

## Multidimensional Medicinal Potential Of Terminalia Chebula Retz.: From Folklore To Pharmacology — A Comprehensive Review

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### ABSTRACT

**Introduction:** Terminalia chebula Retz. (Family: Combretaceae), canonised as Harītakī in Ayurveda and described as the 'king of medicines' in Caraka Saṁhitā and Suśruta Saṁhitā, occupies a preeminent position in classical and folk medicine across the Indian subcontinent and Southeast Asia. Despite its extensive use across Ayurvedic, Siddha, Unani, and Tibetan systems, a unified review integrating tribal ethnomedicinal knowledge with contemporary pharmacological validation has not been systematically presented.

**Methods:** Ethnobotanical data were systematically compiled from 5 standard ethnobotany reference books and 21 peer-reviewed ethno-medicine research articles covering tribal communities across 12 Indian states and 2 neighbouring countries (Bangladesh). Data were categorised by local name, tribal community, geographic area, plant part, dosage form, route of administration, and therapeutic indication. Pharmacological evidence was collated from published in vitro, in vivo (animal), and clinical studies retrieved from PubMed, Scopus, and Google Scholar. Phytochemical data were compiled from authenticated pharmacological and botanical sources. Classical Ayurvedic descriptions were sourced from primary texts.

**Results:** Ethnobotanical analysis documented 35 distinct therapeutic applications across 12 Indian states and Bangladesh, spanning 27 internal, 6 external, and 1 combined route of administration. Principal therapeutic domains included gastrointestinal disorders (constipation, dysentery, haemorrhoids), respiratory ailments (asthma, cough, bronchitis), metabolic conditions (diabetes, jaundice), and dermatological/wound healing applications. Phytochemical investigations identified hydrolysable tannins — chebulagic acid, chebulinic acid, gallic acid, ellagic acid (comprising 32–50% dry weight of fruit) — as dominant bioactives, alongside triterpenoids, flavonoids, anthraquinones, sterols, and volatile oils. Pharmacological evidence established 12 major activity domains: antimicrobial (including anti-HIV, anti-HSV), antioxidant (DPPH IC<sub>50</sub> 5–15 μg/mL), anti-inflammatory (COX-1/COX-2 inhibition; NF-κB suppression), hepatoprotective, cardioprotective, antidiabetic (alpha-glucosidase inhibition), anticancer (apoptosis induction in MCF-7, HeLa, A549, HepG2, HL-60 cell lines; VEGF-mediated anti-angiogenic activity), neuroprotective, nephroprotective, wound-healing, immunomodulatory, and adaptogenic/Rasayana. Clinical evidence supports Triphalā use in constipation, IBS, dental hygiene, diabetes management, and cataract prophylaxis.

**Discussion and Conclusion:** The consistency of ethnomedicinal application across geographically and linguistically diverse tribal communities constitutes a robust cross-validated traditional evidence base, with pharmacological mechanisms now elucidated for virtually every major claim. The anticancer, hepatoprotective, and immunomodulatory properties are of particular significance for integrative oncology. Priority research gaps include large-scale randomised clinical trials for anticancer supportive care and antidiabetic applications, chemotypic characterisation of the seven Ayurvedic varieties, and human pharmacokinetic profiling of key bioactives. Novel drug delivery systems — PLGA nanoparticles, liposomes, SLN, and nanoemulsions — offer pathways to enhanced bioavailability and organ-targeted delivery. T. chebula exemplifies the potential of the

traditional pharmacopoeia as a systematic source for evidence-based drug discovery..

**Keywords:** Terminalia chebula; Harītakī; Ethnobotany; Phytochemistry; Pharmacology; Ayurveda; Triphalā; Gallic acid; Chebulagic acid; Anticancer; Rasayana; Wound healing

## INTRODUCTION

Forests are among the most critical repositories of medicinal knowledge for rural and tribal communities worldwide. In India, over 53 million tribal people belonging to 550 communities across 227 ethnic groups draw approximately half of their annual income from forest resources, with roughly 60% of rural communities directly dependent on forests for daily sustenance.[1] This intimate ecological association has fostered centuries of refined ethnomedicinal knowledge, particularly for plants with broad-spectrum therapeutic utility.

Among the thousands of medicinal plants described in classical Ayurvedic texts — most prominently the Caraka Saṁhitā and Suśruta Saṁhitā — *Terminalia chebula* Retz. (Harītakī) commands an unparalleled position.[2] Classified as 'Pathyā' (always wholesome) and 'Sarvadoṣahara' (eliminator of all diseases), it is the primary ingredient of Triphalā — arguably the most globally recognised Ayurvedic polyherbal preparation.[3] Its use spans Ayurvedic, Siddha, Unani, and Homeopathic systems and is documented across the Indian subcontinent, Southeast Asia, and Africa. Classical texts reference its utility in asthma, bleeding piles, sore throat, vomiting, gout, and a wide spectrum of metabolic and infectious conditions.

Modern pharmacological research has substantially validated these traditional claims, revealing a chemically complex plant whose hydrolysable tannins, triterpenoids, and flavonoids collectively underpin diverse biological activities.[2,41] Despite this, a comprehensive review systematically integrating tribe-specific ethnobotanical data — compiled from primary ethnobotany sources — with phytochemical and pharmacological evidence remains a gap in the literature. The present review addresses this gap through a structured synthesis spanning ethnobotany, botanical characterisation, classical Ayurvedic pharmacology, phytochemistry, pharmacological activities (with mechanistic detail), clinical evidence, safety, and drug delivery strategies for *T. chebula*.

### 2. Botanical Description and Taxonomy

*Terminalia chebula* Retz. belongs to the family Combretaceae. It is a moderate-to-large deciduous tree reaching 25–30 m in height. Leaves are sub-opposite, ovate to elliptic-oblong (7–20 cm long), with two glands at the leaf base near the petiole — a useful morphological identifier. Flowers are monoecious, dull white to yellow, arranged in terminal spikes or panicles with a characteristic fetid odour. The drupe-like fruit (3–5 cm long) transitions from greenish-yellow to dark brown on ripening and bears 5 prominent longitudinal ridges when dried.[2] The pericarp of the mature dried fruit is the principal pharmacological material.

**Table 1: Taxonomic classification and vernacular nomenclature of *Terminalia chebula* Retz. [2,3]**

Taxonomic Category	Classification
Kingdom	Plantae
Order	Myrtales
Family	Combretaceae
Genus	<i>Terminalia</i>
Species	<i>T. chebula</i> Retz.
Common English name	Chebulic Myrobalan
Sanskrit / Ayurvedic names	Harītakī, Abhayā, Pathyā, Kayasthā, Vijayā, Chetakī, Śreyasī, Pūtanā
Hindi	Harad, Harra, Harara
Tamil	Karakkāi, Kadukkāi
Telugu	Karakkāya
Kannada	Alaley, Anale
Marathi	Hirda, Haritaki
Bengali	Haritaki, Hortoki
Distribution	Indian subcontinent (India, Nepal, Bangladesh, Sri Lanka), Myanmar, Thailand, South China, East Africa
Altitude range	Up to 1500 m ASL; common in dry deciduous and mixed forests

#### 2.1 Seven Ayurvedic Varieties (Saptavidha Harītakī)

Classical Ayurvedic pharmacopoeia describes seven varieties — Vijayā, Rohiṇī, Pūtanā, Amṛtā, Abhayā, Jivantī, and Chetakī — each with specific therapeutic indications.[2] Vijayā is considered universally applicable (sarvadoṣahara); Rohiṇī is preferred for wound healing; Chetakī for purgation. This classical typology anticipates modern chemotypic variation and warrants systematic pharmacognostic and phytochemical investigation across varieties.

### 3. Classical Ayurvedic Perspective

#### 3.1 Dravyaguna Properties

Harītakī uniquely possesses five of the six fundamental Ayurvedic tastes (Pañca rasa), excluding only salt (Lavaṇa) — the basis of its tridoṣic action balancing Vāta, Pitta, and Kapha simultaneously.[2] Table 2 summarises its pharmacodynamic properties as described in the *Caraka Saṁhitā* and *Aṣṭāṅga Hṛdayam*.

**Table 2: Dravyaguna properties of Harītakī per Caraka Saṁhitā and Aṣṭāṅga Hṛdayam. [2]**

Property (Guṇa)	Classical Description
Rasa (taste)	Five of six tastes — Kaṣāya (astringent) predominant; also Madhura, Amla, Kaṭu, Tikta
Guṇa (quality)	Laghu (light), Rūkṣa (dry)
Vīrya (potency)	Uṣṇa (hot)
Vipāka (post-digestive)	Madhura (sweet)
Karma (action)	Tridoṣaghna; Rasāyana; Medhya; Lekhanīya; Anulomana
Prabhāva (special)	Sarvadoṣahara; Pathyā (always wholesome)
Part used	Fruit (Phala), principally pericarp; also bark, leaves, seeds, flowers

#### 3.2 Rasāyana and Medhya Classification

Harītakī is classified as a premier Rasāyana (rejuvenative tonic) and Medhya Rasāyana (cognitive enhancer) in multiple classical Ayurvedic texts.[2] Its descriptions as Āyus̄kara (life-extending), Cakṣuṣya (beneficial for eyes), and Indriyaprasādana (sensory enhancer) anticipate modern research on adaptogens, senolytics, and AChE inhibitors — confirming the depth of classical empirical observation.

#### 3.3 Key Classical Formulations

- **Triphalā Cūrṇa:** Equal parts *T. chebula* + *T. belerica* + *Phyllanthus emblica* — most globally recognised Ayurvedic formulation[3]
- **Agastya Harītakī:** Classical Rasāyana for chronic respiratory disease
- **Abhaya Āriṣṭa:** Fermented preparation for constipation and haemorrhoids[2]
- **Triphala Guggulu:** For metabolic syndrome and inflammation
- **Cyavanaprāśa:** Classical tonic Rasāyana containing Harītakī among major ingredients

### 4. Ethnobotanical Survey

#### 4.1 Methodology

Ethnobotanical data on *Terminalia chebula* Retz. were compiled from five standard ethnobotany reference books[3,38] and 21 peer-reviewed ethno-medicine research articles covering tribal communities across 12 Indian states and Bangladesh.[4–37] Data were arranged by local name, tribal/community identity, geographic area, plant part, route of administration, dosage form, and therapeutic claim. Ecological and non-medicinal uses were recorded separately. No new field data were collected; this is a secondary compilation and critical synthesis of documented sources.

#### 4.2 Geographic Distribution of Ethnomedicinal Reporting

*T. chebula* has been documented for ethnomedicinal use in 12 Indian states: Andhra Pradesh/Telangana, Jharkhand, Assam, Gujarat, Uttaranchal, Madhya Pradesh, Maharashtra, Odisha, Rajasthan, Tamil Nadu, Uttar Pradesh, and West Bengal; and additionally in Bangladesh.[3–37] This pan-subcontinent distribution of ethnomedicinal knowledge — across distinct tribal groups with independent oral traditions — constitutes strong cross-validated evidence of therapeutic utility.

#### 4.3 Plant Parts and Routes of Administration

Multiple plant parts are documented in ethnomedicinal use: dried fruit/pericarp (most frequent), bark, leaf, seed, and flower.[3] Across all records, 27 internal administration modes, 6 external application modes, and 1 combined internal-external mode were documented, alongside 4 ecological/non-medicinal uses (hair dye, tannin extraction, ornamental use).

#### 4.4 Ethnomedicinal Data — Compiled Tables

**Table 3A: Ethnomedicinal claims — Internal Administration of *T. chebula* Retz. as single ingredient**

Sr.	Local Name	Tribes / Area	Part	Dosage Form	Therapeutic Claims	Ref.
1	Harna	Tharu / UP, MP, NE India	Fruit	Powdered fruits orally	Diabetes (hypoglycaemic)	4
2	Harra	Tharu / Sub-Himalayan eastern UP	Fruit	Roasted fruit powder orally	Stomachache	5
3	Harra	Bastar / Madhya Pradesh	Fruit	Rasaut + Harra + Amla (3 g each) powder during menstrual cycle	Anti-fertility	6
4	Harra	Rewa / Madhya Pradesh	Fruit	Fruit powder (oral)	Laxative; Stomachache	7
5	Harra	Chitheri Hills / Tamil Nadu	Bark/Fruit	1) Bark decoction (diuretic, cardiotonic); 2) Fruit dentifrice for toothache & gum ulcers; 3) Nut as astringent heart stimulant	Cardiotonic; Chronic ulcers; Toothache; Oliguria	8
6	Hotibari	Jajpur / Orissa	Bark	Bark paste (15–20 g) in hot water once daily for 3 days	Cough; Gastric troubles	9
7	Harida	Narayanapatna / Orissa	Leaf/Bark	1) Bark decoction orally; 2) Leaf paste as purgative	Diabetes; Stomachache; Purgative	10
8	Harro/Dhemaji	Nepal / Assam	Fruit	Fruit powder administered orally	Throat complications	11
9	Karakkaya	Nalgonda & Warangal / Telangana, AP	Leaf/Fruit	Leaf/fruit powder orally	Cough; Constipation	12
10	Karakkaya	Adilabad / Andhra Pradesh	Fruit pulp	Fruit pulp chewed; sap swallowed	Oral/digestive	13
11	Kadukkaimaram	Madurai / Tamil Nadu	Fruit	Powdered fruit in water or milk	Cold and Cough	14
12	Harad	Garhwal Himalaya / Uttaranchal	Fruit	Fruits used internally	Urinary disease; Asthma; Cough; Liver enlargement; Worms; Dysentery; Fever	15
13	Haritaki	Rajasthan	Fruit	Pills (rosebuds + Senna + Amalatas + Haritaki) twice daily for 5 days	Chronic constipation	16
14	Harra	Satpuda region / Maharashtra	Fruit	Gargle; astringent purgative/laxative	Purgative; Laxative; Mucosal inflammation	17
15	Karakkai	Konda Dora Tribes / Visakhapatnam, AP	Fruit	Unripe fruit powder + castor oil paste; 1 spoon twice daily before bed	Sciatica	18
16	Harida	Bondo Tribe / Malkangiri, Odisha	Bark	5 mL bark decoction orally for 1 week	Gastrointestinal disorders	19
17	–	Tribes of Saurashtra / Gujarat	Leaf	Decoction of <i>T. chebula</i> + <i>Embelia ribes</i> + <i>Apium</i>	Haemorrhoids	20

				graveolens seeds twice daily for 1 week		
18	Hardi	Saputara & Purna forests / Dang, Gujarat	Flower	Flower used orally	Laxative; Stomachache	21
19	Horitoki	Kurigram / Bangladesh	Fruit	T. emblica + T. belerica + T. chebula soaked overnight; water drunk empty stomach; 3 powdered fruits twice daily for 7 days	Cough; Spleen disorders; GI disorders; Flatulence; Constipation; Helminthiasis	22
20	Hortoki	Tangail / Bangladesh	Fruit	1) Complex juice (P. emblica + T. chebula + Mucuna pruriens + Ipomoea mauritiana + Bombax ceiba + A. racemosus) with honey; 2) Triphala macerate orally	Dysentery; Cholera; Gastric problems; Spermatorrhoea	23

**Table 3B: Ethnomedicinal claims — Internal Administration as Triphalā formulation**

Sr.	Local Name	Tribes / Area	Part	Dosage Form	Therapeutic Claims	Ref.
1	Hirda	Warli / Thane, Maharashtra	Fruit	Fruit as Triphala component (I)	Laxative; Toothache	24
2	Harar	Kumaun Himalaya	Fruit	Triphala (Awala + Harar) for cough and throat disorder; vomiting	Throat complications	25
3	Harra	Jharkhand	Fruit	Harr + Bahera + Amla (1:2:3) powder + 1/5 Til oil; 2 tbsp with water for 21 days	Asthma	26
4	Harra	Pandhurna / Chhindwara, MP	Fruit carp	Harraa + Baheda + Amla crushed – Triphala Curna	Heart disease	27
5	Harra	Amarakantak / Madhya Pradesh	Fruit	1 spoon Triphala powder + 1/2 tsp honey twice daily	Asthma; Bronchitis	28
6	Harida	Kandhas / Kandhamal, Orissa	Fruit	1) Triphala + cow ghee 3x daily for 1 month (empty stomach); 2) Fruit powder + iron rust powder with milk/honey 2x daily for 7 days	Diabetes; Jaundice	29
7	Harra	Satna / Madhya Pradesh	Fruit	Triphala + Hinga (asafoetida) + salt; 10 g twice daily after meals	Gastric disorders	30

**Table 3C: Ethnomedicinal claims — External Application, Combined Use, and Ecological Uses**

Sr.	Local Name	Tribes / Area	Part	Dosage Form	Therapeutic Claims	Ref.
1	Haira	Bankura / West Bengal	Fruit	Fruit paste applied on 'Haza' (water-contact skin disease) between toes (E)	Skin disease	31
2	Haritaki	Kattunayaka Tribes / Nilgiris, Tamil Nadu	Fruit	Fruit paste applied externally thrice daily for 1 week (E)	Muscular dislocation	32
3	Haritaki	Jalgaon / Maharashtra	Fruit	Fruit powder applied externally (E)	Wound healing	33
4	Karakkaya	Prakasam / Andhra Pradesh	Fruit pulp	Fruit pulp applied externally to wounds and gum ulcers (E)	Wounds; Gum ulcers	34
5	–	Nilgiri Hills / Tamil Nadu	Seed	10 g seed powder + 10 g sandal powder + 10–15 mL coconut oil as body lotion (E)	Cracks; Scales; Rough skin	35
6	Harde	Valsad / Gujarat	Fruit	Burnt Harde + Amla + Baheda powder with honey applied externally (Triphala formulation) (E)	Updamsha (syphilitic ulcers)	36
7	Harra	Birhore Tribes / Jharkhand	Fruit	Dried fruit powder for constipation (I); chewed for lung congestion (I); decoction cooled to wash eyes (E)	Constipation; Lung congestion; Eye wash	37

#### 4.5 Summary of Therapeutic Scope

Across 35 documented disease conditions, the following therapeutic domains are represented:

- **Gastrointestinal (most frequent):** Constipation, laxative, purgative, stomachache, dysentery, cholera, gastric disorders, flatulence, haemorrhoids, helminthiasis[4,7,9,14,16,17,19,20,22,23,24,29,30]
- **Respiratory:** Cough, cold, asthma, bronchitis, throat complications, lung congestion[8,11,12,25,26,28,37]
- **Metabolic:** Diabetes, jaundice, heart disease, cardiogenic[1,5,7,27,29]
- **Genitourinary:** Urinary disease, oliguria, anti-fertility, spermatorrhoea[5,12,15,23]
- **Dermatological / Musculoskeletal:** Skin disease, wound healing, muscular dislocation, cracks and scales, gum ulcers, updamśa[31,32,33,34,35,36]
- **Neurological / Sensory:** Sciatica, eye wash[18,37]
- **Ecological:** Natural hair dye, tannin source (leather industry), ornamental rosaries (Assam)[38,39,40]

#### 5. Phytochemical Constituents

The multidimensional pharmacological activity of *T. chebula* is rooted in its complex phytochemical matrix. The fruit contains one of the highest tannin concentrations reported among medicinal plants — 32–50% of dry weight — alongside diverse secondary metabolite classes.[2,29,38] Table 4 summarises the major phytochemical classes with representative constituents and primary pharmacological activities.

**Table 4: Major phytochemical classes, key bioactive constituents, and primary activities of *T. chebula* Retz.**

Class	Key Constituents	Primary Activities	Ref.
Hydrolysable Tannins	Chebularic acid, Chebulinic acid, Corilagin, Terchebin, Ellagic acid, Gallic acid, Punicalin, Punicalagin	Antioxidant; Antimicrobial; Antidiarrheal; Anticancer; Hepatoprotective	29,38,39
Triterpenoids	Chebuloside I & II, Arjunic acid, Chebulic acid, Bellericoside	Anti-inflammatory; Cardiogenic; Adaptogenic	2,40
Flavonoids	Luteolin, Quercetin, Rutin	Antioxidant; Anticancer; Cardioprotective	41
Anthraquinones	Sennoside A & B	Laxative; Purgative	2,42
Amino acids	Glutamic acid, Alanine, Aspartate, Serine	Nutritive	2
Glycosides	Arjunetin, Chebulin	Cardiotonic; Hypoglycaemic	40,43
Sterols	Beta-sitosterol, Daucosterol	Anti-inflammatory; Anticholesterolaemic	2
Volatile oils	Alpha-pinene, Limonene, Terpineol	Antimicrobial; Antifungal	44
Carbohydrates	Fructose, Glucose, Sucrose	Nutritive; Excipient	2
Vitamins & Minerals	Vitamin C, Selenium, Copper, Manganese	Antioxidant; Micronutrient	2,38

### 5.1 Hydrolysable Tannins — The Dominant Bioactive Class

Chebularic acid and chebulinic acid are ellagitannins characteristic of the *Terminalia* genus and the principal bioactives of *T. chebula*. [29,38] Gallic acid and ellagic acid — their hydrolysis products — are among the most extensively studied plant phenolics globally, with documented anticancer, antiviral, and antioxidant activities. [41,46] Corilagin demonstrates hepatoprotective and antiviral properties. [48] The synergistic interaction among these tannins — producing activity superior to any single isolated compound — is consistent with the Ayurvedic rationale for whole-plant preparation use (Samagra Dravya Prayoga).

### 5.2 Standardisation Markers for Quality Control

Gallic acid (quantified by HPLC), chebulagic acid, and chebulinic acid serve as the primary standardisation markers for *T. chebula* raw material and finished products. [29] Geographic sourcing variability results in fruit tannin content ranging 15–50% — underscoring the necessity of chemotypic characterisation and standardised sourcing for reproducible clinical research and pharmaceutical applications.

## 6. Pharmacological Activities

Table 5 provides a structured overview of documented pharmacological activities with key bioactives, mechanisms, evidence levels, and primary references.

**Table 5: Summary of documented pharmacological activities of *Terminalia chebula* with mechanisms and references**

Activity	Key Bioactives	Mechanism / Findings	Evidence Level	Ref.
Antimicrobial / Antiviral	Gallic acid, Chebulagic acid	Inhibits <i>S. aureus</i> , <i>E. coli</i> , <i>Candida</i> , MRSA; anti-HIV (reverse transcriptase inhibition); anti-HSV via viral entry blockade	In vitro; Preliminary clinical	29,44,45
Antioxidant	Ellagic acid, Chebulinic acid, Vitamin C	DPPH IC50 5–15 µg/mL; inhibits lipid peroxidation; elevates SOD, CAT, GPx in vivo	In vitro; In vivo	38,46
Anti-inflammatory	Chebularic acid, Gallic acid	Inhibits COX-1/COX-2; suppresses TNF-α, IL-1β, IL-6; downregulates NF-κB; reduces carrageenan paw oedema	In vitro; Animal models	41,47

Hepatoprotective	Chebulinic acid, Gallic acid	Reduces ALT/AST; protects vs CCl4-hepatotoxicity; elevates hepatic GSH; promotes hepatocyte regeneration	Animal models	29,48
Cardioprotective	Chebuloaside I & II, Arjunic acid	Reduces LDL oxidation; vasodilatory; positive inotropic; antihyperlipidaemic	Animal models; Clinical observations	2,40
Antidiabetic	Chebulagic acid, Ellagic acid	Alpha-glucosidase inhibition; insulin sensitisation; reduces FBG and HbA1c in STZ-diabetic rodents	Animal models; In vitro; Small RCTs	29,43,49
Anticancer	Gallic acid, Ellagic acid, Chebulagic acid	Apoptosis (caspase-3, Bcl-2/Bax); anti-proliferative vs MCF-7, HeLa, A549, HepG2, HL-60; VEGF-mediated anti-angiogenic	In vitro; Animal models	41,50,51
Neuroprotective	Chebulinic acid, Gallic acid	AChE inhibition; reduces oxidative neuronal damage; memory enhancement in scopolamine-amnesic models	In vitro; Animal models	52
Nephroprotective	Ellagic acid, Gallic acid	Protects vs cisplatin- and gentamicin-induced nephrotoxicity; diuretic	Animal models	31,53
Wound Healing	Tannins, Gallic acid	Promotes collagen synthesis; astringent; anti-infective; accelerates re-epithelialisation	In vitro; Animal; Clinical	33,54
Immunomodulatory	Polyphenols, Chebulagic acid	Enhances macrophage phagocytosis; NK cell activity; balances Th1/Th2	Animal models; In vitro	33,55
Adaptogenic / Rasayana	Polyphenol complex	Reduces cortisol; anti-fatigue; cognitive enhancement (Medhya Rasayana)	Traditional; Preliminary human	2,56

### 6.1 Antimicrobial and Antiviral Activity

Ethanollic and aqueous extracts of *T. chebula* demonstrate inhibitory activity against Gram-positive (*S. aureus*, *B. subtilis*), Gram-negative (*E. coli*, *P. aeruginosa*, *K. pneumoniae*) bacteria, and drug-resistant MRSA strains.[29,44] Antifungal activity against *Candida albicans* and dermatophytes has been established by disc diffusion and minimum inhibitory concentration assays.[44] Of particular significance, chebulagic acid has been shown to inhibit HIV-1 reverse transcriptase and integrase, and anti-HSV activity through interference with viral cell entry has been documented — positioning *T. chebula* bioactives as credible antiviral drug leads.[45]

### 6.2 Antioxidant Activity

*T. chebula* consistently ranks among the highest in comparative DPPH, ABTS, and FRAP antioxidant assays among Indian medicinal plants.[38,46] Standardised aqueous extracts yield DPPH IC50 values of 5–15 µg/mL — comparable to or exceeding synthetic antioxidants BHA and BHT. In vivo rodent studies demonstrate significant elevation of endogenous antioxidant enzymes (SOD, CAT, GPx) and reduction of lipid peroxidation markers (MDA, TBARS) following extract administration.[46]

### 6.3 Anti-inflammatory Activity

Multiple studies document significant inhibition of pro-inflammatory mediators.[41,47] Documented mechanisms include: COX-1 and COX-2 enzyme inhibition comparable to indomethacin; suppression of TNF-α, IL-1β, and IL-6 in LPS-stimulated macrophages; downregulation of NF-κB signalling; and significant reduction of carrageenan-induced paw oedema in animal models.[47] These mechanisms mechanistically explain the ethnomedicinal use in arthritis, gastric inflammation, and respiratory ailments documented across tribal

communities.

#### 6.4 Anticancer Activity

Anticancer activity of *T. chebula* has been explored across multiple malignancy models.[41,50,51] Gallic acid and ellagic acid induce apoptosis through caspase-3 activation, modulation of the Bcl-2/Bax ratio, and disruption of mitochondrial membrane potential. Anti-proliferative activity has been demonstrated in MCF-7 (breast cancer), HeLa (cervical), A549 (lung), HepG2 (hepatocellular carcinoma), and HL-60 (promyelocytic leukaemia) cell lines.[50] Chebulagic acid additionally inhibits VEGF-mediated angiogenesis — a critical step in tumour progression and metastasis.[51] The concurrent hepatoprotective and immunomodulatory activities support integrative oncology applications in managing chemotherapy-induced organ toxicity.

#### 6.5 Hepatoprotective Activity

Preventive and curative hepatoprotective effects are established in CCl<sub>4</sub>-induced hepatotoxicity rodent models.[29,48] Significant reduction in serum ALT, AST, ALP, and total bilirubin was documented alongside improvement in hepatic histopathology. Mechanisms involve hepatocyte free radical quenching, membrane stabilisation, and elevation of hepatic glutathione levels.[48] These findings validate ethnomedicinal use in jaundice — as documented by the Kandha tribes of Orissa[29] — and support the Ayurvedic description of Haritakī as a Yakṛduttejaka (liver stimulant).

#### 6.6 Antidiabetic Activity

Chebulagic acid and ellagic acid demonstrate potent alpha-glucosidase inhibition in vitro, with IC<sub>50</sub> values comparable to acarbose.[43,49] In streptozotocin-induced diabetic rodents, *T. chebula* extract supplementation significantly reduced fasting blood glucose and HbA<sub>1c</sub>, improved insulin sensitivity, and ameliorated oxidative stress in pancreatic tissue.[49] These mechanisms validate ethnomedicinal diabetes use documented across UP, MP, Orissa, and Bangladesh.[1,7,29]

#### 6.7 Neuroprotective Activity

Consistent with its classical Medhya Rasāyana classification, *T. chebula* extracts demonstrate acetylcholinesterase (AChE) inhibition in vitro — suggesting utility in Alzheimer's disease management.[52] In vivo, administration significantly reduced oxidative damage in hippocampal and cortical neurons, and memory-enhancing effects were confirmed in scopolamine-induced amnesic rodent models by Morris Water Maze and passive avoidance testing.[52]

#### 6.8 Nephroprotective Activity

Oral administration of *T. chebula* extract significantly attenuated cisplatin-induced nephrotoxicity in mice, as evidenced by reduction in serum creatinine, blood urea nitrogen, and kidney histopathological injury scores.[31,53] Similar protection against gentamicin-induced tubular injury has been reported. These findings are of direct relevance for cancer patients receiving nephrotoxic chemotherapy regimens — a key integrative oncology application.

### 7. Clinical Evidence and Human Studies

While pharmacological evidence remains predominantly preclinical, clinical observations and small human studies provide translational context:

- *Triphalā* in constipation and IBS: Randomised trials report significant improvement in bowel frequency, stool consistency, and abdominal symptoms versus placebo.[56]
- Dental hygiene: Triphala mouthwash demonstrated reduction in plaque, gingivitis scores, and anaerobic bacterial counts comparable to chlorhexidine — without chlorhexidine's adverse effects (staining, taste alteration).[54]
- Diabetes management: Triphala supplementation over 3 months showed statistically significant reduction in fasting blood glucose and HbA<sub>1c</sub> in Type 2 diabetic patients.[49]
- Cataract prophylaxis: Triphala eye drops showed slowing of nuclear lens opacity progression in a 6-month study, consistent with antioxidant and anti-inflammatory mechanisms.[56]
- Wound healing: Triphala-based formulations in post-surgical and diabetic wound care reported faster re-epithelialisation and reduced infection rates compared to standard dressings.[33,54]

The preponderance of evidence at this stage consists of in vitro and animal data, with small-scale clinical studies for Triphala formulations. Large-scale randomised controlled trials with standardised single-herb *T. chebula* extracts, defined doses, and validated outcome measures for individual clinical indications are a clear research priority.

### 8. Safety Profile, Toxicology, and Contraindications

### 8.1 Preclinical Safety

*T. chebula* has an established history of safe use. Acute oral toxicity studies in rodents yielded LD50 > 2000–5000 mg/kg body weight (no mortality at tested doses).[2] Sub-acute and chronic toxicity studies at therapeutically relevant doses (equivalent to 3–6 g/day in humans) showed no significant changes in haematological, serum biochemical, or histopathological parameters.

### 8.2 Ayurvedic Contraindications

Classical texts specify the following contraindications for Harītakī:[2]

- Pregnancy (Lekhanīya/depleting action)
- Extreme Vāta conditions with severe emaciation or cachexia
- Active dehydration and haemorrhagic conditions (due to drying, astringent action)
- Caution in summer without appropriate Anupāna — use with sugar candy (rock candy) or cow ghee in hot season

### 8.3 Herb-Drug Interactions

Due to high tannin content, complexation with co-administered drugs is a concern — particularly oral iron preparations, quinolone antibiotics, and tetracyclines (administer 2 hours apart).[2] Preliminary data suggest potentiation of anticoagulant effects of warfarin; patients on anticoagulant therapy should be monitored. Whole-plant preparations at standard doses (3–6 g/day) do not typically cause gastric irritation, unlike high-dose isolated gallic acid.

## 9. Novel Drug Delivery Strategies

Contemporary pharmaceutical research has explored advanced delivery systems to address inherent bioavailability limitations of high molecular weight tannins:

- **PLGA nanoparticles:** Nanoparticulate gallic acid and ellagic acid show enhanced cytotoxicity against cancer cell lines with sustained release and improved solubility[50]
- **Liposomal systems:** Liposomal chebulagic acid demonstrates enhanced hepatocyte targeting and improved hepatoprotective efficacy
- **Solid Lipid Nanoparticles (SLN):** SLN formulations for topical delivery demonstrate superior skin penetration and antimicrobial activity against dermatophytes
- **Intranasal nanoemulsions:** For neuroprotective brain-targeted delivery bypassing the blood-brain barrier; an emerging strategy for Alzheimer's disease applications[52]
- **Phytosomes:** Phospholipid complexes of polyphenols improve membrane permeability and oral bioavailability[29]
- **Standardised extracts:** Polyphenol-standardised dry extracts ( $\geq 20\%$  gallic acid equivalent by HPLC) provide reproducible pharmacological activity for clinical research and nutraceutical application

## 10. Discussion

The breadth of ethnomedicinal documentation for *T. chebula* across geographically and linguistically diverse tribal communities — from Sub-Himalayan UP to the Nilgiri hills, and from Rajasthan to Bangladesh — is remarkable in its consistency. The convergent documentation of gastrointestinal, respiratory, metabolic, and wound-healing applications across independent cultural traditions constitutes a cross-validated evidence signal that should systematically guide pharmacological prioritisation.[3–37]

The dominant ethnomedicinal use in gastrointestinal conditions is fully mechanistically grounded: anthraquinone-mediated stimulant laxation (Sennosides A and B),[42] tannin-mediated astringency reducing mucosal permeability and intestinal secretion,[29] and broad antimicrobial activity against enteric pathogens — including *V. cholerae* and *Shigella* spp.[44] The convergence of ethnomedicinal diabetes use with documented alpha-glucosidase inhibition and insulin sensitisation validates the traditional knowledge system and provides a clear clinical trial rationale of particular significance for contemporary oncology is the convergence of multiple anticancer mechanisms in a single plant: pro-apoptotic activity across diverse cancer cell lines, VEGF-mediated anti-angiogenic activity, immunomodulation, and robust antioxidant protection.[41,50,51] The integrative oncology potential — as a supportive agent managing chemotherapy-induced hepatotoxicity, nephrotoxicity, and immune suppression, while potentially potentiating tumour cell apoptosis — represents a high-priority translational research area directly relevant to Ayurvedic cancer research.

A critical unresolved research gap is the systematic phytochemical comparison of the seven Ayurvedic varieties. If these correspond to distinct chemotypes with differential tannin profiles, as classical descriptions imply, variety-specific drug development becomes possible — a precision medicine approach grounded in Ayurvedic

pharmacological typology. Conservation and sustainable cultivation of *T. chebula* must parallel any commercial development to prevent biodiversity erosion.

### 11. Conclusion

*Terminalia chebula* Retz. stands as a paradigmatic exemplar of the depth of knowledge encoded in traditional medical systems. This comprehensive review demonstrates: (i) its ethnomedicinal applications across 35 disease conditions in 12 Indian states and neighbouring countries represent robust, cross-source-validated traditional evidence; (ii) its phytochemical composition — dominated by hydrolysable tannins but spanning multiple bioactive classes — provides mechanistic grounding for its broad therapeutic spectrum; (iii) contemporary pharmacological research has validated traditional claims across 12 major pharmacological domains; and (iv) novel drug delivery systems offer pathways to overcome bioavailability barriers for targeted clinical application.[2,29,38,41]

Priority research directions include: large-scale randomised clinical trials for anticancer supportive care, antidiabetic, and neuroprotective applications; chemotypic characterisation of the seven Ayurvedic varieties; human pharmacokinetic profiling of chebulagic acid and chebulinic acid; and in vivo validation of anticancer nanodrug delivery systems. *T. chebula* exemplifies the bridge between ancient wisdom and evidence-based pharmacology — a bridge that, when rigorously constructed, can meaningfully enrich the global pharmacopoeia and the practice of integrative oncology.

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### Conflict of Interest

The authors declare no conflict of interest..

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