

Medicinal uses and phytochemical diversity of *Terminalia* species: An insight into their therapeutic applications

M. Selvamurugan*, M. Chitra, P. Sivakumar and V. Karunakaran

Tamil Nadu Agricultural University, Coimbatore- 641 003, Tamil Nadu, India
E mail: selvamurugan.m@tnau.ac.in

CONTENTS

1. INTRODUCTION
2. *TERMINALIA BELLIRICA*
 - 2.1. Phytochemical composition
 - 2.2. Therapeutic potential
 - 2.2.1. Angiogenesis activity
 - 2.2.2. Antidepressant activity
 - 2.2.3. Antidiarrheal and analgesic effects
 - 2.2.4. Antimicrobial activity
 - 2.2.5. Hepatoprotective properties
 - 2.3. Mechanism of action
3. *TERMINALIA CHEBULA*
 - 3.1. Phytochemical composition
 - 3.2. Therapeutic potential
 - 3.2.1. Anti-diabetic activities
 - 3.2.2. Anti-cancer activities
 - 3.2.3. Antimicrobial activities
 - 3.2.4. Antioxidant activities
 - 3.3. Mechanism of action
4. CONCLUSIONS

ABSTRACT

Terminalia spp., a genus in the Combretaceae family, includes species widely used in traditional medicine across India, Africa and Southeast Asia. This review explores the phytochemical composition and therapeutic potential of species like *Terminalia bellirica* and *Terminalia chebula*. Despite their extensive use, these species remain underexplored in terms of their bioactive compounds and mechanisms of action. Their medicinal properties are attributed to key phytochemicals, including tannins, flavonoids, phenolic compounds, glycosides, and triterpenes. These contribute to a wide range of pharmacological effects such as antioxidant, anti-inflammatory, antimicrobial, cardioprotective, hepatoprotective and anticancer activities. The mechanisms underlying these effects primarily involve modulation of oxidative stress pathways, inflammatory mediators and cell signaling. However, further research is needed to fully understand the underlying mechanisms and unlock the full therapeutic potential of *Terminalia* spp. in modern medicine.

Key words: *Terminalia* spp., phytochemical composition, bioactive compounds, therapeutic potential, pharmacology, mechanism of actions

*Correspondence author,

1. INTRODUCTION

Medicinal plants have long been integral to traditional healing practices worldwide, primarily due to their rich bioactive compounds (9). Despite significant advancements in modern medicine, herbal remedies remain popular for their affordability, accessibility, and deep cultural roots (3). According to the World Health Organization (WHO), around 80 % of the global population still relies on traditional herbal remedies and supplements (44), with over 80 % of individuals in India utilizing herbal treatments within the framework of Ayurveda (15). Globally, traditional medicines, particularly those derived from herbs, are increasingly recognized for their safety, effectiveness, and cost-efficiency in drug development (3). Recent innovations in vertical farming and biotechnology are poised to enhance the appeal of medicinal herbs in developed countries, broadening their applications in pharmaceuticals, nutraceuticals and food products (2).

Ancient texts indicate that approximately 500 plants possess therapeutic potential, with about 800 utilized in traditional medicine. The Indian subcontinent is particularly rich in medicinal flora (13), especially within the Combretaceae family, which encompasses 20 genera and 600 species (38). Among these, the *Terminalia* genus is noteworthy, comprising about 250 species predominantly found in South Asia, Australia and South Africa, with India hosting around 24 species that can grow to heights of 20 to 30 m.

One of the most prominent herbal formulations in Ayurveda is *Triphala*, a polyherbal remedy composed of the fruits of *Emblica officinalis*, *Terminalia bellirica* and *Terminalia chebula* (42). *Triphala* is revered for its efficacy in treating gastrointestinal issues and promoting overall rejuvenation. For centuries, the individual components, particularly *Terminalia bellirica* and *Terminalia chebula*, have been utilized to address infections, digestive disorders, hypertension and even cancer (16,30). However, the phytochemical profiles and the mechanisms underlying their therapeutic effects remain largely unstudied. *Terminalia* species are abundant in bioactive compounds, including tannins, flavonoids, phenolic acids, glycosides and triterpenes, which contribute to their antioxidant, anti-inflammatory, antimicrobial, cardioprotective and anticancer properties (21). These phytochemicals, produced through complex metabolic processes, are significant not only in therapeutic contexts but also in agriculture and research (61). Their potential in preventing degenerative diseases and inhibiting various microorganisms further underscores their medicinal value (34).

Understanding the chemical constituents of these plants is essential for the development of complex therapeutic compounds (41). While preliminary studies indicate promising bioactivity, further research is needed to fully elucidate the pharmacological mechanisms of *Terminalia bellirica* and *Terminalia chebula*. This review aims to provide a comprehensive overview of the phytochemistry and therapeutic potential of these two species, highlighting the critical need for ongoing research into their medicinal significance.

2. *TERMINALIA BELLIRICA*

Terminalia bellirica Roxb. is a significant medicinal plant used in traditional medical systems across South Asia, including Ayurveda, Unani, Siddha and traditional Chinese

medicine (62). It grows in India, Pakistan, Nepal, Bangladesh, Sri Lanka and Southeast Asia. This deciduous tree can grow up to 35 m tall, featuring buttressed trunks and smooth, blackish-grey bark. It has simple, clustered leaves and produce bisexual greenish-yellow flowers and yellowish-brown drupes (Fig. 1). The fruit is valued for treating conditions like hypertension, dysuria, inflammation, and cancer, and ongoing research is exploring its medicinal potential (24). Studies reveal a rich array of bioactive compounds in *T. bellirica* that contribute to its pharmacological effects. It is particularly noted for its antimicrobial, antioxidant, hepatoprotective, antidiarrheal and antihypertensive properties, showing promise in managing chronic diseases, including cardiovascular and liver conditions (14,24). Despite its established use, further research is needed to fully harness the therapeutic potential of *T. bellirica*. Key active compounds include glucosides, tannins, gallic acid, ellagic acid, ethyl galate, galloyl glucose and chebulanic acid, responsible for various medicinal activities such as analgesic, antidiabetic, antioxidant, antiulcer and anticancer effects (33).

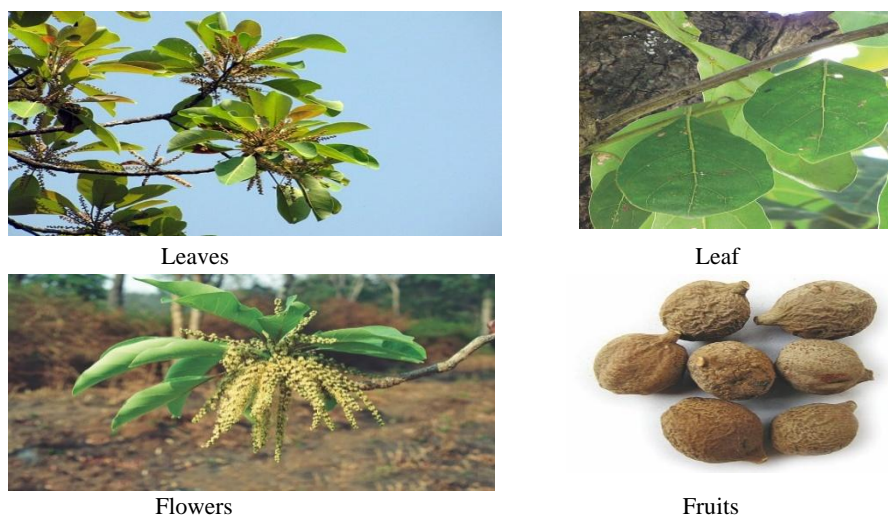


Figure 1. Leaves, flowers and fruits of *Terminalia bellirica*

2.1. PHYTOCHEMICAL COMPOSITION

Terminalia bellirica is characterized by a diverse array of phytochemical constituents, varying by plant part. The stem bark contains compounds such as arjungenin and its glycosides, belleric acid and bellericosides. In contrast, the fruit is abundant in hexahydroxydiphenic acid methyl ester, β -sitosterol, gallic acid, ellagic acid, ethyl gallate, galloyl glucose, chebulagic acid, mannitol, glucose, galactose and rhamnose (64).

The bark exhibits mild diuretic properties and is useful for treating anemia and leucoderma. The fruit possesses various therapeutic effects, including anti-inflammatory, antihelminthic, expectorant, antipyretic and antiemetic properties, making it effective for conditions like asthma, bronchitis, dropsy, dyspepsia, cardiac disorders, skin diseases and ulcers (33). Ripe fruits are often used in traditional Ayurvedic formulations like *Triphala*,

to address eye issues such as cataracts and glaucoma (33). In Ayurveda, *T. bellirica* is commonly employed to manage hypertension, rheumatism and diabetes (58). Its broad therapeutic potential can be attributed to key compounds like glucosides, tannins, ellagic acid, ethyl gallate, galloyl glucose and chebulanic acid. The plant is recognized for its anti-HIV-1, antimalarial and antifungal properties, as well as its roles as an antioxidant, antimicrobial, antidiarrheal, anticancer, antidiabetic, antihypertensive and hepatoprotective agent, along with analgesic, antipyretic and anti-ulcer effects (8,53).

Extensive research has identified over 85 secondary metabolites in the leaves, including ellagitannins, phenolics, saponins, and lignans, which contribute to the medicinal efficacy of *T. bellirica* (49). Notable compounds like ellagic acid and gallic acid are particularly recognized for their potent antioxidant properties, essential for combating oxidative stress and inflammation. The rich and varied phytochemical profile of *T. bellirica* underpins its wide-ranging therapeutic applications, promoting overall health and well-being (55).

2.2. THERAPEUTIC POTENTIAL

2.2.1. Angiogenesis activity

Angiogenesis is a key therapeutic target for cardiovascular diseases, as it enables the body to compensate for reduced blood supply by forming new collateral vessels to alleviate ischemia. *Terminalia bellirica* has shown notable pharmacological effects that support its use in treating cardiovascular disorders (33). In a study by Prabhu et al. (43) the angiogenic potential of *T. bellirica* was evaluated using an in vivo sponge implantation model in mice. Gelatin sponges infused with ethanolic extract of *T. bellirica* leaves (at 0.3 and 0.5 mg) were subcutaneously implanted in Swiss albino mice. After 14 days, histological analysis of the sponges revealed significant angiogenic activity in those containing the extract. This underscores the pharmacological properties and its potential effectiveness of *T. bellirica* in managing cardiovascular conditions.

2.2.2. Antidepressant activity

Terminalia bellirica has demonstrated antihypertensive properties, with fruit extracts shown to effectively reduce arterial blood pressure in anesthetized animal models. This effect is vital for managing hypertension, a significant risk factor for heart disease, stroke and kidney damage. The antihypertensive action is largely attributed to a blend of bioactive compounds, notably ellagic acid, which helps regulate blood pressure by modulating blood vessel tone and endothelial function (33). Additionally, Dhingra and Valecha (19) investigated the antidepressant effects of aqueous and ethanolic extracts of *T. bellirica* in mice using the forced swim test (FST) and tail suspension test (TST). Over 10 days, these extracts were administered orally to young male Swiss albino mice. Both the aqueous extract (50, 100 and 200 mg/kg) and the ethanolic extract (100 mg/kg) significantly decreased immobility time in a dose-dependent manner, without affecting locomotor activity.

The efficacy of the aqueous extract (200 mg/kg) and ethanolic extract (100 mg/kg) was comparable to that of imipramine (15 mg/kg) and fluoxetine (20 mg/kg) and both extracts reversed reserpine-induced immobility. Further investigation using prazosin (62.5 µg/kg), sulphiride (50 mg/kg) and p-chlorophenylalanine (100 mg/kg) revealed that

these substances diminished the antidepressant effects of the extracts. Overall, these findings suggest that *T. bellirica* extracts produce significant antidepressant-like effects through interactions with adrenergic, dopaminergic and serotonergic systems (33,54).

2.2.3. Antimicrobial Activity

T. bellirica exhibits strong antibacterial properties, positioning it as a promising source for developing new antimicrobial agents. Its bioactive compounds can be harnessed to create effective treatments for various infections, particularly in light of the escalating challenge of antibiotic resistance (33). Research has shown that extracts from *T. bellirica* such as methanol, ethyl acetate, butanol, and aqueous extracts demonstrate significant antimicrobial activity against numerous pathogenic microorganisms. Notably, these extracts have shown impressive antibacterial effects against *Micrococcus flavus*, *Staphylococcus aureus*, *Escherichia coli*, and other multidrug-resistant strains, including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum β -lactamase (ESBL)-producing *E. coli* (6,18,20). The effectiveness of *T. bellirica* extracts often surpasses that of traditional antibiotics like streptomycin and ampicillin, underscoring its potential as a natural alternative in the treatment of infectious diseases. The pharmaceutical industry could leverage these unique properties to develop targeted therapies, leading to innovative strategies for managing infections (11).

2.2.4. Antidiarrheal and Analgesic Effects

Extracts from the fruit of *Terminalia bellirica* demonstrate noteworthy antidiarrheal and analgesic properties. Both aqueous and ethanolic extracts have been shown to effectively reduce diarrhea, as indicated by their capacity to inhibit intestinal fluid secretion induced by castor oil in various animal models. Notably, at a dosage of 100 mg/kg, these extracts significantly diminished the number of writhes in mice subjected to acetic acid, which serves as a reliable indicator of pain and discomfort (28).

These results highlight the potential of *T. bellirica* in the management of gastrointestinal disorders, particularly diarrhea and associated pain. The fruit pulp exhibits a specific ability to alleviate dysenteric diarrhea, with pronounced antidiarrheal effects observed at doses of 334 mg/kg, 200 mg/kg, and 143 mg/kg for both the aqueous and ethanolic extracts (31). This evidence underscores the significance of *T. bellirica* as a promising candidate for further research and development as an effective antidiarrheal and analgesic agent.

2.2.5. Hepatoprotective Properties

Terminalia bellirica has demonstrated significant hepatoprotective effects, particularly against liver damage induced by aceclofenac, a widely used nonsteroidal anti-inflammatory drug (NSAID). Research indicates that extracts from *T. bellirica*, especially those high in ellagic acid and gallic acid, can combat oxidative stress and help restore normal liver function markers in Wistar rats experiencing liver damage (35).

This hepatoprotective activity is crucial in preventing liver-related diseases such as hepatitis and cirrhosis, positioning *T. bellirica* as a promising candidate for therapeutic use in managing hepatic disorders (33). Studies have evaluated the protective effects of

T. bellirica fruit extract and its active component, gallic acid (3,4,5-trihydroxybenzoic acid), against carbon tetrachloride-induced intoxication. The toxin significantly elevated serum transaminases and alkaline phosphatase levels, increased hepatic lipid peroxidation and reduced glutathione levels, indicating oxidative stress and liver injury. Additionally, carbon tetrachloride exposure led to a decrease in glycogen content in the liver and kidneys and inhibited the activities of key enzymes such as adenosine triphosphatase and succinic dehydrogenase (54).

Treatment with *T. bellirica* extracts (at doses of 200, 400 and 800 mg/kg) and gallic acid (at doses of 50, 100, and 200 mg/kg) resulted in a dose-dependent recovery of biochemical parameters, including serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), and reduced glutathione levels. Notably, the effects were more pronounced with gallic acid, which proved particularly effective against liver and kidney damage caused by carbon tetrachloride (54).

Moreover, both ethyl acetate and aqueous extracts of *T. bellirica* fruit, along with ellagic acid, exhibit potent antioxidant and anti-inflammatory properties in vitro. In rat studies, prolonged administration of diclofenac resulted in hepatotoxicity characterized by impaired oxidative stress responses and altered liver function biomarkers. However, *T. bellirica* extracts and ellagic acid effectively mitigated this liver damage, showcasing hepatoprotective effects comparable to those of silymarin, a well-established liver protective agent (25). These findings emphasize the need for further research to elucidate the mechanisms by which its various constituents exert their protective effects, paving the way for the development of new natural therapeutic agents.

2.3. Mechanism of Action

The therapeutic effects of *Terminalia bellirica* arise from various mechanisms that target key physiological pathways. Its antihypertensive properties are mainly due to the relaxation of vascular smooth muscle, facilitated by the inhibition of angiotensin-converting enzyme (ACE) and the increased production of nitric oxide (NO) in endothelial cells, leading to vasodilation and reduced blood pressure (5). Additionally, the aqueous-methanolic extract acts as a calcium channel antagonist, blocking calcium influx and release in vascular tissues, further enhancing its ability to lower blood pressure (29). Moreover, *Terminalia bellirica* demonstrates hepatoprotective effects against oxidative stress and liver damage, particularly from substances like aceclofenac, by boosting antioxidant defences and restoring normal liver function (23). It also effectively lowers glucose levels in alloxan-induced hyperglycemia and increases antioxidant enzyme activity (16).

The extract influences immune responses by enhancing T cell and B cell proliferation, thereby promoting cellular-mediated immunity (52). Its antimicrobial properties stem from bioactive compounds that disrupt bacterial membranes and inhibit enzymatic functions, affecting a broad spectrum of bacteria. Additionally, antioxidant effects of *T. bellirica*, largely attributed to its phenolic compounds, scavenge free radicals and reduce inflammation, contributing to its anti-inflammatory benefits. This reduction in oxidative stress is also linked to its anticancer effects, where the extract induces apoptosis in cancer cells by modulating Bcl-2 family proteins and activating caspases (39). Finally, *Terminalia bellirica* exhibits antidiarrheal and analgesic properties by suppressing intestinal fluid

secretion and inhibiting pro-inflammatory mediators, making it effective for managing gastrointestinal disorders and alleviating pain (28).

3. *TERMINALIA CHEBULA*

Terminalia chebula, commonly known as haritaki or myrobalan, is a medium-sized deciduous tree belonging to the Combretaceae family, typically reaching heights of 25 to 30 m. It features a cylindrical trunk that is often relatively short, less than 10 m. The bright-green leaves are spirally arranged, measuring 12 to 15 cm in length and 5 to 6 cm in width, and they shed during the cold season. Young leaves, buds, and branches are covered with soft, shiny reddish-brown hairs (Fig. 2). Revered in Tibetan culture as the “King of Medicine” and in Ayurveda, *T. chebula* is celebrated for its wide range of medicinal properties, including digestive support, antipyretic effects and antiviral activity (10). Rich in bioactive compounds such as tannins, flavonoids and sterols, it exhibits significant antibacterial, antifungal, antioxidant, anti-inflammatory, antidiabetic and anti-aging effects (22).



Leaves



Flowers



Ripe Fruits



Unripe Fruits

Figure 2. Leaves, flowers and fruits of *Terminalia chebula*

3.1. Phytochemical Composition

Terminalia chebula is abundant in a diverse range of phytochemical and nutritional compounds, including proteins, carbohydrates, vitamin C, tannins, flavonoids, triterpenoids and phenolic compounds (57). Its fruits are particularly rich in bioactive constituents such as corilagin, ellagic acid and gallic acid, which contribute to its notable biological activities, including anti-diabetic effects (4). Other significant phytochemicals in *T. chebula* include shikimate, gallate, sitosterol, tannic acid, chebulic acid and various esters of gallic acid (59).

The fruit also contains compounds like ellagitannin, interchebulin, punicalagin, terflavin-A and several fatty acids and sterols, including beta-sitosterol (59). The chemical structures of some of the phytochemicals present in *T. chebula* are shown in Fig. 3 and Fig. 4. Advanced extraction techniques, such as microwave and ultrasonication, enhance the therapeutic potential of *T. chebula* by increasing the yield of phytochemicals and introducing additional beneficial compounds (60). Studies on various parts of the tree viz., fruits, seeds, galls, and bark - extracted with different solvents have identified key bioactive components like chebulic acid, chebulinic acid and chebulaginic acid, which demonstrate significant pharmacological properties, including antioxidant, anti-aging, anti-inflammatory and cardioprotective activities (10).

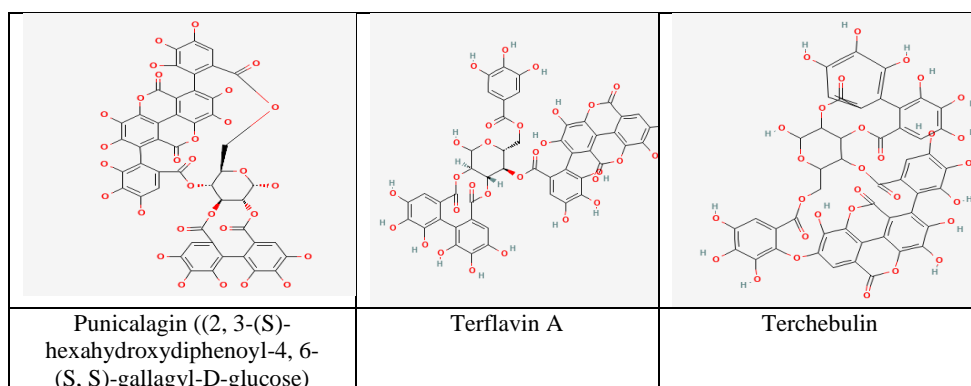


Figure 3. Chemical structure of tannins in *Terminalia chebula* Retz.

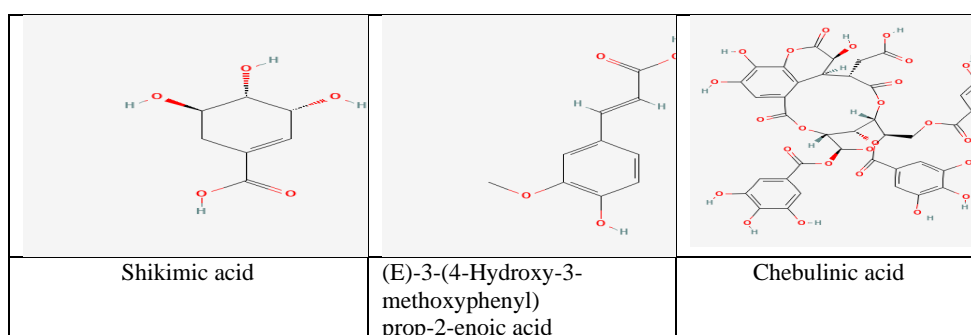


Figure 4. Chemical structure of phenolic carboxylic compounds in *Terminalia chebula* Retz.

3.2. THERAPEUTIC POTENTIAL

3.2.1. Anti-diabetic activities

The anti-diabetic effects of *Terminalia chebula* are primarily due to its active compounds, including corilagin, ellagic acid and gallic acid, which act as α -glucosidase inhibitors, effectively lowering blood glucose levels (4). The tannin-rich

fraction of *T. chebula* leaf extract also accelerates wound healing, reducing the epithelialization period by approximately 40 % in experimental models (12). The dried immature fruit exhibits significant α -glucosidase inhibition, stimulating insulin secretion and enhancing intestinal glucose transport (32,48). Ethanol extracts notably decrease blood glucose and glycosylated hemoglobin levels while improving carbohydrate metabolism (46). Chloroform extracts boost insulin secretion from β -cells of Langerhans and the methanol extract serves as a potent noncompetitive inhibitor of intestinal α -glucosidase, aiding in the management of postprandial hyperglycemia (46). Additionally, chebulic acid normalizes metabolic parameters and oxidative stress, making *T. chebula* a promising antidiabetic agent compared to acarbose (27).

3.2.2. Anti-cancer activities

Terminalia chebula exhibits promising antimicrobial properties, particularly in the context of cancer prevention. Its ethanol fruit extract demonstrates dual inhibitory effects on cyclooxygenase (COX-2) and lipoxygenase (5-LOX) enzymes, showcasing antiproliferative activity against various cancer cell lines, including colon adenocarcinoma (COLO-205) and breast cancer (47). Notably, gallic acid, a key component, induces apoptotic cell death in human stomach and colon cancer cells (47). Studies have revealed moderate cytotoxicity from methanol extracts against lung and colon cancer lines (10). Additionally, the extracts of *T. chebula* are rich in phenolic compounds that may inhibit cancer cell proliferation and lipid peroxidation (50). Chebulinic and chebulagic acids, found in the fruit, enhance apoptotic processes and downregulate drug resistance mechanisms, making *T. chebula* a potential candidate for natural antimicrobial and anticancer therapies (10).

3.2.3. Antimicrobial activities

The antimicrobial activity of *Terminalia chebula* has been extensively researched, demonstrating its efficacy against a wide range of pathogens. Studies indicate that *T. chebula* possesses significant antibacterial properties against both gram-positive and gram-negative bacteria, including *Escherichia coli*, *Shigella sp.*, *Vibrio cholerae* and *Salmonella sp.* (37). Its leaf extracts are particularly potent, while triterpenoids isolated from the stem bark show effectiveness against *Bacillus subtilis* and *Staphylococcus aureus* (17). Notably, gallotannin from *T. chebula* enhances the effectiveness of antibiotics like gentamicin by acting as an efflux pump inhibitor, thereby combating multidrug-resistant strains (7). The fruit extracts have also exhibited considerable antibacterial activity, particularly against *Staphylococcus mutans* and *Staphylococcus aureus*, with acetone extracts demonstrating the highest potency (12). However, these extracts were less effective against other pathogens such as *Lactobacillus acidophilus*, *Candida albicans* and *Saccharomyces cerevisiae* (4). Additionally, ellagic acid from *T. chebula* reduces the virulence of *Pseudomonas aeruginosa* by downregulating essential survival genes, while methyl gallate effectively targets *Shigella sp.* and *Helicobacter pylori* (1). Beyond its antibacterial effects, *T. chebula* exhibits antiviral properties, inhibiting viruses like herpes simplex virus-1 (HSV-1), cytomegalovirus (CMV), influenza A and human immunodeficiency virus type 1 (HIV-1) by blocking

their replication and entry into host cells (40). Furthermore, its extracts demonstrate antifungal activity against various fungi, including *Candida* species and dermatophytes (10).

3.2.4. Antioxidant activities

Terminalia chebula demonstrates strong antioxidant activity, effectively counteracting the harmful effects of reactive oxygen species (ROS) linked to chronic diseases such as cancer, diabetes and cardiovascular conditions. Key compounds, including Casuarinin, chebulanin and ellagic acid, extracted from various solvents, exhibit antilipid peroxidation effects and lower lipid peroxidase levels (56). The polyphenols in *T. chebula* scavenge free radicals and bolster cellular defences by protecting proteins and DNA from oxidative damage (26). Its aqueous extract is particularly effective in preventing lipid peroxidation and boosting glutathione levels. Moreover, the ability of *T. chebula* to inhibit advanced glycation end products (AGEs) links its antioxidant properties to metabolic health, positioning it as a powerful natural remedy for oxidative stress-related conditions (45). Additionally, zinc oxide (ZnO) nanoparticles derived from *T. chebula* fruits show significant scavenging and reducing activities against ROS, as well as efficient photodegradation of methylene blue dye, underscoring the antioxidant and environmental potential of *T. chebula* extracts (12).

3.3. Mechanism of Action

The therapeutic effects of *Terminalia chebula* stem from its rich phytochemical profile, which supports a variety of mechanisms of action. In the context of diabetes management, compounds such as corilagin, ellagic acid and gallic acid play a crucial role by inhibiting α -glucosidase, the enzyme responsible for converting carbohydrates into glucose (4). This inhibition helps regulate blood sugar levels. Additionally, chebulic acid enhances glucose uptake by upregulating GLUT4 and adiponectin expression, while also increasing C/EBP- α mRNA levels, a target of PPAR γ . This combination promotes insulin-stimulated glucose transport in 3T3-L1 adipocytes (27). In cancer therapy, *T. chebula* can alleviate renal complications associated with doxorubicin, an anthracycline chemotherapy drug (36). This protective effect is likely linked to its wound healing, antimicrobial and antioxidant properties, which work synergistically to mitigate treatment-related side effects (12).

The antimicrobial activity of *T. chebula* is primarily attributed to its tannins, flavonoids and other bioactive compounds, which disrupt bacterial cell walls and inhibit microbial growth. Its effectiveness against *Staphylococcus* species suggests promising potential as a treatment for bacterial infections. Additionally, gallotannin from *T. chebula* fruit can work synergistically with antibiotics such as gentamicin and trimethoprim by acting as efflux pump inhibitors, thereby combating multidrug resistance in bacteria (7). *Terminalia chebula* also exhibits significant antiviral properties. It works by downregulating the IKK-NF- κ B and MAPK signaling pathways, which are vital in mediating viral infections. Chebulagic acid, in particular, has been shown to suppress viral replication and reduce cytopathic effects in cells infected with enterovirus 71 (63).

Furthermore, ellagic acid and its derivatives diminish the virulence of *Pseudomonas aeruginosa* by downregulating phosphate kinase-1 (PPK-1), which leads to reduced expression of RpoS, a regulator of survival genes in microorganisms (51). The tannins and phenolic compounds in *T. chebula* also scavenge free radicals, helping to mitigate oxidative stress. Its wound-healing effects are attributed to enhanced epithelialization and tissue regeneration. Moreover, zinc oxide (ZnO) nanoparticles derived from *T. chebula* further enhance its antioxidant capabilities, providing additional protection against oxidative damage (12).

4. CONCLUSIONS

In conclusion, this review emphasizes the therapeutic potential of *Terminalia* species, particularly *T. bellirica* and *T. chebula*, which are rich in bioactive compounds such as tannins, flavonoids, phenolic compounds, glycosides and triterpenes. These phytochemicals contribute to a range of pharmacological effects, including antioxidant, anti-inflammatory, antimicrobial, cardioprotective, hepatoprotective and anticancer activities. However, despite their extensive use in traditional medicine, the mechanisms underlying these therapeutic effects remain inadequately explored. Given the significant reliance on herbal remedies worldwide, particularly in regions where traditional practices dominate, further research is crucial to uncover the bioactive profiles and mechanisms of action of *Terminalia* species. This could not only enhance our understanding of their medicinal properties but also facilitate the development of novel therapeutic agents. Continued investigation into the phytochemistry of *Terminalia* spp. is essential for unlocking their full potential in modern medicine and promoting their integration into contemporary healthcare practices.

ACKNOWLEDGEMENTS

The authors would like to thank the Dean of HC&RI(W), Trichy for their support in writing this manuscript.

AUTHOR CONTRIBUTIONS

M. Selvamurugan - Literature collection and writing of the manuscript. M. Chitra - Manuscript conceptualization. P. Sivakumar - reviewing and editing. V. Karunakaran - reviewing and editing.

DECLARATIONS

We declare that all authors of this Ms. have made substantial contributions. We did not exclude any author who substantially contributed to this Ms. We have followed our ethical norms established by our respective institutions.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

ETHICAL APPROVAL

The authors declare that the study was carried out following scientific ethics and conduct. However, this study did not involve any use of animals, hence no ethical approval has been obtained from the concerned committee.

REFERENCES

- Acharyya, S., Sarkar, P., Saha D.R., Patra, A., Ramamurthy, T. and Bag, P.K. (2015). Intracellular and membrane-damaging activities of methyl gallate isolated from *Terminalia chebula* against multidrug-resistant *Shigella* spp. *Journal of Medical Microbiology* **64**(8): 901-909.
- Ahmed, K.K.M., Gupta, G.B.M., Singh, N. and Kumar, A. (2021). Global Research on *Terminalia arjuna*: A Quantitative and Qualitative Assessment of Publications during 2004-18. *Pharmacogn. Review* **14**: 45-52.
- Amalraj, A. and Gopi, S. (2017). Medicinal properties of *Terminalia arjuna* (Roxb.) Wight and Arn.: A review. *Journal of Traditional Complement Medicine* **7**: 65-78.
- Anam, K., Widharna, R.M., Kusriani D. (2009). α -Glucosidase inhibitor activity of *Terminalia* Species. *International Journal of Pharm* **5**: 277-280.
- Asif, M., Lisa, S. and Qais, N. (2021). Exploring the Anti-Hypertensive Properties of Medicinal Plants and Their Bioactive Metabolites: An Extensive Review. *American Journal of Plant Sciences*, **12**: 1705-1740.
- Ayoob, F.A., Awad, H.M., El-Kousy, S.M., Rashed, K.N. and Al-Sayed, N.H. (2014). Phytochemical and biological investigations of *Terminalia bellirica* Roxb. Leaves. *Journal Pharmacist Research* **8**(4): 500-510.
- Bag, A. and Chattopadhyay, R.R. (2014). Efflux-pump inhibitory activity of a gallotannin from *Terminalia chebula* fruit against multidrug-resistant uropathogenic *Escherichia coli*. *Natural Products Research* **28**(16): 1280-1283.
- Biradar, Y.S., Jagatap, S., Khandelwal, K.R. and Singhania, S.S. (2008). Exploring of antimicrobial activity of triphala mashi-an ayurvedic formulation. *Complement Alternat Med* **5**(1): 107-113.
- Buenz, E.J., Verpoorte, R. and Bauer, B.A. (2018). The ethnopharmacologic contribution to bioprospecting natural products. *Annu. Rev. Pharmacol. Toxicol* **58**: 509-530.
- Bulbul, M.R.H., Chowdhury, M.N.U., Naima, T.A., Sami, S.A., Imtiaj, M.S, Huda, N. and Uddin, M.G. (2022). A comprehensive review on the diverse pharmacological perspectives of *Terminalia chebula* Retz. *Heliyon* **8**(8): e10220. doi: 10.1016/j.heliyon.2022.e10220.
- Chakraborty, T.S. Chatterjee., Datta, L. and Sengupta, A. (2021) Antimicrobial activity of *Terminalia bellirica* (Gaertn.) Roxb. against multidrug resistant *Staphylococcus saprophyticus*. *International Journal of Pharmaceutical Sciences and Research* **12**: 5353-5363.
- Chanda, S., Menpara, D. and Desai, D. (2013). Antimicrobial Activity of *Terminalia bellirica* leaf and stem collected from two different sites. *American J Phytomed Clinic Therapeut* **(9)**: 721-733.
- Chitra, M., Selvamurugan, M, Karunakaran, V., Sakila, M. and Marimuthu, M. (2024). Allelopathic medicinal plants: Major *Terminalia* spp. *International Journal of Advanced Biochemistry Research* **SP-8**(10): 740-746.
- Chitra, M., Selvamurugan, M, Sivakumar, P., Karunakaran, V., Anuratha, A. and Kavithashree, G.G. (2024). Phytoceutics and medicinal pharmacology of *Terminalia* spp.: A recent review. *International Journal of Advanced Biochemistry Research* **8**(9S): 679-686.
- Das, G., Kim, D.Y., Fan, C., Gutiérrez-Grijalva, E.P., Heredia, J.B., Nissapatom, V., Mitsuwana, W., Pereira, M.L., Nawaz, M., Siyadatpanah, A., Norouzi, R., Sawicka, B., Shin, H.S. and Patra, J.K. (2020) Plants of the Genus *Terminalia* : An Insight on Its Biological Potentials, Pre-Clinical and Clinical Studies. *Front Pharmacol* **(10)**8: 11:561248.
- Das, M.S. and Devi, G, (2015). *In vitro* cytotoxicity and glucose uptake activity of fruits of *Terminalia bellirica* in Vero, L-6 and 3T3 cell lines. *J App Pharm Science* **5**(12): 92-95.
- Datta, S., Pal, N.K. and Nandy A.K. (2017). In-vitro antibacterial activity of bioactive potent compounds from *Terminalia chebula* against some common human pathogens. *Pharmacol Pharm* **8**(9): 283-291.
- Dharmaratne, M.P.J., Manoraj, A., Thevanesam, V., Ekanayake, A., Kumar, NS., Liyanapathirana, V., Abeyratne, E. and Bandara BMR. (2018). *Terminalia bellirica* fruit extracts: in-vitro antibacterial activity against selected multidrug-resistant bacteria, radical scavenging activity and cytotoxicity study on BHK-21 cells. *BMC Complement Alternate Medicine* **18**(1): 325.
- Dhingra, D. and Valecha, R. (2007). Evaluation of antidepressant like activity of aqueous and ethanolic extracts of *Terminalia bellirica* Roxb. fruits in mice. *Indian Journal of Experimental Biology* **45**(7): 610-616.
- Elizabeth, K.M., (2005). Antimicrobial activity of *Terminalia Bellirica*. *Indian Journal of Clinical Biochemistry* **20**(2): 150-153.
- Eloff, J.N., Katerere, D.R. and McGaw L.J., (2008). The biological activity and chemistry of the southern African Combretaceae. *Journal of Ethnopharmacology* **119**(3):686-699

22. Elsadek M.F. and Al-Numair K.S. (2024). Profiling of phytochemical constituents of *Terminalia chebula* fruit extract by different solvent effects and synchronized analysis of FTIR and GCMS. *Journal of King Saud University – Science* **36(9)**: 103414.
23. Gupta, A. and Pandey, A. (2020). Aceclofenac-induced hepatotoxicity: An ameliorative effect of *Terminalia bellirica* fruit and ellagic acid. *World Journal of Hepatology* **12(11)**: 949-964.
24. Gupta, A., Kumar, R., Bhattacharyya, R., Bishayee, A. and Pandey, A.K. (2020). *Terminalia bellirica* (Gaertn.) roxb. (Bahera) in health and disease: A systematic and comprehensive review. *Phytomedicine* **77**: 153278.
25. Gupta, A., Kumar, R., Ganguly, R., Singh, A.K., Rana, H.K. and Pandey, A.K. (2020). Antioxidant, anti-inflammatory and hepatoprotective activities of *Terminalia bellirica* and its bioactive component ellagic acid against diclofenac induced oxidative stress and hepatotoxicity. *Toxicology Report* **8**: 44-52.
26. Hedina, A., Kotti, P., Kausar, J. and Anand V. (2016). Phytopharmacological overview of *Terminalia chebula* Retz. *Pharmacognosy Journal* **8(4)**: 307-309.
27. Huang Y.N., Zhao, D.D., Gao, B., Zhong, K., Zhu, R.X., Zhang, Y., Xie, W.J., Jia, L.R. and Gao, H. (2012). Anti-hyperglycemic effect of chebulagic acid from the fruits of *Terminalia chebula* Retz. *International Journal of Mol Science* **13(5)**: 6320-6333.
28. Khan, A.K. and Gilani, A.H. (2010). Antisecretory and analgesic Activities of *Terminalia bellirica*. *African Journal of Biotechnology* **9(18)**: 2717-2719.
29. Khan, A.U. and Gilani, A.H. (2008). Pharmacodynamic evaluation of *Terminalia bellirica* for its antihypertensive effect. *Journal of Food and Drug Analysis* **16(3)**: 6-14
30. Konczak, I., Maillot F. and Dalar A. (2014). Phytochemical divergence in 45 accessions of *Terminalia ferdinandiana* (Kakadu plum). *Food Chem* **151**: 248–256.
31. Kumar, B., Divakar, K., Tiwari, P., Salhan, P. and Goli D. (2010). Evaluation of anti-diarrhoeal effect of aqueous and ethanolic extracts of fruits pulp of *Terminalia bellirica* in rats. *International Journal of Drug Development Research* **2(4)**: 769-779.
32. Kumar, G.P.S., Arulseivan, P., Kumar D.S. and Subramanian, S.P. (2006). Anti-diabetic activity of fruits of *Terminalia chebula* on streptozotocin induced diabetic rats. *Journal of Health Science* **52(3)**: 283-291.
33. Kumar, N. and Khurana S.M.P. (2018). Phytochemistry and medicinal potential of the *Terminalia bellirica* Roxb. (Bahera). *Indian Journal of Natural Products and Resources* **9(2)**: 97-107.
34. Lukmanul, H., Girija, A. and Boopathy, R. (2008). Antioxidant property of selected *Ocimum* species and their secondary metabolite content. *Journal of Medicinal Plants Research* **2(9)**: 250-257.
35. Manohar, V.R., Sowmya., Mohandas, R., Gopalakrishna, H.N. and Chandrashekar, R. (2021). Effect of aqueous extract of *Terminalia bellirica* fruit pulp on alcohol affected learning in swiss albino mice. *IP International Journal of Comprehensive and Advanced Pharmacology* **6**: 76-78.
36. Muneer, A., Alhowail, A., Aldubayan, M. and Rabbani S.I. (2020). The activity of *Terminalia chebula* Retz. extract on doxorubicin-induced renal damage in rats. *Journal of Pharm Pharmacogn Research* **8(3)**: 237-246.
37. Mussarat, S., Adnan, M., Begum, S., Ur Rehman, S., Hashem, A. and Abd Allah, E.F. (2021). Antimicrobial screening of polyherbal formulations traditionally used against gastrointestinal diseases. *Saudi Journal of Biological Science* **28(12)**: 6829-6843.
38. Muthu, C., Ayyanar M., Raja N. and Ignacimuthu S. (2006). Medicinal plants used by traditional healers in Kancheepuram District of Tamil Nadu, India. *Journal of Ethnobiol Ethnomedicine* **2(1)**: 1-10.
39. Nishida, K., Yamaguchi, O. and Otsu, K. (2008). Crosstalk between autophagy and apoptosis in heart disease. *Circ Research* **103**: 343-351.
40. Oyuntsetseg, N.M.A., Khasnatinov, P., Molor-Erdene, J., Oyunbileg, A.V., Liapunov, G.A., Danchinova, S., Oldokh, J., Baigalmaa and Chimedragchaa C. (2014). Evaluation of direct antiviral activity of the Deva-5 herb formulation and extracts of five Asian plants against influenza A virus H3N8. *BMC Compl. Alternative Medicine* **14(1)**: 1-9.
41. Parekh, J. and Chanda, S. (2008). Phytochemicals screening of some plants from western region of India. *Plant Arch* **8**: 657-662.
42. Peterson, C.T., Denniston, K. and Chopra, D. (2017). Therapeutic Uses of *Triphala* in Ayurvedic Medicine. *Journal of Alternate Complement Medicine* **23(8)**: 607-614.
43. Prabhu, V.V., Chidambaranathan, N. and Gopa, V. (2012). Evaluation and quantification of angiogenesis activity of *Terminalia Bellirica* Roxb. by mice sponge implantation method. *J Young Pharm* **4(1)**: 22–27.
44. Ramesh, P. and Palaniappan A. (2023). *Terminalia arjuna*- a Cardioprotective Herbal Medicine–Relevancy in the Modern Era of Pharmaceuticals and Green Nanomedicine- A Review. *Pharmaceuticals* **16(1)**: 126.

45. Ramkissoon, J., Mahomoodally, M., Ahmed, N. and Subratty, A. (2013). Antioxidant and anti-glycation activities correlates with phenolic composition of tropical medicinal herbs. *Asian Pacific Journal of Tropical Medicine* **6(7)**: 561-569.
46. Rao, N.K. and Nammi, S. (2006). Antidiabetic and renoprotective effects of the chloroform extract of *Terminalia chebula* Retz. seeds in streptozotocin-induced diabetic rats. *BMC Compl. Alternative Medicine* **6(1)**: 1-6.
47. Reddy, D.B., Reddy, T., Jyotsna, G., Sharan, S., Priya, N., Lakshmipathi, V. and Reddanna, P. (2009). Chebulagic acid, a COX-LOX dual inhibitor isolated from the fruits of *Terminalia chebula* Retz., induces apoptosis in COLO-205 cell line. *Journal of Ethnopharmacol* **124(3)**: 506-512.
48. Sabu, M. and Kuttan R. (2002). Anti-diabetic activity of medicinal plants and its relationship with their antioxidant property. *Journal of Ethnopharmacol* **81(2)**: 155-160.
49. Saha, P.K., Patrab, P.H., Pradhan, R., Dey, R. and Das. (2011). Effect of *Terminalia bellirica* and *Terminalia chebula* on wound healing in induced dermal wounds in rabbits. *Pharmacol Online* **2**: 235-241.
50. Saleem, A., Husheem, M., Harkonen, P. and Pihlaja, K. (2002). Inhibition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula* Retz. Fruit. *Journal of Ethnopharmacol* **81(3)**: 327-336.
51. Sarabhai, S., Harjai, K., Sharma P. and Capalash, N. (2015). Ellagic acid derivatives from *Terminalia chebula* Retz. increase the susceptibility of *Pseudomonas aeruginosa* to stress by inhibiting polyphosphate kinase. *Journal of Applied Microbiology* **118(4)**: 817-825.
52. Saraphanchotiwitthaya, A., Sripalakit, P. and Ingkaninan, K. (2008). Effects of *Terminalia bellirica* Roxb. methanolic extract on mouse immune response in vitro. *Mj Int J Sci Techology* **2**: 400-407.
53. Saraswathi, M.N., Karthikeyan, M., Kannan M. and Rajasekar, S. (2012), *Terminalia bellirica* Roxb.-A phytopharmacological review. *Int J Pharm Biomed Research* **3(1)**: 96-99.
54. Shukla, S., Jadon, A. and Bhadauria, M. (2006). Protective effect of *Terminalia bellirica* Roxb, and gallic acid against carbontetra chloride induced damage in albino rats. *Journal of Ethanopharmacology* **109**: 214-218.
55. Sobeh, M., Mahmoud, M.F., Hasan, R.A., Abdelfattah, M.A.O, Osman, S., Rashid, H.O., El-Shazly, A.M. and Wink, M. (2019). Chemical composition, antioxidant and hepatoprotective activities of methanol extracts from leaves of *Terminalia bellirica* and *Terminalia sericea* (Combretaceae). *PeerJ* **7**: e6322.
56. Subramaniyan, S., Chennam, S. and Devi, S. (2005). Antioxidant activity of ethanolic extract of *Terminalia chebula* fruit against isoproterenol-induced oxidative stress in rats. *Indian Journal of Biochem. Biophysics* **42**: 246-249.
57. Sultan, M.T., Anwar, M.J., Imran, M., Khalil, I., Saeed, F., Neelum, S. and Al-Jbawi, E. (2023). Phytochemical profile and pro-healthy properties of *T. chebula*: a comprehensive review. *International Journal of Food Properties* **26(1)**: 526-551.
58. Tanaka, M., Kishimoto, Y., Saita, E., Suzuki-Sugihara, N., Kamiya, T., Taguchi, C., Iida, K. and Kondo, K. (2016). *Terminalia bellirica* extract inhibits low-density lipoprotein Oxidation and macrophage inflammatory response in vitro. *Antioxidants* **5**: 20.
59. Tariq, A.L and Reyaz, A.L. (2013). Significances and importance of phytochemical present in *Terminalia chebula*, *International Journal of Drug Development and Research* **5**: 256-262.
60. Thomas, R.E., Kamat, S.T. and Kamat, D.V. (2015). HPTLC and HPLC analysis *T. chebula* extracts prepared using microwave and ultrasonication assisted extraction methods. *Journal of Pharmacognosy and Phytochemistry* **4**: 192-196.
61. Vasu, K., Goud, J.V, Suryam, A. and Singara-Chary, M.A. (2009). Biomolecular and phytochemical analyses of three aquatic angiosperms. *African Journal of Microbiol Research* **3(8)**: 418-421.
62. Xiang, H., Zhang Y., Jiaming, L., Li, L., Ziwei, L., Rui, N., Dan P., Lining, J., Jianhong, C. and Yao, L. (2025). *Terminalia bellirica* (Gaertn.) Roxb. Extracts reshape the perifollicular microenvironment and regulate the MAPK pathway for androgenetic alopecia treatment. *Journal of Ethnopharmacology* **337(1)** 118778.
63. Yang, Y., J. Xiu, J. Liu, L. Zhang, X. Li, Y. Xu, C. and Zhang, Q.L. (2013). Chebulagic acid, a hydrolyzable tannin, exhibited antiviral activity in vitro and in vivo against human enterovirus 71. *International Journal of Mol Science* **14(5)**: 9618-9627.
64. Yoganasimhan, S.N. (2000). Medicinal plants of India, **Vol. 2**. Tamil Nadu, Bangalore: Vedams Books (P) Ltd., 443.