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A REVIEW ON POTENTIAL PHARMACOLOGICAL ACTIVITIES OF *TERMINALIA CHEBULA*

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ABSTRACT
A common medicinal plant found in India, Burma, and Sri Lanka is *Terminalia chebula* Retz. Throughout the beginning of time, numerous Indian plants have been employed in traditional medical systems to cure a wide range of illnesses and infections. This plant is frequently utilized in India's traditional medical systems. *Terminalia Chebula* is known as the "King of Medicine" in Tibet and is always ranked first in Ayurvedic material medicine due to its amazing healing capacity. TC has anti-inflammatory, antibacterial, antiviral, anti dermatophytic, antimutagenic, hypoglycaemic, hypolipidemic, and hepatoprotective properties. It also has no toxicity and the least amount of negative effects. This study aims to compile the numerous pharmacological and biochemical investigations on *Terminalia chebula* that provide a comprehensive understanding of the herb and its significance in personal hygiene and health care.

KEYWORDS: *Terminalia chebula*, Pharmacological Effect, Gastrointestinal Activity, Anticariogenic Effect, Antidiabetic Effects, Cardiotonic Activity.

1. INTRODUCTION
Terminalia chebula Retz. is called the "King of medicines" in Tibet and is always listed first in the Ayurvedic materia medica because of its extraordinary powers of healing with a wide spectrum of biological activity.[1] *Terminalia chebula* is a moderate tree used in traditional medicines. It is commonly called as Black myrobalan, Ink tree (or) Chebulic myrobalan. It is extensively used in unani, ayurveda and homeopathic medicine. *Terminalia chebula* is a popular traditional medicine not only used in India but also in other countries of Asia and Africa.[2] This is used in traditional medicine due to the wide spectrum of pharmacological activities associated with the biologically active chemicals present in this plant. It is used for the treatment of number of diseases like cancer, paralysis, cardiovascular diseases, ulcers, leprosy, arthritis, gout, epilepsy etc. It has been reported as antioxidant, antidiabetic, antibacterial, antiviral, antifungal, ant cancerous, antiulcer, ant mutagenic, wound healing activities etc.[3] The estimation of World Health Organization reported 80% of the world population are chiefly depends on traditional medicals that is involving the use of plant extracts or their active chemical constituents. Thus, the economic importance of medicinal plants is much more in countries like India & rest of the world. In the last few decades, the position of herbal medicine is getting popularized in both developed and developing countries. This is due to the herbal medicines are, economic, natural origin with higher safety margins and lesser or no side effects.[4]

2. Plant Profile[5]
2.1 Biological source: It consists of dried fruit, root, bark of plant knows as *Terminalia chebula*.
2.2 Geographical Source: Dhaka, Bangladesh.
2.3 Family: Combretaceae
2.4 Common name: Haritaki

3. Types of *Terminalia Chebula*
In Ayurvedic literature *Terminalia Chebula* has been mentioned in Brihatrayee viz. Charak, Susruta and

Vagbhatt main classics but its varieties have first time been described by Nighantus. These verities have diverse in habitat, identification criteria, therapeutic uses as mentioned in following table.[6]

Sr. No.	Types	Habitat	Identification from Fruit shape	Therapeutic uses
1.	Vijaya	Vindhya	Gourd shaped	All disease, purificationary measures & preparation of malt
2.	Rohini	Sindh	Round shaped	Internal use & Wounds
3.	Putana	Vindhya	Proportionately bigger stone	Externa application
4.	Amrita	Champa	Fleshy	Purgative
5.	Abhaya	Champa	Has 5 ridges	Eye disease
6.	Jivanti	Saurashtra	Golden in colour	Oleation theory
7.	Chetaki	Himalaya	Has 3 ridges	Purgative

4. Traditional uses of *Terminalia chebula*

- Fruits work well to minimise swelling, speed up healing, and clean wounds and ulcers.
- prevents pus from building up in skin disorders.
- wound healing, particularly for burns.
- Due to its anti-inflammatory qualities, fruit is also applied on conjunctivitis to provide comfort.
- An anticancer agent is used as a mouthwash.[7]

5. Pharmacological activities of *T chebula*

5.1 Anti-bacterial activity

Kannan et al has investigated on two anti-bacterial compounds, Gallic acid and ethyl ester against methicillin resistant Staphylococcus, have been isolated from ethyl alcohol extract of fruits of *Terminalia chebula. Terminalia chebula* is well effective against Helicobacter pylori, a bacterium responsible for gastritis, ulcer and stomach cancers.[8]

5.2 Anti-fungal activity

Alcoholic and ethyl acetate extracts of *Terminalia chebula* leaves were also tested pathogenic fungi using paper disc method and were found effective compared to that of the reference standard carbendazim.[9]

5.3 Anti-amoebic and immune-modulatory activities

The anti-amoebic effect of a crude drug formulation of *Terminalia chebula* was investigated in experimental caecalamoebias is in rats. In immunomodulation studies, humoral immunity was enhanced where T-cells counts remained unaffected in the animals, but cell mediated immune response was stimulated.[10]

5.4 Molluscicidal activity

The molluscicidal activity of ethanolic extract of *Terminalia chebula* fruit powder was studied against the vector snail Lymnaea acuminata and was found time and concentration dependent.[11]

5.5 Anti-helminthes activity

The ovicidal and larvicidal activities of ethyl acetate, acetone, and methanol extracts of dried leaves and seeds of *Terminalia chebula* were examined by the in vitro on Haemonchuscontortus based on egg hatch and larval development assays at 50, 25, 12.5, 6.25 and 3.13mg/ml. The extracts of leaves and seeds of *Terminalia chebula* showed complete inhibition at 50mg/ml.[12]

5.6 Anti-viral activity

The Fruits extract of *Terminalia chebula* showed inhibitory effects on human immunodeficiency virus-1 reverse transcriptase. Hot water extract of *Terminalia chebula* showed anti-herpes simplex virus (HSV) activity in-vivo and anti-cytomegalovirus (CMV) activity both in-vitro and in vivo in a study. *Terminalia chebula* inhibited HSV-1 entry at non-cytotoxic doses in A549 human lung cells by preventing binding, penetration, and cell to cell spread, as well as secondary infection.[13]

5.7 Anti-mutagenic and anti-carcinogenic activities

The fruit extract of *Terminalia chebula* was studied on growth of several malignant cell lines. One of the fractionated compounds from ethanolic fruit extract of *Terminalia chebula*, chebulagic acid, showed potent dual inhibition against COX and 5-LOX. It also showed antiproliferative activity against HCT-15, COLO-205, MDAMB-231, DU-145 and K562 cell lines. A recent study has shown the ability of triphala to inhibit cytochrome P450.[14]

5.8 Anti-oxidant activity

The *Terminalia chebula* is an excellent anti-oxidant. In a study, 6 extracts and 4 pure compounds of *Terminalia chebula* exhibited in-vitro antioxidant properties of anti-lipid peroxidation, antisuperoxide radical formation and DPPH activities at different concentration. The results demonstrated that triethyl-chebulate was a strong antioxidant and free-radical scavenger, which might contribute to the anti-oxidative ability of *Terminalia chebula.*[15]

5.9 Anti-diabetic activity

75% methanolic extract of *Terminalia chebula* (100 mg/kg body weight) reduced the blood sugar level in normal and alloxan diabetic rats significantly within 4 h by the oral administration. The chloroform extract of *Terminalia chebula* seeds (100, 200 and 300 mg/kg body weight) produced dose-dependent reduction in blood glucose of diabetic rats in both short term and long term study (300 mg/kg body weight for 8 weeks).[16]

5.10 Anti-anaphylactic activity

The *Terminalia chebula* along with several other medicinal plants helps to resist against a number of stressors in different ways. *Terminalia chebula*, when given following anaphylactic shock, reduces the serum histamine levels showing a strong Antianaphylactic activity.[17]

5.11 Anti-nociceptive activity

The Fruits extract of *Terminalia chebula* with petroleum ether, chloroform, and ethanol and water were evaluated for the analgesic activity by using the tail immersion method in mice. The ethanolic extract of the plant exhibited analgesic response at 200,400 and 800mg/kg body weight day.[18]

5.12 Anti-ulcerogenic active

The hydro alcoholic extract of *Terminalia chebula* showed reduction in lesion index, total affected area and percentage of lesion in comparison with control groups in the aspirin, ethanol and cold restraint stress induced ulcer models.[19]

5.13 Anti-arthritic activity

The hydro-alcoholic extract of *Terminalia chebula* produced a significant inhibition of joint swelling as compared to control in both formaldehyde-induced and CFA-induced arthritis. *Terminalia chebula* treatment also reduced serum TNF-α level and synovial expression of TNF-R1, IL-6 and IL-1β.[20]

5.14 Wound healing activity

The alcoholic extract of the leaves of *Terminalia chebula* caused much faster healing of rat dermal wounds in-vivo due to improved rates of contraction and a decreased period of epithelialization for the topical administration. Biochemical studies revealed increase in total protein, DNA and collagen contents in the granulation tissues of treated wounds.[21]

5.15 Cyto-protective activities

The different concentrations of gallic acid and chebulagic acid, isolated from fruit extract of *Terminalia chebula*, blocked cyto-toxic T lymphocyte (CTL)-mediated cyto-toxicity. Granule exocytosis in response to anti-CD3 stimulation was also blocked by the above phyto-chemicals at the equivalent concentrations.[22]

5.16 Radio-protective activity

The aqueous extract of the fruit of *Terminalia chebula* (50µg) was able to neutralize 1, 1-diphenyl-2picrylhydrazyl, a stable free radical by 92.9% and protected the plasmid DNA pBR322 from undergoing the radiation-induced strand breaks.[23]

5.17 Cardio-protective activity

Tthe Cardio-protective effect of ethanolic extract of *Terminalia chebula* fruits (500 mg/kg body weight) was investigated in isoproterenol induced myocardial damage in rats. It was reported that the pre-treatment with *Terminalia chebula* extract had cardioprotective effect due to the lysosomal membrane stabilization preventing myocardial necrosis and inhibition of alterations in the heart mitochondrial ultra-structure and function in the experimental rats.[24]

5.18 Hepato-protective activity

The 95% ethanolic extract of *Terminalia chebula* fruit showed hepatoprotective activity against anti-tuberculosis (anti-TB) drug induced toxicity which could be attributed to its prominent anti-oxidative and membrane stabilizing activities.[25]

5.19 Anti-Spermatogenic activity

oral administration (300 mg/kg body weight for 28 days) of bark of *Terminalia chebula* extracted in acetone, methanol, 50% ethanol, and in aqueous solvents caused histological alterations in seminiferous tubules in testes of treated mice.[26]

5.20 Chemoproventive Activity

T. chebula extract treatment prevened nickel chloride induced renal oxidative stress, toxicity and cell proliferation response in male Wistar rats. The authors suggested *that T. chebula* extract could be used as a therapeutic agent for cancer prevention as it blocked or suppressed the events associated with chemical carcinogenesis.[27]

5.21 Hypolipidemic and Hypocholesterolemic Activity

T. chebula extract administration showed hypolipidaemic activity against experimentally induced atherosclerosis and hypocholesterolemic activity against cholesterol-induced hypercholesterolemia and atherosclerosis.[28] Triphala formulation was found to have hypolipidaemic effects on the experimentally induced hypercholesteremic rats.[29]

5.22 Antiplasmodial activity

T. chebula, water extract revealed antiplasmodial activity in vitro because it inhibits the uptake of [3H] hypoxanthine into the Plasmodium falciparum K1 multidrug-resistant strain and in vivo.[30]

5.23 Anti-dermatophytic effect

An aqueous extract of *Terminalia chebula* showed inhibitory effects on three dermatophytes (Trichophyton spp.) and three yeasts (Candida spp.). An aqueous extract of *T. chebula* showed pronounced inhibitory effects than ethanol extracts indicating the tannins are the plausible candidates for the antidermatophytic effects of *T. chebula*.[31]

5.24 Acetylcholine inhibition activity

Acetylcholinesterase inhibitors have been extensively used for the symptomatic treatment of Alzheimer's disease. The phytochemical isolated form TC named 1,2,3,4,6-penta-O-galloyl-β-D-glucose showed

significant acetylcholinesterase and butyrylcholinesterase inhibitory effects comparable with Tacrine.[32] The aqueous extract of *T. chebula* showed highest efficacy to inhibit acetylcholinesterase when tested in comparison with other herbs viz. *Terminalia bellirica*, and Emblica officinalis and Triphala.[33]

5.25 Hypoglycemic activity

The ethanolic extract of TC fruit has potential hypoglycemic action in STZ induced diabetic rats. The hypoglycemic effect was found to be more effective than standard therapeutic drug Glibenclamide.[34] Further in another short term and long term study the chloroform extract of T. chebula produced dose-dependent reduction in blood glucose of diabetic rats comparable with standard drug, Glibenclamide. The results indicate a prolonged action of TC in reduction of blood glucose probably mediated through enhanced secretion of insulin from the β-cells of Langerhans or through extra pancreatic mechanism. Significant reno-protective activity is also observed in T. chebula treated rats.[35] In another animal study methanolic extract of *Terminalia chebula*, *Terminalia belerica*, Emblica officinalis and their combination 'Triphala' were found to reduce the blood sugar level significantly within 4 h comparable to standard control.[36]

5.26 Anticaries agent

The mouth rinsing with aqueous extract of *Terminalia chebula* strongly inhibited the growth, sucrose induced adherence and glucan induced aggregation of Streptococcus mutans in the saliva samples up to 3 h after rinsing and glycolysis of salivary bacteria for up to 90 min post rinsing as well.[37]

5.27 Myocardial protection

Myocardial infarction, the most dreaded sequel among ischemic heart diseases, is invariably followed by several biochemical alterations. *T. chebula* extract pretreatment was found to ameliorate the effect of isoproterenol on myocardial damage and retained the activities of the altered diagnostic marker enzymes and hence display cardioprotective effect.[38]

5.28 Antinociceptive Activity

The ethanol extract TC is exhibited antinociceptive effect claimed to be contributed to triterpenoids present in TC and may be partially related to the cholecystokinin receptor pathways.[39]

5.29 Antianaphylaxis Activity

The aqueous fraction of *Terminalia chebula* showed inhibition of 48/80-induced anaphylaxis in local as well as systemic level. The effect is pronounced in pretreatment when compared with post induction of anaphylactogen. The serum histamine release levels from rat peritoneal mast cells were reduced in a dosedependent manner.[40]

5.30 Effect of TC on NF-kB

Nuclear factor kappa-light chain-enhancer of activated B cells (NF-κB) is responsible for the expression of numerous genes involved in cell survival, proliferation, angiogenesis, inflammation, invasion and metastasis, among other processes. Treatment with TC extract inhibited NF-κB activity and protected against IκBα degradation and strongly suppressed IκBα phosphorylation in Jurkat-NF-κB-RE-bla cells. In addition, the TC extract downregulated certain NF-κB regulated genes, including IL-8 and MCP-1, in JurkatNF-κB-RE-bla cells. Moreover, gallic acid was identified from the TC extract demonstrating its ability to inhibit NF-κB activity in Jurkat-NF-κB-RE-bla cells.[41,42]

5.31 Effect of TC on Bronchial Asthma

An Ayurvedic clinical study has been reported evaluating two Ayurvedic formulations on bronchial asthama (Tamak shvasa) viz. Shvasaharaleha and Vasaharitakiavaleha. The results of the study indicate that the Vasa Haritaki avaleha containing Terminalia chebula provided better relief than Shvasahara Leha in Tamaka Shvasa.[43]

5.32 Anti-inflammatory activity

Anti-inflammatory effect of fruit extract of *T. chebula* on cultured RAW 264.7 cell lines was determined by COX/LOX assay. Cyclooxygenases (COX-2) and 5-lipoxygensases (5- LOX) are key marker enzymes for the diseases with impaired arachidonic acid metabolism.[44,45] In this attempt to isolate a natural product with COX-LOX dual inhibition, it was identified *Terminalia chebula* as a potential source. Preliminary studies with the methanolic fruit extract of *T. chebula* showed potent inhibition of COX-2 and 5-LOX with IC50 values of 50.54 and 100.254µg/ml respectively.[46]

5.33 Neuroprotective activity

Terminalia chebula methanol and water extracts have neuroprotective activity against H2O2-induced PCI2 cell toxicity and are possible candidates for the treatment of H2O2-induced neurodegenerative diseases. The water extract's effective neuroprotective activity is due to its OH and H2O2 scavenging activities, its highest extraction yield and its overall phenolic and tannin material.[47]

5.34 Prokinetic Effect

Proper gastric emptying has been associated with the correct therapeutic effects shown by the drug therapy and thus, it is essential that the gastric emptying process remains proper. The oral administration of *Terminalia chebula* on gastric emptying has been investigated to confirm its potent prokinetic effect. Metoclopramide significantly increased the gastric emptying (76.33 +/- 12.37%; $p < 0.01$) and atropine inhibited the motility percent gastric emptying (7.26 +/- 19.76%; $p < 0.01$). TCE was found to increase the percent gastric emptying (86.57 +/- 6.65%; $p < 0.01$), which showed that TCE

may serve as an useful alternative to prokinetic drugs available.[48]

5.35 Antiprotozoal activity

A combination of *T. chebula* and four other botanicals (Boerhavia diffusa, Berberis aristata, Tinospora cordifolia, and Zingiber officinale) had a maximum cure rate of 73% in experimental amoebic liver abscess in hamsters[49] and 89% in experimental caecal amoebiasis in rats showing its antiamoebic activity against Entamoeba histolytica.[50] The acetone extract of *T. chebula* seeds showed anti plasmodial activity against Plasmodium falciparum.[51]

5.36 Adaptogenic and antianaphylactic activities

T. chebula fruit was one of the six Ayurvedic herbs administered to animals to test their adaptogenic potential. All six traditional rasayana plants were able to aid the animals against a variety of different stressors working in different ways.[52] Besides, animal studies show that when extract of T. chebula was administered following induction of anaphylactic shock, the serum histamine levels were reduced, indicating its strong antianaphylactic action 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.[53]

5.37 Purgative property

Purgative action of an oil fraction from *T. chebula* has been documented.[54]

5.38 Anti-allergic activity

Aller-7, a polyherbal formulation of seven medicinal plants including *T. chebula* exhibited potent in vitro antiallergic activity in isolated guineapig ileum substrate.[55]

CONCLUSIONS

There is a lot of medical potential for *Terminalia chebula* to investigate. Because of its exceptional therapeutic abilities, it is referred to as the "king of medicines" and is always mentioned first in the Ayurvedic meteria medica. The pharmacological and therapeutic effects are described in this review. Due to its use in medicine, this adaptive plant is a rare source of a variety of compounds with unique chemical structures. The plant's potential medical application, notably against multidrug-resistant bacterial infections, has received very little research attention despite the fact that it contains a number of bioactive chemicals with a variety of pharmacological effects. The unique medicinal herb *Terminalia chebula* has been utilised for centuries in the Indian, Tibetan, and Unani systems of medicine.TC may be used as an important source for discovery of new and potential drug molecules in contemporary health science.

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