

Research Article

Phytochemical Analysis and Ocular Benefits of *Terminalia chebula* Extracts for Myopia

Treatment: In Vitro and In Silico Approaches

Abstract

Terminalia chebula, commonly known as Haritaki, is a medicinal plant with a long history of use in Ayurvedic medicine for various health conditions. It is rich in bioactive compounds such as tannins, flavonoids, and phenolic acids, demonstrating significant antioxidant and anti-inflammatory properties. Myopia, or nearsightedness, is a prevalent refractive error that typically begins in childhood and can lead to an increased risk of other ocular complications if severe. While genetic and environmental factors contribute to myopia, inflammation, and oxidative stress within ocular tissues may exacerbate its progression. Given Haritaki's documented therapeutic properties, this study investigates its potential in treating myopia. This research explores the phytochemical composition and biological activities of *Terminalia chebula* extracts concerning myopia treatment. Utilizing Soxhlet extraction with methanol, hexane, and ethyl acetate solvents, followed by GC-MS analysis, this research identified key bioactive compounds in *T. chebula*. Antioxidant and anti-inflammatory activities were assessed via DPPH, and TCA, with all three extracts demonstrating superior efficacy. In silico ADME evaluation and molecular docking studies using Discovery Studio revealed several promising ligands, particularly from methanol and ethyl acetate extracts, showing favorable drug-like properties and strong interactions with myopia-related target proteins. These findings suggest *T. chebula* extracts hold potential for developing novel myopia treatments. This study lays the groundwork for future pre-clinical and clinical investigations to validate *T.*

chebula's therapeutic efficacy in ophthalmology, potentially offering a natural alternative in myopia management.

Keywords: *Terminalia chebula*, Myopia, Soxhlet, GC-MS, Antioxidant, anti-inflammatory, DPPH, TCA, ADME, Discovery Studio, Molecular Docking

1.Introduction

Medicinal plants have been an integral component of human civilization since antiquity, serving as vital tools in the battle against various diseases. In recent decades, herbal medicine has garnered heightened attention on a global scale due to its economic viability, natural provenance, and perceived superior safety profiles characterized by minimal or absent adverse effects. A pertinent illustration of this botanical pharmacopeia is *Terminalia chebula* (*T. chebula*), a perennial flowering tree belonging to the Combretaceae family¹. Black myrobalan, ink tree, or chebolic myrobalan are some of its common names; other names include Haritaki (Sanskrit and Bengali), Harad (Hindi), Harada (Marathi and Gujarati), Karkchettu (Telugu), and Kadukkai (Tamil)². Because of the wide range of pharmacological characteristics associated with the physiologically active chemicals found in this plant, *Terminalia chebula* (Haritaki) is used in Ayurvedic medicine. The wild Haritaki tree is a medium-sized tree that may be found in Iran, Bangladesh, Turkey, Egypt, India, and Myanmar³. In Ayurveda, Haritaki (*Terminalia chebula* Retz) is highly valued for its ability to both prevent and treat illness. Antibacterial, antifungal, antiviral, antidiabetic, antimutagenic, antioxidant, antiulcer, and wound-healing qualities are all present in *T. chebula* (Table 1.). In conventional medicine, it is considered a moderate, safe, and efficient laxative. *T. chebula* and its phytoconstituents are non-toxic and have medicinal effects⁴.

Sl.	Plant	Bioactive	Pharmacological	Effects
-----	-------	-----------	-----------------	---------

No.	part	compounds	activity	
1.	Leaves, bark, and fruit	Chebolic acid	Antioxidant and free radical scavenging activity	Aqueous extract of fruit reduced xanthine/xanthine oxidase activity and hemolysis ^{5,6,7} .
2.	Fruit	Gallic acid	Radioprotective	Reduction in the development of strand breaks in plasmid PBR322 DNA caused by gamma radiation. It also protected human lymphocytes from gamma radiation-induced DNA damage when they were exposed in vitro ^{7, 8} .
3.	Fruit	Chebolic acid	Chemopreventive activity	Fruit extract demonstrated a chemopreventive effect in male Wistar rats against nickel chloride-induced renal oxidative stress, toxicity, and cell proliferation response ⁹ .
4.	Fruit	Ellagic acid	Anticarcinogenic activity	Haritaki phenolics have an inhibitory effect on cancer cell proliferation. Chebulinic acid, tannic acid, and ellagic acid were determined to be the main growth-inhibiting phenolics ¹⁰ .
5.	Fruit	Gallic acid and chebulagic	Cytoprotective activity	It caused duodenal ulcers to form and appeared to have a cytoprotective effect on the stomach mucosa in vitro. T-lymphocyte-mediated cytotoxicity was also

		acid		inhibited ^{11,12} .
6.	Fruit	Neochebulic acid	Hepatoprotective activity	Haritaki is a herbal preparation (HP-1) demonstrated hepatoprotective effects in rat hepatocytes when exposed to carbon tetrachloride ¹³ .
7.	Fruit and seeds	Chebulagic acid	Antidiabetic and renoprotective activity	Fruit and seeds demonstrated dose-dependent decreases in blood glucose and renoprotective benefits in streptozotocin-induced diabetic rats in both short and long-term experiments ^{14,15} .
8.	Fruit	Gallic acid	Antibacterial activity	It was shown to have antibacterial action against a variety of human pathogenic bacteria, including Gram-positive and Gram-negative ^{16,17} .
9.	Fruit	Tannins	Cardioprotective activity	In isoproterenol-induced cardiac injury in rats, to reduce the effect of isoproterenol on lipid peroxide production and maintain the activities of diagnostic marker enzymes ¹⁸ .
10.	Fruit and seed	Ellagic acid	Antiprotozoal activity	Acetone extract from seed has anti-plasmodial action against <i>Plasmodium falciparum</i> . Antiamoebic activity against <i>Entamoeba histolytica</i> was found to be 89% in rats with experimental caecal amoebiasis ^{19,20} .
11.	Fruit	Gallic acid	Antifungal	Antifungal activity was found in an aqueous extract of

			activity	haritaki against a variety of dermatophytes and yeasts. In vitro, the anticandidal activity of methanol extract against clotrimazole-resistant <i>Candida albicans</i> was found ^{21,22,23} .
12.	Dried fruit	Chebularic acid	Anti-inflammatory	Haritaki is a polyherbal formulation (Aller-7) that inhibited Freund's adjuvant-induced arthritis in rats in a dose-dependent manner. Inhibits inducible nitric oxide production, making it anti-inflammatory ²⁴ .
13.	Seed	Chebularic acid	Antiarthritic activity	Chebularic acid derived from immature seeds inhibited the development and progression of collagen-induced arthritis in rats ²⁵ .
14.	Fruit	Gallic acid	Adaptogenic and anti-anaphylactic activities	Haritaki fruit was one of six Ayurvedic herbs given to animals to see whether they were adaptogenic. In animal experiments, blood histamine levels were decreased when fruit extract was given after inducing anaphylactic shock, showing that it has a powerful anti-anaphylactic effect ²⁶ .
15.	Fruit	Gallic acid	Antiviral activity	On human immunodeficiency virus-1 reverse transcriptase, methanol and aqueous extracts of haritaki demonstrated a strong inhibitory action with $IC_{50} \leq 5 \mu\text{g/mL}$. Haritaki tannins are efficient against

				potato virus x ^{27, 28.}
16.	Fruit	Chebulinic acid and corilagin	Hypolipidemic	Haritaki extract has been shown to have hypolipidemic action against experimentally generated atherosclerosis ^{29.}
17.	Fruit	Chebulinic acid and corilagin	Hypocholesterolemic activity	It also has hypocholesterolemic activity in rabbits with hypercholesterolemia and atherosclerosis caused by cholesterol ^{30.}
18.	Fruit	Flavonol aglycones	Gastrointestinal motility improving	The fruit of haritaki has been proven to speed up gastric emptying. This impact seems to be counterbalanced by a protective effect on the mucosa of the gastrointestinal tract ^{31.}
19.	Fruit	Flavonol aglycones	Antiulcerogenic activity	Brunner's gland secretory condition improves, which aids in the prevention of duodenal ulcers ^{32.}
20.	Fruit	Gallic acid	Antispasmodic activity	Anti-spasmodic effects were proven in one of several investigations by the decrease of aberrant blood pressure and intestinal spasms ^{33.}
21.	Fruit	Tannins	Anticaries activity	<i>Streptococcus mutans</i> adherence was induced by sucrose, and glucan aggregation was produced by glucan. Salivary bacterial count and glycolysis were lowered for up to 90 min after washing with a 10%

				solution of the extract ³⁴ .
22.	Leaves	Tannins	Wound healing activity	Wounds treated with haritaki healed quicker, as evidenced by faster contraction rates and shorter epithelialization times ³⁵ .
23.	Fruit	Gallic acid	Immunomodulatory activity	The crude extract induced a cell-mediated immune response in golden hamsters with an amoebic liver abscess ³⁶ .
24.	Fruit	Gallic acid	Anti-allergic activity	An isolated guinea pig ileum substrate, showed significant antiallergic action in vitro ³⁷ .
25.	Fruit	Tannins	Purgative property	An oil fraction from fruit has been shown to have purgative properties ³⁸ .

Table 1. Summary of pharmacological studies on *Terminalia chebula*³⁹.

Haritaki also contains 18 amino acids in small amounts of phosphorus. Additionally, it is known for promoting eyesight⁴⁰. The eye is a vital organ of vision that plays a very important role not only in life but also in the Human body. The human eye is the organ that gives the sense of sight, allowing one to learn more about the surrounding world⁴¹.

Myopia, often referred to as nearsightedness or shortsightedness, is a highly common disorder that usually first manifests in childhood. There are around 70 genetic loci to which the primary myopias have been traced⁴². They are often caused by mutations in transcriptional activator-encoding genes, the majority of which have been found in individuals with developmental disorders by sequencing candidate genes⁴³. However, to what extent many genes of small effect and gene-environment

interactions contribute to variations in myopia within populations remains to be established. There are promising optical and pharmacological interventions for preventing the development of myopia or slowing its progression, which require further validation, and promising vision-sparing treatments for pathological myopia⁴⁴.

Despite the broad spectrum of health benefits associated with Haritaki, there is a notable gap in research regarding its impact on myopia. To address this gap, we conducted a comprehensive study involving Soxhlet extraction of Haritaki using Hexane, Methanol, and Ethyl Acetate to obtain the extracts. The chemical composition of these extracts was analyzed via Gas Chromatography-Mass Spectrometry (GCMS). Following this, we evaluated the anti-inflammatory and antioxidant activities of the extracts using DPPH and TCA assays. Finally, molecular docking studies were performed to explore the interaction of the compounds identified from the Haritaki extracts with target proteins related to myopia.

2. Methods and Methodology:

2.1. Extraction of Plant Compounds

The initial stage in assessing the characteristics of *Terminalia chebula* (Haritaki) involves creating a syrup by converting the seed into a fine powder. This powder is then subjected to Soxhlet extraction using three different solvents: hexane, ethyl acetate, and methanol. The Soxhlet extraction method, which is widely used for efficiently extracting bioactive compounds from plant materials, involves repeatedly washing the powder with the chosen solvent until the extraction is complete. This results in the continuous extraction of the desired compounds, yielding three distinct extracts. These extracts undergo Gas Chromatography-Mass Spectrometry (GCMS) analysis to identify their chemical constituents, referred to as ligands.

2.2. Gas Chromatography-Mass Spectrometry (GCMS) Analysis

Gas Chromatography-Mass Spectrometry (GCMS) is a powerful analytical technique that combines the capabilities of gas chromatography and mass spectrometry to identify various compounds present in the given sample. By using GCMS, the chemical profiles of the extracts from *T. chebula* were accurately determined, providing detailed spectra that facilitated the identification of molecular structures and compositions.

2.3. DPPH Assay

In the study of *T. chebula*, DPPH assay is crucial for determining the antioxidant potential of its extracts (Ethyl Acetate, Hexane, and Methanol). By measuring the scavenging ability of these extracts against DPPH radicals, the assay identifies which extracts exhibit the highest antioxidant activity, thus supporting their potential therapeutic use and validating their efficacy in reducing oxidative stress.

2.4. TCA Test

For the study of *T. chebula*, TCA assay helps identify the antioxidant potential of various extracts (Ethyl Acetate, Hexane, and Methanol) based on their ability to reduce ferric ions. This insight is crucial for determining the extracts with the highest antioxidant capacity and their potential use in combating oxidative stress.

2.5. Anti-Inflammatory

To evaluate the anti-inflammatory activity of Haritaki (*T. chebula*) seed extracts, the seeds were extracted using methanol, ethyl acetate, and hexane. The anti-inflammatory activity was assessed by treating an inflammatory model with each extract and measuring the reduction in inflammatory markers at 600 nm. This assay helps in identifying which solvent extracts the most effective anti-inflammatory compounds, guiding further development and potential therapeutic applications.

2.6. Protein Preparation:

Four target proteins associated with myopia were selected for molecular docking studies: 7LBG (HCMV Trimer with human TGF- β receptor type 3 and neutralizing Fabs), 5DSG (M4 muscarinic acetylcholine receptor bound to tiotropium), 5AER (Neuronal calcium sensor-1 with D2 dopamine receptor peptide), and 1BY4 (homodimeric RXR on DNA). These proteins were prepared using Discovery Studio for accurate docking.

2.7. Ligand Preparation

Following GCMS analysis, the identified *T.chebula* ligands from the three extracts were prepared for computational studies using Discovery Studio. The ligands were prepared for maintaining the structural integrity and chemical properties, ensuring they were suitable for subsequent pharmacokinetic and pharmacodynamic evaluations.

2.8. ADME Prediction and Toxicity Analysis

The next phase involved predicting the Absorption, Distribution, Metabolism, and Excretion (ADME) properties of the ligands using Discovery Studio's inbuilt tools. Concurrently, a toxicity analysis was conducted to evaluate the safety profiles of the ligands. Rat oral LD50 was predicted to assess acute oral toxicity, and ocular irritation was evaluated to predict potential eye irritation effects. Each ligand was also evaluated against Lipinski's Rule of Five to determine its drug-likeness.

2.9. Molecular Docking

The molecular docking phase involved the interaction of the prepared ligands with the four target proteins 7LBG, 5DSG, 5AER, and 1BY4 using Discovery Studio. The ligands were docked into the active sites of these proteins using LibDock, and the resulting interactions were analyzed.

3. Results:

3.1. Differential Phytochemical Extraction from Plant Seeds via Soxhlet Method

The syrup preparation performed using Soxhlet extraction of 10 grams of plant seed powder using methanol, hexane, and ethyl acetate (200 ml each) as solvents yielded 1 mL of extract for each solvent, suitable for GC-MS analysis. Multiple Soxhlet cycles were completed for each solvent, with noticeable color changes indicating successful extraction (Fig. 1.).

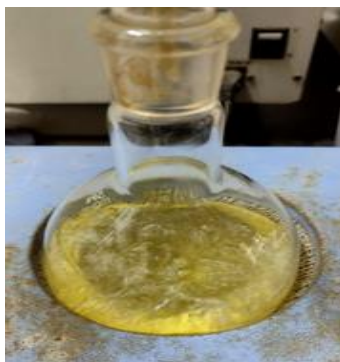


Fig.1. Color Changes During Soxhlet Extraction

3.2. Preliminary Phytochemical Screening of Plant Seed Extracts

Preliminary phytochemical screening confirmed the presence of phenolic compounds and flavonoids in the methanol extract, oils and fatty acids in the hexane extract, and a mix of flavonoids and terpenoids in the ethyl acetate extract providing a comprehensive profile of the *T.chebula* plant's bioactive compounds suitable for further GC-MS analysis.

3.3. GC-MS Profiling of Bioactive Compounds in Haritaki (*T. chebula*) Seed Extracts

The GC-MS analysis of the plant seed extracts obtained using methanol, hexane, and ethyl acetate solvents revealed 103 distinct profiles of bioactive compounds. The methanol extract was rich in phenolic compounds and flavonoids, hexane extract contained high levels of fatty acids and lipids, and ethyl acetate extract had a mix of flavonoids, terpenoids, and phenolic compounds. Key

compounds include 1,2,3-Benzenetriol (923) and 1,2,4-Benzenetriol (868), known for strong antioxidant properties, and 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl- (850) and 5-Hydroxymethylfurfural (830), both with antioxidant and antimicrobial activities. Hexane extract identified 3-Allyl-6-methoxyphenol (score 899) and Phenol, 2-methoxy-3-(2-propenyl)- (Eugenol) (score 896), both known for strong antioxidant, antimicrobial, and anti-inflammatory properties. Ethyl acetate extract includes 1,2,3-Benzenetriol (score 953) and 1,2,4-Benzenetriol (score 857), both known for strong antioxidant properties and 2,4-Di-tert-butylphenol (score 899), which has potent antioxidant and antimicrobial activities.

3.4. Antioxidant Activity of Haritaki (*T. chebula*) Seed Extracts: DPPH and TCA Assays

The antioxidant activity (Fig. 2.) of the plant seed extracts obtained using methanol, hexane, and ethyl acetate solvents was evaluated by DPPH analysis at 517nm. Overall, the results confirm that the methanol extract possesses the most potent antioxidant properties among the three solvents used (Table 2.).

Sl.No	Solvent	Concentration (mg)	Control (Ac)	Absorbance (As)	% of Anti-Oxidant
1.	Ethyl Acetate	0.5	0.68	0.51	25
2.	n-Hexane	0.5	0.72	0.56	22.3
3.	Methanol	0.5	0.70	0.50	28.5

Table 2. Antioxidant activity of *T.chebula* with DPPH

Calculation of Antioxidant activity of *Haritaki* with DPPH; % of antioxidant activity = $[(Ac - As) \div Ac] \times 100$; % of antioxidant activity (Ac being Absorbance of Control and As being Absorbance of Sample).

The antioxidant activity of plant seed extracts was evaluated using the TCA test at 700 nm. Overall, the results highlight the superior antioxidant activity of the methanol extract, followed by ethyl acetate, and then hexane, with methanol proving most effective in extracting polar antioxidants (Table.3).

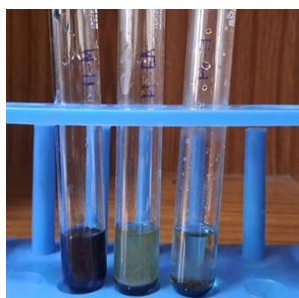


Fig.2. Anti-Oxidant activity of *T.chebula*

Sl.No	Solvent	Concentration (mg)	Absorbance (As)	% of Anti-Oxidant
1.	Ethyl Acetate	0.5	0.50	26.5
2.	n-Hexane	0.5	0.55	23.6
3.	Methanol	0.5	0.45	35.7

Table.3. Anti-Oxidant activity of *T.chebula* with TCA

3.5. Anti-inflammatory Activity of Haritaki (*T. chebula*) Seed Extracts

The anti-inflammatory activity (Fig.3) of plant seed extracts was assessed with measurements taken at 600 nm. Overall, methanol proved to be the most effective solvent for extracting anti-inflammatory compounds, followed by ethyl acetate and then hexane (Table 4.).

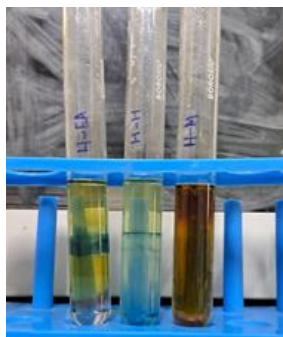


Fig.3. Anti-inflammatory test of *T.chebula*

SI.No	Solvent	Concentration (mg)	Absorbance (As)	% of Anti- Inflammatory
1.	Ethyl Acetate	0.5	0.55	36.4
2.	n-Hexane	0.5	0.60	30
3.	Methanol	0.5	0.50	40

Table 4. Anti-inflammatory activity of *T.chebula*

3. 6. In silico ADME Evaluation of *T.chebula* Compounds using Discovery Studio

The in silico ADME evaluation using Discovery Studio identified a diverse range of ADME properties among the three types of *T.chebula* compounds from the three extracts. This analysis provides valuable insights for prioritizing promising candidates for further investigation (Fig.4.).

From GC-MS analysis of Ethyl Acetate extract of *T.Chebula*, 36 ligands were extracted out of which only 19 ligands were selected in ADME prediction based on the exhibition of favorable HIA, low BBB permeability, and appropriate physicochemical properties that warrant further exploration in pre-clinical models to validate their therapeutic potential and assess their overall drug-likeness profile. Similarly, 28 out of 51 ligands and 18 out of 19 ligands were chosen for Hexane and Methanol extracts through ADMET prediction.

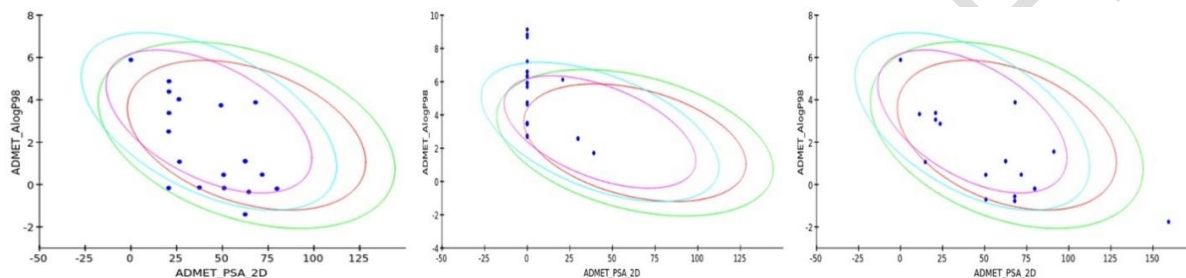


Fig.4. ADMET Plot - Ligands of Ethyl acetate, Hexane and Methanol extract of *T.Chebula*

3.7. Docking Analysis of Target Protein and *T.Chebula* Compounds

A total of 65 *T.Chebula* ligands were selected from all three extracts Ethyl Acetate, Hexane, Methanol were selected based on the ADMET and toxicity prediction. The 65 *T.Chebula* ligands are docked with the selected four target proteins - 7LBG, 5DSG, 5AER, and 1BY4 using LibDock in Discovery Studio (Table 5.).

S.No	Target Proteins	Extracts	Ligands	LibDock Energy Score	Amino acids	Distance
1.	7LBG	Ethyl Acetate	-	-	-	-

		Hexane	4,7-Dimethylundecane - 519389	74.2151	ASN,ASP	2.05,2.72
		Methanol	-	-	-	-
2.	5DSG	Ethyl Acetate	8-methylnonanoic acid ethyl ester - 53428935	80.8528	PHE, VAL, TYR, LEU, ILE	2.75, 4.22, 4.78, 4.82, 4.94, 4.98, 5.01, 5.45
		Hexane	Tridecane - 12388	81.8818	ILE, PHE, LEU, VAL, LYS, ARG	3.97, 5.34, 4.39, 4.36, 5.34, 4.60, 4.06, 5.44, 3.64, 4.87
		Methanol	Doxylamine - 3162	92.64	LEU, VAL, ASN, THR, ARG, ILE	5.12, 2.71, 5.35, 2.56, 2.68, 3.02, 3.00, 2.39, 5.06, 2.66, 2.43

3.	5AER	Ethyl Acetate	Naratriptan N-Oxide - 46782454	125.834	PHE, TRP, GLU, ALA, LYS, ASP, ASP, LEU	2.79, 2.18, 1.72, 4.89, 2.00, 2.94, 2.90, 3.09, 2.29, 4.02, 2.44, 4.75, 5.53, 5.44, 4.81, 2.16, 2.80, 2.21, 2.51, 2.37
		Hexane	Dodecane - 35768	91.4202	TRP, VAL, LYS	5.11, 4.47, 4.14, 5.03
		Methanol	-	-	-	-
4.	1BY4	Ethyl Acetate	7-Chloro-6-[4- (diethylamino)phenyl]- 5,8-quinolinedione - 10042917	127.959	DA	2.49, 5.41, 3.09, 4.63, 5.21, 2.43, 2.54, 3.64
		Hexane	Dodecane- 35768	100.039	DA, DG, DT	5.40, 4.12, 4.85, 5.23, 5.50
		Methanol	1-Methyl-3,4-bis(indol-	116.75	DA, DT,	3.06, 2.71,

			3-yl)maleimide - 2400		DG, ASN, GLN	2.79, 1.70, 2.25, 5.34
--	--	--	-----------------------	--	-----------------	---------------------------

Table 5. Docking Results

4. Discussion:

Haritaki is rich in bioactive compounds such as tannins, flavonoids, and phenolic acids, which can inhibit pro-inflammatory cytokines and enzymes, reducing inflammation and potentially improving eye health. This experiment involved the Soxhlet extraction of plant seed powder using methanol, hexane, and ethyl acetate as solvents, followed by GC-MS analysis and antioxidant and anti-inflammatory assays⁴⁵. The methanol extract yielded a high concentration of polar compounds which demonstrated the highest antioxidant and anti-inflammatory activities⁴⁶ in the DPPH and TCA assays. In contrast, hexane extract predominantly extracted non-polar compounds. While this extract showed the lowest antioxidant activity, it still exhibited notable antimicrobial properties, making it useful for applications in the cosmetic and food industries⁴⁷. The ethyl acetate extract provided a balanced extraction of both polar and non-polar compounds. This extract showed moderate antioxidant and anti-inflammatory activities, making it a versatile option for both therapeutic and cosmetic uses.

In our antioxidant activity test using the DPPH assay on plant seed extracts, we observed significant variations in antioxidant capacity based on the solvent used for extraction. Methanol extracts exhibited the highest antioxidant activity, likely due to the efficient extraction of polar phenolic compounds and flavonoids known for their strong free radical scavenging properties. Because hexane is nonpolar and largely removes lipids and non-polar chemicals that are less

effective at neutralizing free radicals, it exhibited the lowest antioxidant efficacy across extracts. Intermediate antioxidant activity was shown by ethyl acetate extracts.

Myopia can sometimes be exacerbated by inflammation and oxidative stress within ocular tissues. The anti-inflammatory properties of *Terminalia chebula* can help mitigate these effects by reducing oxidative stress and promoting tissue repair. The in silico ADME evaluation and docking analysis of *Terminalia chebula* extracts highlight the drug-likeness and therapeutic potential of its compounds. Docking studies performed indicate significant binding interactions of Naratriptan N-Oxide from the Ethyl Acetate extract with 5AER, Tridecane from the Hexane extract and Doxylamine from the Methanol extract with 5DSG. Additionally, the ethyl acetate extract's 7-Chloro-6-[4-(diethylamino) phenyl]-5,8-quinolinedione shows the highest binding affinity for 1BY4, supporting its potential in treating eye disorders. These analyses highlight new applications of several promising ligands with favorable drug-like properties and strong target interactions, indicating the need for further pre-clinical studies to confirm their therapeutic potential. Future research should focus on validating these in silico predictions through pre-clinical and clinical studies. This will help to fully explore and confirm the therapeutic efficacy of *Terminalia chebula* extracts and pave the way for innovative natural product-based treatments, bridging the gap between traditional medicinal knowledge and modern pharmacological advancements.

Conclusion

The study demonstrates that *Terminalia chebula* (Haritaki) extracts, particularly those obtained with methanol and ethyl acetate, exhibit notable efficacy in the treatment of myopia. The research combined comprehensive computational methods with laboratory experiments to explore the medicinal benefits of these extracts. These combined findings underscore the diverse therapeutic potential of *Terminalia chebula* extracts. The integration of computational analysis with

experimental results not only enhances our understanding of these bioactive compounds but also supports the development of novel therapeutic agents. Future research should focus on validating these in silico predictions through pre-clinical and clinical studies.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

5. References:

1. Gupta P. Biological and pharmacological properties of Terminalia chebula Retz. (Haritaki) – An overview. *Int J Pharm Sci.* 2012 Jan 1; 4:62–8.
2. K Ra, R J. Evaluation Of Antimicrobial Properties Of Fruit Extracts Of Terminalia Chebula Against Dental Caries Pathogens. 2009 Jan 1;2(34):105–11.
3. Babar T, Gokhale V, Deshpande DrM. A Review Of Haritaki (Terminalia Chebula) And Its Pharmacological Actions. 2022 Jan 1;
4. Meher SK, Pandas P, Das B, Bhuyan GC, Rath KK. Pharmacological profile of Terminalia chebula Retz. and Willd. (Haritaki) in Ayurveda with evidences. *Res J Pharmacol Pharmacodyn.* 2018;10(3):115–24.
5. Chande KalyaniU, Ekhande NikhilS, Deshpande PL, Aher SS. Haritaki A Review. *World J Pharm Res.* 11(7):302–17.
6. Mahesh R, Bhuvana S, Hazeena Begum VM. Effect of Terminalia chebula aqueous extract on oxidative stress and antioxidant status in the liver and kidney of young and aged rats. *Cell Biochem Funct.* 2009;27(6):358–63.
7. Naik GH, Priyadarsini KI, Naik DB, Gangabthagirathi R, Mohan H. Studies on the aqueous

extract of *Terminalia chebula* as a potent antioxidant and a probable radioprotector. *Phytomedicine*. 2004 Sep 20;11(6):530–8.

8. Gandhi NM, Nair CKK. Radiation protection by *Terminalia chebula*: Some mechanistic aspects. *Mol Cell Biochem*. 2005 Sep 1;277(1):43–8.
9. Prasad L, Husain Khan T, Jahangir T, Sultana S. Chemomodulatory effects of *Terminalia chebula* against nickel chloride induced oxidative stress and tumor promotion response in male Wistar rats. *J Trace Elem Med Biol*. 2006 Dec 4;20(4):233–9.
10. Saleem A, Husheem M, Härkönen P, Pihlaja K. Inhibition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula* retz. fruit. *J Ethnopharmacol*. 2002 Aug 1;81(3):327–36.
11. Chang CL. Influence of *Terminalia chebula* extracts on the effect of PC12 cell growth. *J Trad Med*. 2010;23–30.
12. Lee HS, Koo YC, Suh HJ, Kim KY, Lee KW. Preventive effects of chebulic acid isolated from *Terminalia chebula* on advanced glycation endproduct-induced endothelial cell dysfunction. *J Ethnopharmacol*. 2010 Oct 5;131(3):567–74.
13. Tasaduq SA, Singh K, Sethi S, Sharma SC, Bedi KL, Singh J, et al. Hepatocurative and antioxidant profile of HP-1, a polyherbal phytomedicine. *Hum Exp Toxicol*. 2003 Dec 1;22(12):639–45.
14. Rajesh Kannan V, Rajasekar G, Pandiyan R, Balasubram V, Nachimuthu R, Ebenezer K, et al. Anti-diabetic Activity on Ethanolic Extracts of Fruits of *Terminalia chebula* Retz. Alloxan Induced Diabetic Rats. *Am J Drug Discov Dev*. 2012 Mar 1; 2:135–42.
15. Senthilkumar GP, Subramanian SP. Biochemical studies on the effect of *Terminalia chebula* on the levels of glycoproteins in streptozotocin-induced experimental diabetes in rats. *J Appl*

- Biomed. 2008 Jul 31;6(2):105–15.
16. Khan K. Regular intake of *Terminalia chebula* can reduce the risk of getting typhoid fever. *Adv BioTech*. 2009 Jan 1;8.
 17. Malekzadeh F, Ehsanifar H, Shahamat M, Levin M, Colwell RR. Antibacterial activity of black myrobalan (*Terminalia chebula* Retz) against *Helicobacter pylori*. *Int J Antimicrob Agents*. 2001 Jul 1;18(1):85–8.
 18. Suchalatha S, Shyamala Devi CS. Protective effect of *Terminalia chebula* against experimental myocardial injury induced by isoproterenol. *Indian J Exp Biol*. 2004 Feb;42(2):174–8.
 19. Bagavan A, Rahuman AA, Kamaraj C, Kaushik NK, Mohanakrishnan D, Sahal D. Antiplasmodial activity of botanical extracts against *Plasmodium falciparum*. *Parasitol Res*. 2011 May 1;108(5):1099–109.
 20. Sohni YR, Kaimal P, Bhatt RM. The antiamebic effect of a crude drug formulation of herbal extracts against *Entamoeba histolytica* in vitro and in vivo. *J Ethnopharmacol*. 1995 Jan 1;45(1):43–52.
 21. Dutta BK, Rahman I, Das TK. Antifungal activity of Indian plant extracts: Antimyzetische Aktivität indischer Pflanzenextrakte. *Mycoses*. 1998;41(11–12):535–6.
 22. Shahidi Bonjar GH. Inhibition of Clotrimazole-resistant *Candida albicans* by plants used in Iranian folkloric medicine. *Fitoterapia*. 2004 Jan 1;75(1):74–6.
 23. Vonshak A, Barazani O, Sathiyamoorthy P, Shalev R, Vardy D, Golan-Goldhirsh A. Screening South Indian medicinal plants for antifungal activity against cutaneous pathogens. *Phytother Res*. 2003;17(9):1123–5.
 24. Moeslinger T, Friedl R, Volf I, Brunner M, Koller E, Spieckermann PG. Inhibition of inducible nitric oxide synthesis by the herbal preparation Padma 28 in macrophage cell line. *Can J*

- Physiol Pharmacol. 2000 Nov;78(11):861–6.
25. Nair V, Singh S, Gupta YK. Anti-arthritic and disease modifying activity of *Terminalia chebula* Retz. in experimental models. J Pharm Pharmacol. 2010 Dec 1;62(12):1801–6.
 26. Shin TY, Jeong HJ, Kim DK, Kim SH, Lee JK, Kim DK, et al. Inhibitory action of water soluble fraction of *Terminalia chebula* on systemic and local anaphylaxis. J Ethnopharmacol. 2001 Feb 1;74(2):133–40.
 27. Gambari R, Lampronti I. Inhibition of immunodeficiency type-1 virus (HIV-1) life cycle by medicinal plant extracts and plant-derived compounds. In: Khan MTH, Ather A, editors. Advances in Phytomedicine [Internet]. Elsevier; 2006 [cited 2024 Aug 3]. p. 299–311. (Lead Molecules from Natural Products; vol. 2). Available from: <https://www.sciencedirect.com/science/article/pii/S1572557X05020179>
 28. Ma H, Diao Y, Zhao D, Li K, Kang T. A new alternative to treat swine influenza A virus infection: extracts from *Terminalia chebula* Retz.
 29. Maruthappan V, Shree KS. Hypolipidemic Activity Of Haritaki (*Terminalia Chebula*) In Atherogenic Diet Induced Hyperlipidemic Rats. J Adv Pharm Technol Res. 2010 Jun;1(2):229.
 30. Israni DA, Patel KV, Gandhi TR. Anti-hyperlipidemic activity of aqueous extract of *Terminalia chebula* & Gaumutra in high cholesterol diet fed rats. Pharma Sci Monit. 2010;1(1):48–59.
 31. Tamhane MD, Thorat SP, Rege NN, Dahanukar SA. Effect of oral administration of *Terminalia chebula* on gastric emptying: an experimental study. J Postgrad Med. 1997 Mar;43(1):12.
 32. Sharma P, Prakash T, Kotresha D, Ansari MA, Sahrm UR, Kumar B, et al. Antiulcerogenic activity of *Terminalia chebula* fruit in experimentally induced ulcer in rats. Pharm Biol. 2011

- Mar 1;49(3):262–8.
33. Mard SA, Veisi A, Naseri MKG, Mikaili P. Spasmogenic Activity of the Seed of *Terminalia chebula* Retz in Rat Small Intestine: In Vivo and In Vitro Studies. *Malays J Med Sci MJMS*. 2011;18(3):18–26.
 34. Bag A, Bhattacharyya SK, Chattopadhyay RR. The development of *Terminalia chebula* Retz. (Combretaceae) in clinical research. *Asian Pac J Trop Biomed*. 2013 Mar 1;3(3):244–52.
 35. Li K, Diao Y, Zhang H, Wang S, Zhang Z, Yu B, et al. Tannin extracts from immature fruits of *Terminalia chebula* Fructus Retz. promote cutaneous wound healing in rats. *BMC Complement Altern Med*. 2011 Oct 7;11(1):86.
 36. Dwevedi A, Dwivedi R, Sharma YK. Exploration of Phytochemicals Found in *Terminalia* sp. and their Antiretroviral Activities. *Pharmacogn Rev*. 2016;10(20):73–83.
 37. Pratibha N, Saxena VS, Amit A, D'Souza P, Bagchi M, Bagchi D. Anti-inflammatory activities of Aller-7, a novel polyherbal formulation for allergic rhinitis. *Int J Tissue React*. 2004 Jan 1;26(1–2):43–51.
 38. Vani T, Rajani M, Sarkar S, Shishoo CJ. Antioxidant Properties of the Ayurvedic Formulation Triphala and Its Constituents. *Int J Pharmacogn*. 1997 Jan 1;35(5):313–7.
 39. Jha AK, Sit N. Methods of extraction of bioactive compounds from *Terminalia Chebula* (Haritaki) and their application in food and pharmaceutical industry: A review. *Food Bioeng*. 2023;2(2):139–50.
 40. Biswal DrA, Mohanty PK. Clinical Study on Simple Myopia with Reference to the Effect of Triphala Ghreeta. *Int J Innov Res Med Sci*. 2017;2(1):481–3.
 41. Jadhav N, Auti. Ayurvedic treatment modalities in management of myopia: Critical review. *Int Ayurvedic Med J*. 2023;7(3):651–5.

42. Baird P, Seang-Mei S, Carla L, Guggenheim J, Xiangtian Z, Kyoko-Ohno M, et al. Myopia (Primer). *Nat Rev* [Internet]. 2020 [cited 2024 Aug 3];*Disease Primers*(6(1)). Available from: <https://www.proquest.com/openview/123703ef1a5f50987ccdb921a6597752/1?pq-origsite=gscholar&cbl=2069613>
43. Kim MH, Zhao D, Kim W, Lim DH, Song YM, Guallar E, et al. Heritability of Myopia and Ocular Biometrics in Koreans: The Healthy Twin Study | *IOVS* | *ARVO Journals*. *Invest Ophthalmol Vis Sci*. 2013;54(5):3644–9.
44. Morgan IG, Ohno-Matsui K, Saw SM. Myopia. *The Lancet*. 2012 May 5;379(9827):1739–48.
45. Harborne AJ. *Phytochemical Methods A Guide to Modern Techniques of Plant Analysis*. Springer Science & Business Media; 1998. 504 p.
46. Momodu IB, Okungbowa ES, Agoreyo BO, Maliki MM. Gas Chromatography – Mass Spectrometry Identification of Bioactive Compounds in Methanol and Aqueous Seed Extracts of *Azanza garckeana* Fruits. *Niger J Biotechnol*. 2022 Jun 6;38(1):25–38.
47. Afrin NS, Hossain MA, Saha K. Phytochemical screening of plant extracts and GC-MS analysis of n-Hexane soluble part of crude chloroform extract of *Cuscuta reflexa* (Roxb.). *J Pharmacogn Phytochem*. 2019;8(2):560–4.