioactive phytochemicals extracted from plants are discussed in this study along with their uses to treat various disorders in traditional medicine. However, in order to understand the mechanisms involved causing these activities and eventually identify the active constituents in *Terminalia chebula* fruit extract that are responsible for each action, extensive molecular-level pharmacological research is needed and more investigation for identifying the active components and to understand the plant's role in indigenous medicine, one must understand its modes of action.

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