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REVIEW ARTICLE

Phytochemical Richness and Medicinal Efficacy of *Terminalia*: Bridging Traditional and Modern Medicine

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Abstract

The *Terminalia* genus of plants, which has over 200 species, is known for its wide range of chemical composition and high medicinal value. Considerable research has been carried out in this area; however, there are still gaps in understanding the full range of its therapeutic capabilities, hence the need for a focused review to fill these gaps. This paper attempts to synthesize existing information concerning the plant chemical composition and biological properties of *Terminalia* species while resolving the abovementioned issues and providing prospects on their clinical importance and sociomedical relevance in the present era. The analysis identified a range of bioactive compounds, such as tannins, flavonoids, and triterpenoids, which are known to have antioxidant, anti-inflammatory, and hepatoprotective activities. Major challenges include the lack of defined protocols and poor clinical validation. The review provided an outline of future directions in the field, making it clear that there is a need for relevant procedures and clinical trials. This review amalgamates historical perspectives and presents scientific research to provide new perspectives, especially focusing on the lesser-known species of *Terminalia* and their novel applications in nanotechnology. Unlike previous assessments, it addresses the inconsistencies in the methods employed and proposes a holistic strategy for understanding the therapeutic attributes of the genus.

Key words: Ethnomedicine, nanomaterials, natural products, pharmacology, phytochemistry, *Terminalia*, therapeutics.

INTRODUCTION

The *Terminalia* genus, comprising over 200 species, is widely recognized for its diverse chemical composition and significant medicinal potential. Over recent years, substantial progress has been made in identifying various *Terminalia* species' bioactive compounds and therapeutic applications. Yet, critical gaps remain in our comprehensive understanding of their full pharmacological potential. Previous reviews have largely focused on isolated aspects such as phytochemistry or specific therapeutic uses, often overlooking recent advances in drug delivery systems, clinical trials, and toxicological evaluations.[1] This review seeks to integrate the phytochemical diversity and therapeutic potential of *Terminalia* species, connecting traditional use with modern scientific validation.[2] This work integrates ethnobotanical knowledge with contemporary pharmacological ideas, identifies deficiencies in existing research, and examines the potential therapeutic applications of *Terminalia* substances in modern medicine.

This review expands the focus by examining new developments in nanotechnology applications related to the *Terminalia* genus. It investigates how nanoformulations improve the bioavailability and therapeutic effectiveness of *Terminalia* phytochemicals, tackling the constraints of conventional applications. This review offers a thorough examination of *Terminalia*'s potential in drug transport, targeting, and bioactive stability through the integration of nanotechnological breakthroughs, thereby laying the groundwork for future therapeutic advancements.

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Studies were incorporated according to the following criteria: Published from 2015 to 2024, this body of work concentrated on *Terminalia* species with established phytochemical profiles or medicinal attributes,[3] encompassing both empirical and review studies on nanotechnology applications pertinent to *Terminalia*, peer-reviewed and disseminated in esteemed journals, and offering insights into pharmacological efficacy, bioavailability improvements, or molecular mechanisms. Studies devoid of methodological clarity, non-peer-reviewed sources, or those pertaining to unrelated species were removed. This selection guarantees thorough coverage of current research connecting traditional and innovative therapeutic applications.

Research contributions

This study explains the differences in phytochemical components and therapeutic values of *Terminalia* species, emphasizing the reason for the traditional use and present-day medicinal potential. It incorporates contemporary findings, provides insight for future research development, practices standardization, and stresses innovative uses, including game-changing nanotechnology technology.

Genus *Terminalia* is derived from the Latin word terminus, which means the ending or a limit. This is why the leaves appear to be situated at the apex of the shoots. Plants of the genus *Terminalia* usually originate from shrubs and grow into tall trees found in tropical moist forests. They are mostly large trees whose height can reach even 75 m above the ground.[4] Many *Terminalia* species are found throughout southern Asia, including the Himalayas, Madagascar, Australia, and tropical or subtropical Africa. Conduct study on the therapeutic benefits of plants; the southern region of Asia has garnered significant interest in *Terminalia* species, which are widely utilized in traditional medicine throughout nations such as India, Tibet, and China. Rephrase. Nanotechnology is a new strategy that is used to improve the absorption and solubility of active components in biological systems. Genus *Terminalia* consists of plants that have been used for treating various diseases in different regions of the world.[5] The peoples of the world have systems of traditional medicine that make use of these plants to help in the treatment of several diseases: From problems of the stomach and its bacterial infections to common flu, sore throat, conjunctivitis, diarrhea, or dysentery; such as a viral disease characterized by high fever with pain of the stomach ulceration, pregnancy-related migraines, and heart diseases that have tissue necrosis due to hookworm infestation. High blood pressure, throat pain (sore throat), hypertensive crises (over 180), jaundice (yellowing of the skin due to liver dysfunction), leprosy (a long-lasting disease caused by the bacillus *Mycobacterium leprae*), epistaxis – or nasal bleeding – and edema (a condition where excess fluid accumulates), pneumonia (lung inflammation). Different traditional healing systems across the globe have used the various *Terminalia* species to treat diseases.[6]

The reason why artificial drugs have not appealed to so many people across the globe in the past decade is because of the belief that natural herbal medicines are far more effective than manmade drugs. Diagnosis and treatment in India existed before Western medicine with the help of indigenous practitioners who would utilize over 2500 plant species, whereas in the world's traditional medicine plants, over 70,000 have been utilized. In the world, healing plants are gaining importance at an approximate rate of 7–15% annually. According to the statistical data of the WHO, herbal treatment has been utilized by nearly 4 billion individuals.

Contemporary scientists understood this only recently, while the fact that plants that produce and store secondary metabolites, including but not limited to glycosides, alkaloids, tannins, essential oils, vitamins, and other minerals, have always been viewed as healing plants.[7] The application of therapeutic plants in health care for human beings has become common in practice either as a standalone drug or in combination with other forms of treatment. Cultural practices related to plant foods often include their utilization in the pharmacological sense as source materials using seeds, roots, barks, flowers, leaves, and berries, among others; hence, their use is often referred to as phytomedicine or botanical medicine.[8] *Terminalia mollies* is employed for treating diarrhea, gonorrhea, and malaria, while the *T. branchy* stemma plant is applied for the purpose of HIV treatment in several regions of Africa; other than that, it cures schistosomiasis and stomach diseases. *T. mollies* is employed for treating diarrhea, gonorrhea, and malaria, whereas the *Terminalia brachystemma* plant is used in different parts of Africa for HIV management. Other than that, it treats schistosomiasis and digestive issues.[9]

A thorough review of the literature available on the subject has been oriented towards the different active phytochemicals and physiological activities, respectively, in an effort to provide novel account documents on certain *Terminalia* species that have been focused on their phytochemical constituents, various biological activities, and objective data within this genus.[10] This present review comprises two main parts: The first part discusses the phytochemistry of certain *Terminalia* species. In contrast, the second part consists of literature studies undertaken by various researchers regarding the biological studies found in the genus *Terminalia*. In the literature, a total of 39 *Terminalia* species have been reported, and their phytochemicals were found to contain, among others, terpenes, flavonoids, simple phenols, tannins, and lignans.[11]

Research gaps

Existing studies often neglect an in-depth investigation of the less studied *Terminalia* species and their possible synergistic actions. Furthermore, established pharmacological activity evaluative methods and clinical applications addressing

studies are clamored for but hardly ever explored in prior studies, thus limiting their usefulness in practice.

Many reviews tend to focus on a narrow range of taxa or particular bioactive compounds, ignoring the wide range of forms that the *Terminalia* genus contains. For instance, a review might deal with the effects of *Terminalia arjuna* in managing heart conditions. Yet, the potential of other related species with either similar or different pharmacological properties is poorly presented.

It is common that standardized methodologies are missing in assessing the pharmacological potential of species of *Terminalia*. Variability in extraction techniques and assay conditions can produce conflicting outcomes, jeopardizing the results' validity. There have been recent reviews that recommend the use of standard procedures to achieve uniformity of outcomes. Most of the currently available reviews focus on in vitro and animal studies without paying much attention to the clinical implications of these findings. This might create a disparity between the orthodox ways of practice and modern scientific validation of practices, suggesting reasons why there ought to be many more clinical studies done to prove the efficacy of the use of the *Terminalia* species. Many publications focus on a particular evidence-based bioactive compound. This might lead to the neglect of the whole-plant extract synergy.[12] Such a limitation may not account for the different phytochemical interactions that are synergistic to the holistic bioactivity of *Terminalia* spp. Most reviews, however, fail to account for the more recent developments in nanotechnology and its uses in increasing the bioavailability and efficacy of *Terminalia* extracts. These advances are crucial for optimizing the therapeutic potential of these plants. In addition to more widespread *Terminalia* species, this article seeks to implement the standard approach and also cover the clinical and other aspects. It aims to fill this gap by bringing together the existing and potential resources in the medicinal utilizations of *Terminalia*, thus eliminating the imbalance between ethnomedical applications and modern drug development research.

The intended review will assist in ameliorating the understanding of the phytochemical variation and medicinal utilization, address standardization of evaluation procedures, and improve the clinical application of traditional uses. It will discuss insights on multiple action therapy and review the progress on nanomedicine to enhance therapy.

Research questions

What are the under-researched *Terminalia* species' phytochemical compositions and pharmacological effects? In what ways may the standardization of methodologies enhance the trustworthiness of results? What novel applications, such as nanotechnology, can improve the therapeutic effectiveness of *Terminalia* extracts in clinical environments?

This article thoroughly examines the *Terminalia* genus, highlighting its lesser-known species, unique phytochemical characteristics, and contemporary uses of nanotechnology. It seeks to integrate traditional knowledge with modern pharmacological ideas, addressing gaps in the literature regarding therapeutic promise and clinical validation.

REVIEW METHODOLOGY

The review technique employs a systematic strategy for collecting and analyzing literature concerning *Terminalia* species. The preliminary actions involve executing thorough literature searches in databases such as PubMed, Scopus, and Google Scholar, concentrating on studies released during the past 5 years. Chosen publications will be assessed rigorously concerning their techniques, results, and significance to phytochemical and pharmacological attributes. Data will be analyzed to discern trends, deficiencies, and requirements for uniformity in current research. The review will integrate historic medicinal applications with contemporary scientific findings, providing a comprehensive viewpoint. This methodology seeks to establish a comprehensive framework for subsequent study and applications.

OVERVIEW

Due to its establishment in the heavens, *Terminalia* comprises large trees. This means that it belongs to the flowering plant family commonly known as Combretaceae, which has numerous species. Its trees are found throughout tropical regions, including Asia, Australia, and Africa. Here are some interesting features concerning this intriguing genus.[13]

Species diversity

Around three hundred kinds of *Terminalia* are considered valid. It's a pretty big figure for one class of vegetation!

Etymology

What a captivating title for this family! The basis for the name of a genus in Latin is considered an intriguing thing.[14] This meaning actually means leaves that exist at the shooting points of trees. Hence, imagine them like nature in disguise, saying: "We might as well make our foliage visible."

Traditional medicinal use

Through the ages, various species from the genus *Terminalia* have been used for medicinal purposes as substitutes by different societies from all continents. Many native groups around the globe used these trees in many ways because of their healing power.

Geographical spread

In support of each other's existence, they can thrive in different ecological zones in the world. As an illustration, there are some examples such as the large *Terminalia catappa* (Indian almond tree or tropical almond) or less recognized *Terminalia elliptica* (also called the crocodile tree).[15]

Phytochemical investigations conducted on varied *Terminalia* species have exhibited the presence of multiple categories of bioactive compounds, for instance, tannins, pentacyclic triterpenes including their glycosides, flavonoids, and further phenolic substances. Reviewing the existing literature indicates that the plant genus *Terminalia* has proven to be a good source of tannins and pseudo-tannins such as gallic acid and its mono-gallates, chebulic ellagitannins, and non-chebulic ellagitannins, as well as the ellagic acid derivatives like glycosides of ellagic acid.[16]

Terminalia chebula

Antioxidants mitigate reactive oxygen species, which induce oxidative stress and damage proteins, lipids, and DNA, contributing to diseases such as cancer, cardiovascular conditions, and neurological disorders. Natural antioxidants, including vitamins C and E, flavonoids, and polyphenols, are prevalent in fruits, vegetables, and plant-derived meals. Adhering to a balanced diet abundant in antioxidants is typically more advantageous than high-dose supplementation, which may have negative effects if used excessively. Consequently, natural sources of antioxidants are favored for health maintenance.[17] The research work involved using a process known as chemiluminescence to assess the antioxidant activities of three extracts from *T. chebula* Rentzias, a known medicinal plant. Chemiluminescence is a method where light is generated through chemical reactions, and free radicals and antioxidants are detected in this study.[18]

T. arjuna

Initially, it was uncovered that the plant's bark had 34% ash, entirely composed of pure calcium carbonate. This means high calcium levels in the bark. Further analysis of the water extract of this bark was revealed. The general composition of minerals is enhanced by 23% calcium salts. With antioxidant and astringent properties, 16% of tannins are present. The water extract would seem fairly more efficient as a source of these particular items than the alcohol one since it contains only small amounts of tannins and traces of coloring matter. This difference between aqueous and alcoholic extracts can help better utilize healing qualities possessed by this plant.[19]

Terminalia bhadra

Specimens infected with diseases and those with no visible signs of disease were collected from various parts of *Terminalia* species to diagnose their diseases in the laboratory, determine their severity limitations, and classify them into three groups. (i) Samples with green and healthy leaves (samples with no obvious disease symptoms at the time of picking), (ii) Samples with partially infected leaves (where severity varies depending on the host and pathogen) and (iii) Samples with dead or totally affected/diseased leaf areas (100% disease severity). The dried samples were powdered to a size of 0.5 mm particles using a coffee grinding hand mill and again using a pestle and mortar. Proline, which is a primary metabolite, as well as secondary metabolites such as alkaloids, flavonoids, phenols, and steroids, were assessed from all three samples following standard methodologies.[20]

Terminalia tomentosa

Phytochemical exploration of the extracts from plants revealed varying types of phytochemicals such as carbohydrates, alkaloids, cardiac glycosides, anthocyanins, flavonoids (apigenin, kaempferol, luteolin, myricetin, quercetin, rutin), α and β amyrin, lupeol, mudarine resin, non-toxic proteolytic enzyme calotropin, a potent bacteriolytic enzyme calactin, phytosterols, tannins, triterpenoids, saponins, proteins, and fixed oils and fats, respectively.[21] Among the isolated phytoconstituents are tannins such as arjunetin, gallic acid, arjunic acid, ellagic acid, and triterpenoids such as betulinic acid and oleanolic acid with steroid β-sitosterol being included. Furthermore, present were some new substances, 1333–1343, among them being di-n-octyl phthalate, arjunahomosesquiterpenol, dibutyl phthalate, di-isobutyl phthalate, terpene glycoside, flavone, and chalcone glycoside. These biologically functional materials are responsible for the healing properties of *T. tomentosa*. Chemical constituents as provided in Table 1.[22]

Terminalia brownii

Since traditional medicine often makes use of *T. brownii*, certain extracts have noticeable effects on the body. Therefore, we carried out analysis focusing on it as well as you that began working on them with that data. Here, we have extracted oleanane-type triterpenoids together with some alkylated ellagic acid from the plant that were used for estimating the antiplasmodial and antimicrobial properties. The ethyl acetate fraction was found to be antiplasmodial active based on a liquid/liquid partitioning of fractions from the stem bark's EtOH extract. The chromatographic procedures carried out on this fraction yielded a total of fifteen known compounds and one new oleanane-type triterpenoid as discussed in the experimental section. According to published information

on arjunic acid, the identified and isolated compounds were recognized through NMR and MS data.[23]

Comparison with similar medicinal plants with *Terminalia*'s unique properties

This review evaluates distinct *Terminalia* species- *T. chebula* (Haritaki), *T. arjuna*, *Terminalia bellirica* (Bibhitaki), *T. catappa* (Indian Almond), *Terminalia glaucescens*, *Terminalia ivorensis*, *T. brownii*, and *T. tomentosa* to emphasize their specific characteristics in comparison to other medicinal flora. *T. arjuna* is distinguished for its cardioprotective attributes, stemming from its elevated levels of triterpenoids and flavonoids, whilst *T. chebula* provides significant antioxidant and hepatoprotective benefits, which are ascribed to its ellagitannins and polyphenols.

In contrast to plants such as *Phyllanthus emblica* and *Azadirachta indica*, *Terminalia* species have unique phytochemical compositions and bioactivities, notably through bioactive tannins, glycosides, and phenolic compounds. These chemicals exhibit improved bioavailability, stability, and tailored therapeutic efficacy when included in nanotechnology formulations. This thorough comparison emphasizes the diversity and adaptability of *Terminalia* species in various health applications and showcases their distinct potential in both traditional and contemporary therapeutic contexts [Figure 4].

Traditional uses of *Terminalia* species

T. arjuna

Ayurveda practitioners acknowledge *T. arjuna* as a widely used Ayurvedic herb. The herb was used by practitioners for the treatment of various heart ailments, including hypertension, angina, and arterial obstruction. Besides, it is effective against all sorts of chest pains, such as falls, spermatorrhoea, ecchymosis, and sexually transmitted diseases, including gonorrhea, based on its properties as an astringent, cooling agent, aphrodisiac, etc. In addition, it is thought to be cardio-tonic in its ability to improve heart function in cases of ulcers, leukorrhea, diabetes, coughs, tumors with too much sweating, asthma inflammation, etc.[24]

T. chebula (Haritaki)

Ayurvedic uses far as Ayurveda is concerned, Haritaki is also referred to as the "king of medicines," and this herb is usually thought to be a perfect rasayana, potent purgative, astringent, and has anti-aging properties. Treat digestive disorders such as constipation and indigestion. Improves heart health and lowers cholesterol. Used as a wound healer, anti-inflammatory, and to enhance cognitive functions [Figure 2].[25]

Terminalia bellerica (Bibhitaki)

Ayurvedic use: For ages, Bibhitaki has been valued for its quality of balancing the body's three doshas (Vata, Pitta and Kapha) and powerful cleansing action. Treats respiratory conditions like asthma, cough, and bronchitis. Northern India is a region affected by diarrhea, dysentery, and indigestion, among other gastrointestinal illnesses. It also shows antioxidant, antimicrobial, and anti-inflammatory properties.[26]

T. catappa (Indian almond or tropical almond)

In traditional practices, the foliage is used for healing purposes and curbing inflammatory processes. Employed for various dermatological disorders like dermatitis and eczema. The bark, along with the leaves, is thought to provide protection and enhancement of the liver's activity.

T. glaucescens

In African traditional medicine, the bark is valued for its ability to prevent microbial growth and combat infections caused by bacteria. This applies particularly to febrile states, malaria,and other infectious diseases. Like the other species, it is also employed in healing injuries and sores internally and externally.[27]

T. ivorensis

As per the practice of traditional African medicine, the cure for malaria and fever in general is obtained from the herbal bark and leaves. Moreover, the inner bark is also used to treat digestive issues such as diarrhea and dysentery.[28]

Research conducted on the pharmacological properties of the *Terminalia* genus in plants of this group has shown that there are a number of important activities including but not limited to antimicrobial and antioxidant effects, cytotoxicity, anti-inflammatory, hypoglycemic, and cardiotonic effects as well as Mosquito repellent and antiviral actions.

Antimicrobial activity

Extracts from multiple *Terminalia* species exhibit considerable antibacterial efficacy. *Terminalia australis's* methanol and water extracts demonstrated efficacy against *Candida albicans* and *Candida kruzzei*. Moreover, aqueous extracts of *T. brownii* stem bark, wood, and roots showed significant efficacy against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and antifungal properties against *C. albicans*. The data indicate that *Terminalia* species possess potential as antibacterial agents. The antibacterial properties of certain *Terminalia* species, including *T. bellerica and T. catappa,* are ascribed to their abundant presence of tannins, flavonoids, and essential oils. These phytochemicals demonstrate extensive antibacterial efficacy by compromising microbial cell membranes,

obstructing biofilm development, and affecting the metabolic processes of infections.[29]

Antioxidant activity

Numerous plants within the *Terminalia* genus exhibit significant antioxidant capabilities. Methanol extracts from the trunk bark of *Terminalia alata*, *T. bellirica*, and *Terminalia corticosa* exhibited considerable antioxidant activity comparable to that of ascorbic acid, a recognized antioxidant. Furthermore, flavonoid glycosides, including apigenin derivatives, were detected in the leaves of *T. catappa*, enhancing its antioxidant capacity. These findings underscore the considerable capacity of *Terminalia* species to mitigate oxidative stress and their potential in therapeutic applications. The antioxidant properties of *Terminalia* species, especially *T. chebula,* are mainly ascribed to their elevated concentrations of tannins, flavonoids, and phenolic substances. These phytochemicals counteract free radicals, diminishing oxidative stress and safeguarding cellular components from harm.[30]

Anti-inflammatory

Inflammation significantly contributes to numerous diseases, with macrophages serving a pivotal role in pathogen defense. The outer membrane components of Gram-negative bacteria can induce macrophage activation, resulting in the secretion of inflammatory mediators. Research indicates that CETB exposure can diminish the expression of critical inflammatory molecules, including tumor necrosis factor, interleukin, cyclooxygenase, and nuclear factor, thereby decreasing the creation of pro-inflammatory cytokines. This indicates CETB's capacity to modulate inflammation and diminish disease-related inflammatory responses. Compounds such as arjunic acid and flavonoids present in *T. arjuna* impede the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), resulting in reduced production of inflammatory mediators.[31]

Cardiovascular

Some *Terminalia* species demonstrated cardiovascular activities. For example, the barks of *T. arjuna* displayed strong inotropic and hypotensive effects, mild diuretic activity, and antithrombotic effects with the ability to enhance prostaglandin E2 and lower cholesterol levels. In this study, the cardioprotective properties of *T. pallida* fruit ethanolic extract were tested on rats with isoproterenol-induced myocardial infarction. Due to its high antioxidant properties, it provides significant myocardial protection dose-dependently. This can work as an encouraging factor in the fight against cardiovascular diseases as a therapeutic food for their control.[32]

Mosquitocidal

Insect-transmitted diseases remain a significant worldwide health issue, as escalating mosquito resistance to chemical insecticides challenges vector management. This research examines the larvicidal and ovicidal properties of *T. chebula* extracts utilizing solvents such as methanol, ethyl acetate, and chloroform against the mosquito species *Anopheles stephensi*, *Aedes aegypti*, and *Culex quinquefasciatus*. Methanolic extracts had the greatest larvicidal efficacy, while the ovicidal impact was most pronounced at elevated doses, resulting in full mortality in certain species. No fatalities were observed in the untreated control group.[33]

Hepatoprotective activity

Arjuna and Chebula are a couple of species in the *Terminalia* genus that contain distinct phytochemistry. They have been found to defend the liver against harmful substances like toxins, ethanol, and other stressors. These active compounds are useful in promoting detoxification and liver cell regeneration. The above statement mentions that two species of the genus *Terminalia – arjuna and Chebula* - have different pharmacological properties. Among these properties are the effects on hepatic protection against alcohol, toxins, and other forms of stressors. In this way, they assist the detoxification process as well as help restore damaged liver cells. The hepatoprotective properties of *Terminalia* species, including *T. chebula and T. tomentosa*, are linked to their capacity to improve liver detoxification mechanisms and facilitate hepatocyte regeneration. Bioactive substances, such as ellagic acid and other tannins, regulate the production of phase I and phase II detoxifying enzymes (e.g., glutathione S-transferase) and safeguard liver cells from oxidative damage.[34]

Anticancer activity

Several species in the *Terminalia* genus have shown cytotoxic effects against various cancer cell lines: *T. chebula* exhibits antiproliferative activity against colorectal cancer and breast cancer cells, primarily through its tannins and flavonoids. *T. bellerica*: Has shown anti-tumor effects in *in vitro* and *in vivo* studies. *T. arjuna*: Some studies suggest its compounds can inhibit the growth of cancerous cells in leukemia and breast cancer.[35]

Investigation of obscure phytochemicals in various *Terminalia* species

Different *Terminalia* species possess lesser-known phytochemicals that substantially enhance their medicinal properties, with each species exhibiting a distinct assortment of secondary metabolites:

- *T. chebula*: Besides prevalent polyphenols and tannins, *T. chebula* encompasses chebulagic acid, chebulinic acid, and ellagic acid. These chemicals exhibit potent anti-inflammatory, antibacterial, and hepatoprotective

activities, with new research indicating their potential to alter immune response and promote wound healing

- *T. arjuna*: Renowned for its cardioprotective attributes, *T. arjuna* comprises arjunic acid, arjungenin, and arjunetin, in addition to lesser-known saponins such as arjunolone. These enhance its antioxidant and cardiotonic properties, facilitating lipid management and vasodilation, which are advantageous for cardiovascular health
- *T. bellirica*: This plant contains bellericanin, belliricanin A and B, which exhibit potential neuroprotective properties, as well as gallotannins that offer distinctive hepatoprotective and antidiabetic effects. Recent studies indicate that these phytochemicals may also mitigate oxidative stress in cerebral tissues
- *T. catappa,* often known as Indian almond, contains substances including punicalagin, catappanin, and other flavonoids such as quercetin derivatives, which demonstrate significant anti-inflammatory and anticancer effects. Research underscores the significance of these chemicals in skin health owing to their anti-photoaging properties
- *T. glaucescens*: This West African species is abundant in lupane-type triterpenoids, including glaucenone, which has antibacterial and antiparasitic properties, especially against malaria and bacterial infections. *T. glaucescens* possesses distinctive flavonoids that may enhance metabolic health by modulating blood glucose levels
- *T. ivorensis*: This African species contains chemicals such as ellagitannins and ivorenin, a distinctive lignan known for its anti-inflammatory and possibly anticancer activities. This species is conventionally employed in pain and infection management, and research indicates that these phytochemicals may possess analgesic properties
- *T. brownii*: This lesser-known species contains brownie flavone and other distinctive tannins and flavonoids that exhibit potent antioxidant and antibacterial effects. Studies suggest possible therapeutic advantages in the treatment of gastrointestinal infections and the promotion of wound healing
- *T. tomentosa*: Abundant in tannins like tomentosin, as well as saponins and flavonoids, *T. tomentosa* demonstrates potential in diabetes management and renal health support owing to its nephroprotective attributes [Figure 3].[36]

Innovative discoveries from insufficiently studied *Terminalia* species

This study highlights innovative findings obtained from insufficiently studied *Terminalia* species, including *T. glaucescens*, *T. ivorensis*, and *T. brownii*. In contrast to well-researched species like *T. arjuna* and *T. chebula*, these lesser-known variations include distinctive phytochemicals, namely glaucenone, ivorenin, and browniiflavone, that demonstrate potential bioactivities but are predominantly unexamined. The identification and characterization of these molecules unveil novel therapeutic potentials, especially in antibacterial, anti-inflammatory, and anticancer applications. These findings substantially address deficiencies in *Terminalia* research, indicating more pharmacological potential within the genus and emphasizing prospects for additional studies and novel applications in contemporary medicine.[37]

Mechanisms of *Terminalia* bioactive compounds exert therapeutic effects

The comprehensive mechanistic insights into the therapeutic actions of *Terminalia* species. This may include delineating certain pathways, such as the Nrf2-ARE route associated with antioxidant activity, the NF-κB pathway facilitating anti-inflammatory effects, and signaling processes pertinent to hepatocyte protection and regeneration. Moreover, using pathway diagrams and interaction models would graphically elucidate these intricate processes, enhancing comprehension for readers. This methodology elucidates the mechanisms by which bioactive substances manifest their pharmacological effects while enhancing the scientific integrity of the review by contextualizing these findings with pertinent literature.[38]

Phytochemical variations among different *Terminalia* species

Phytochemical differences across several *Terminalia* species underscore their distinct bioactive characteristics and their medicinal uses. *T. chebula* is abundant in tannins and phenolic chemicals, which enhance its potent antioxidant and hepatoprotective effects. Conversely, *T. arjuna* possesses triterpenoids, such as arjunic acid, which promote cardiovascular health. *T. bellerica* possesses a unique ellagic and gallic acid profile, recognized for their anti-inflammatory properties. The phytochemical variations highlight the distinct medicinal potentials within the *Terminalia* genus, indicating that each species may have unique advantages that merit further exploration for therapeutic applications in traditional medicine [Figure 1].[39]

Safety and toxicological evaluation

Preclinical studies

Available literature shows that few clinical and preclinical studies have been done on different species in *Terminalia*. The methanolic extract is rich in hydrolyzable tannins from *T. chebula* Retz. fruit clearly demonstrates its influence on acute toxicity. Imparting strong, nontoxic properties for 14 days at a dose of 5000. Therefore, it can be concluded that *T. chebula* Retz. fruit extracts are safe to consume. High-performance liquid chromatography analysis confirmed the presence of chebulagic acid, corilagin, and chebulinic acid; their molecular structures were further elucidated through NMR spectroscopic data, which also confirmed their structures. In contrast, other members of the genus *Terminalia*

showed varying degrees of toxicity. The influential changes in certain biochemical indices of both male and female rats were significantly attributed to *T. chebula* Retz. extracts causing a reduction in their body weight. This could be due to the connection between the increased number of tannins found within these plant extracts and reduced forms of feeding habits (low intake), growths hindered by inadequate food, poor feed efficiency rates as well as a reduced net MPME and protein digestion rates.

Clinical studies

The therapeutic potential of *Terminalia* species is constrained by a paucity of clinical investigations into their bioactivities. It consolidates essential data, emphasizing the analgesic properties of *T. chebula* Retz. A placebo-controlled, double-blind crossover trial involved the administration of 500 mg of *T. chebula* fruit extract, which contains chebulinic acid, chebulagic acid, and hydrolyzable tannins, to 14 participants. The results evaluate the safety and analgesic effectiveness of the extract, underscoring the necessity for further comprehensive clinical studies.

Challenges and future directions

Challenges: Habitat loss and deforestation

Many *Terminalia* species are found in regions prone to deforestation due to agricultural expansion, logging, and urbanization. This habitat destruction threatens the natural populations of these species.

Overharvesting

Species like *T. chebula* (Haritaki) and *T. arjuna* are heavily harvested for their medicinal and commercial value. Overharvesting can lead to population declines, especially in regions where these species are not sustainably managed.

Limited phytochemical and genetic studies

Although several species in the genus are recognized for their medicinal properties, there is limited research on the full range of phytochemicals present in many *Terminalia* species. Understanding the genetic diversity and phytochemical composition of under-researched species is crucial for their conservation and use.

Taxonomic uncertainty

The genus *Terminalia* is taxonomically complex, with overlapping morphological traits among species. This can make accurate species identification challenging, confusing ecological studies and conservation efforts.

Climate change

Terminalia species are sensitive to changes in rainfall patterns, temperature, and other climate variables. Climate change significantly threatens these species' habitats, potentially affecting their growth, reproduction, and survival rates.

Lack of sustainable management practices

In numerous areas, the methods supporting the continued cultivation and harvesting of *Terminalia* species are still non-existent. Because of the absence of guidelines and practices, wild populations keep on over-exploiting.

Future directions

Conservation initiatives

It is important to implement programs geared toward the protection and restoration of habitats. Including in-situ conservation (i.e., conservation of species within their natural habitats) and *ex-situ* (for example, botanic gardens and seed banks) efforts would help conserve species and genetic variability.[40]

Phytochemical research and drug development

Further exploration of the bioactive components found in the species of the *Terminalia* family can bring new dimensions into the field of medicine. Increasing demand for natural and plant-derived products has brought *Terminalia* into the limelight as a rich source of bioactive materials that can be formulated into innovative treatments [Figure 5].

Genetic and genomic studies

Applying genomic technologies, including DNA barcoding and genome sequencing, is essential for clarifying taxonomic ambiguities and enhancing phylogenetic comprehension. These instruments are essential in evolutionary research and substantially aid conservation efforts by detecting genetic variety and safeguarding endangered species. Genomic research underpins breeding methods focused on improving desirable features, such as disease resistance and growth rates, offering significant insights for taxonomy and conservation initiatives.[41]

Sustainable cultivation and agroforestry

Encouraging the growth of *Terminalia* species within agroforestry systems would come with various advantages, such as a source of livelihood for locals, less exploitation of wild species, and the promotion of biodiversity. It will also be possible to guarantee the sustainability of the species for both ethnomedicine and economic activities.

Ecological restoration

The *Terminalia* genus is important in forest ecosystems, especially in maintaining soil health, hydrology, and biodiversity. It is possible to reintroduce these species into the ecological restoration processes to rehabilitate degraded land areas, strengthen ecosystem services, and support wildlife.[42]

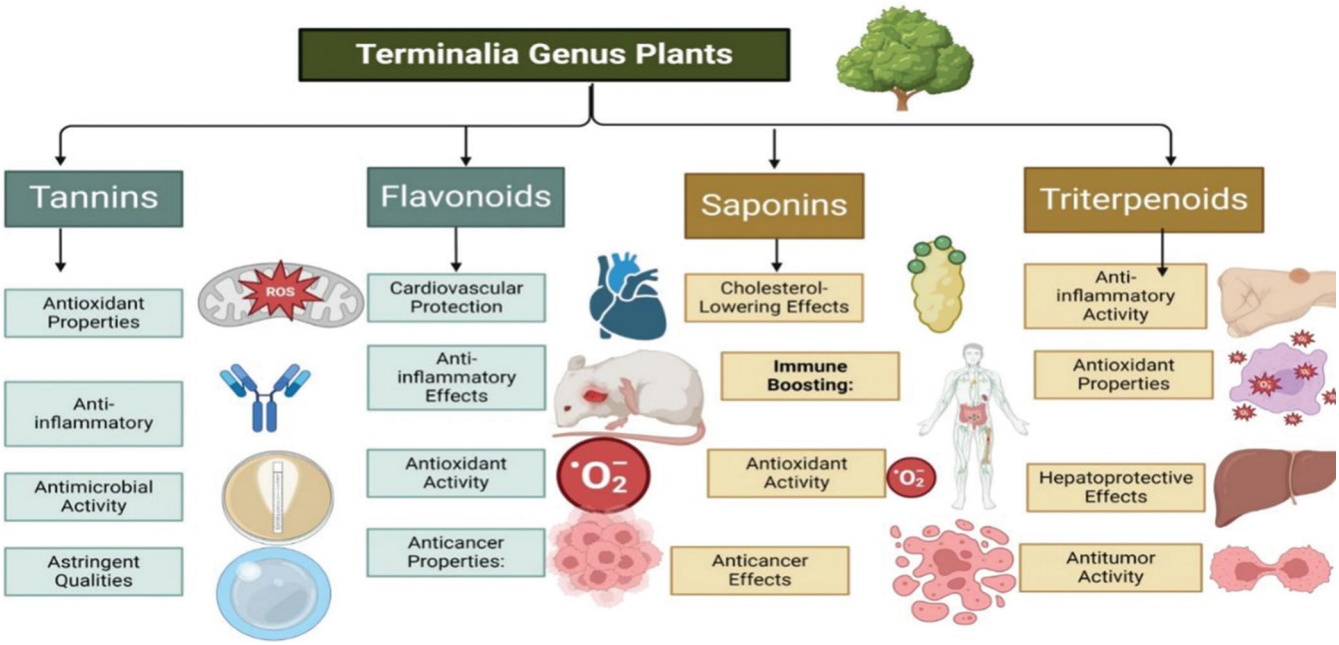


Figure 1: Bioactive compounds derived from *Terminalia* genus plants—tannins, flavonoids, saponins, and triterpenoids—demonstrate significant antioxidant, anti-inflammatory, cholesterol-lowering, hepatoprotective, and immune-enhancing properties, underscoring their potential in the management of cardiovascular, inflammatory, and cancer-related disorders



Figure 2: *Terminalia chebula* fruit



Figure 3: *Terminalia tomentosa* plant

Ethnobotanical research

Delving deeper into the cultural practices regarding the use of *Terminalia* species, especially in native communities, may open up new horizons concerning the copious unexplored medicinal applications. The ethnobotanical research would also help demonstrate how these plants can be used without compromising their ecological niches in their areas of origin.

Biotechnology and tissue culture

The advancement of biotechnology through tissue culture and genetic modification, for instance, can enable the conservation of threatened species, increase productivity, and maximize the synthesis of specific bioactive substances. Furthermore, these approaches may also promote the extensive growth of *Terminalia* species in foreign areas.[43]

RESULTS AND FINDINGS

The investigation of *Terminalia* species threw up several important findings regarding the phytochemistry and pharmacology of these plant species. A broad range of bioactive compound classes, including tannins, flavonoids, phenolic acids, saponins, and triterpenoids, were found among the diverse species. These phytochemicals are linked with numerous pharmacological activities such as antioxidant, anti-inflammatory, hepatoprotective, or cardioprotective, further encouraging their medicinal use.

The comparative study found significant shortcomings in existing studies, especially the lack of established processes for evaluating the pharmacologic activity of *Terminalia* formulations. This difference of ten often

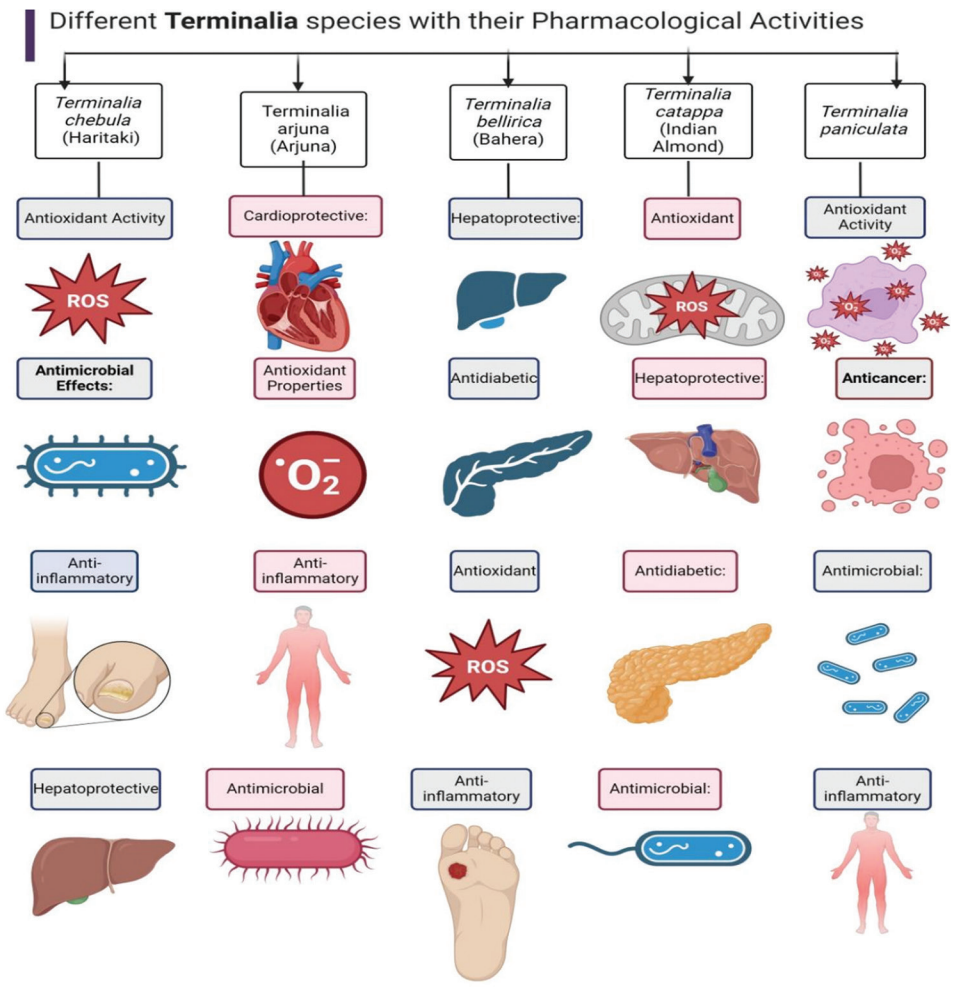


Figure 4: Pharmacological properties of diverse *Terminalia* species, such as *Terminalia chebula, Terminalia arjuna, Terminalia bellirica, Terminalia catappa,* and *Terminalia paniculata*, demonstrate their antioxidant, cardioprotective, hepatoprotective, antimicrobial, anti-inflammatory, antidiabetic, and anticancer capabilities, underscoring their therapeutic potential in disease management

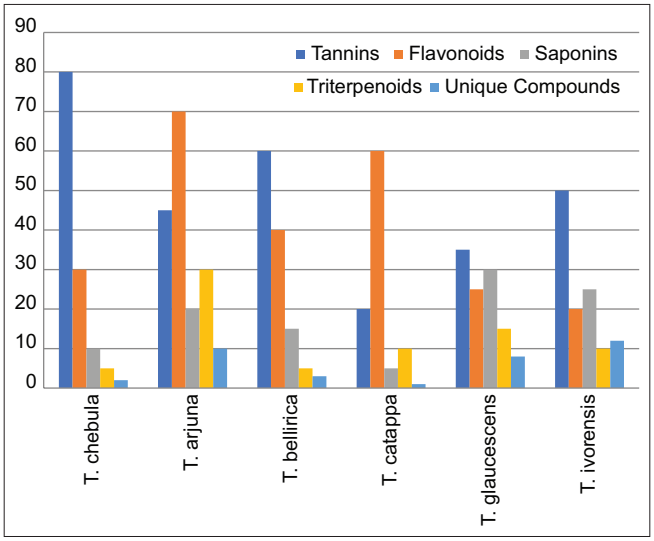


Figure 5: Investigations of the phytochemical composition of various *Terminalia* species. A comparative investigation of the phytochemical composition among different *Terminalia* species, emphasizing the diversity and prevalence of essential bioactive components that enhance their distinctive therapeutic qualities and advantages

Table 1: *Terminalia tomentosa*

S. No.	Phytoconstituents	Plant part
1	Tannins: Arjunic acid, Arjnolic acid, Gallic acid, Ellagic acid	Bark
2	Triterpenoids: oleanolic acid, botulinic acid	Bark and Roots
3	Steroid: B Sitosterol	Bark
4	Flavonoids: Apigenin, Kaempferol, Rutin, Quercetin Luteolin	Levies
5	Polyphenolic Compound: Barringtogenol and Tomentose acid, Dimethyl Ellagic acid, Dimethyl Flavellagicacid, Thymine, Epigallocatechin	Bark

leads to contradictory results, making implementing the findings in real life difficult. Furthermore, whereas many ethnomedicinal uses are documented on various species of *Terminalia*, particularly for conditions such as heart diseases and infections, new studies have pharmacologically validated these uses in experimental studies. The appraisal indicates the

need for additional investigations on stygobitic species and their combined effects. In addition, there is a strong argument for using modern technology, such as Nanotechnology, to enhance the bioavailability and therapeutic efficacy of *Terminalia* extracts. This overall approach is expected to help formulate new herbal medicines, the limitations of which have been pointed out in earlier reviews.

A concentrated discourse on the difficulties of translating *Terminalia*'s pharmacological attributes into clinical applications is essential for various reasons. The heterogeneity in phytochemical content among species can hinder extracts' standardization and quality control. Furthermore, the intricate interactions of bioactive substances may result in unforeseen therapeutic outcomes or unfavorable reactions in clinical environments. Restricted clinical trials and regulatory obstacles further impede the incorporation of *Terminalia* into conventional medicine. Confronting these issues through meticulous study, extensive pharmacokinetic investigations, and well-defined regulatory frameworks is crucial to realizing *Terminalia* species' complete therapeutic potential in clinical practice and improving their integration into contemporary healthcare.

CONCLUSION

By focusing on the *Terminalia* genus's phytochemical constituents and medicinal properties, this review presents a valuable addition to the existing knowledge base. It emphasizes the importance of neglected species as well as the importance of standardized methods to enhance the quality of data. The review proposes including traditional practices with modern techniques to develop new possibilities, such as using nanotechnology to improve treatment outcomes.

There are still drawbacks, such as insufficient clinical validation and lack of agreement on the methods of extraction and assessment. On the other hand, previous studies have often focused on a small number of species within the genus and neglected its greater possibilities.

Future plans must emphasize the adherence to strict protocols in clinical methodologies and clinical trials aimed at assessing the safety and efficacy of interventions and examining the interactions of phytochemicals in detail. There is also the need to establish a research framework supportive of mobilizing researchers, doctors, and industry to ensure that findings and new technologies are rolled into clinical practice quickly. This Includes Suggestions such as focusing on the relatively unexplored species and their potential, carrying out large-scale clinical studies, and utilizing advanced techniques to enhance bioavailability and therapeutic effects.

This assessment is particularly relevant, especially because it integrates classic and modern perspectives regarding the *Terminalia* genus while stressing its untapped therapeutic potential. The resulting structure will act as a comprehensive foundation for future studies, calling for procedural uniformity and the use of recent advances in nanotechnology for enhanced clinical performance.

The outstanding phytochemistry and pharmacological diversity of the plants of the *Terminalia* genus are highlighted by the presence of tannins, flavonoids, phenolic acids, and other active ingredients of therapeutic use. These species exhibit many therapeutic effects, including antioxidant, antimicrobial, anti-inflammatory, anticancer, cardioprotective, hepatoprotective, antidiabetic, and neuroprotective. Various *Terminalia* species have been used extensively in traditional medicine for numerous diseases for ages. Modern scientific research has equally shown their effectiveness in managing chronic illness and maintaining wellness. Nevertheless, while the genus is beneficial in many ways for health, further clinical studies are required, extraction protocols need to be standardized, and hazard characterization gauged to enable the functional and safe use of *Terminalia* species in medical practices. If the research continues at this pace, *Terminalia* might be even more useful than it is now in generating new drugs.

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