

Current Medical Applications of Terminalia Chebula: An Overview

Dhiya Altememy¹, Akram Alizadeh^{2*}, Sorayya Ghasemi^{3*}

¹Department of Pharmaceutical, College of Pharmacy, Al-Zahraa University for Women, Karbala, Iraq

²Department of tissue engineering and applied cell sciences, Semnan University of medical sciences, Semnan, Iran

³Cellular and Molecular Research Center, Basic Health Sciences Institute, Shahrekord University of Medical Sciences, Shahrekord, Iran

Email: alizadehbio@gmail.com², sorayya.ghasemi@gmail.com³

Abstract

Medicinal plants have long been used, and many of them are known today as drug production sources. The study and research of medicinal plants used in traditional medicine and their various effects in the treatment of some diseases can help produce new drugs. Terminalia chebula, known as the Haritaki plant, has always been at the top of Chinese, Tibetan, Ayurveda, and Iranian traditional medicines. Its classification is based on the size, shape, and growth of the fruit. We have done a thorough literature search in databases and collected the data and research results indexed in PubMed, Elsevier, and Institute for Scientific Information (ISI), Scientific Information Database, Google Scholar databases, and various books up to 2020. It has pharmacological uses such as neuroprotective, hepatoprotective, cardioprotective, antidiabetic, renoprotective, antifungal, antiviral, antibacterial, antimicrobial, antimutagenic, antiproliferative, antioxidant, antiarthritic, and antifertility properties. It also can act as an immunomodulator and anticancer agent. There are some available drugs obtained from T. chebula. Due to the different and wide pharmacological uses of Terminalia chebula, further studies are required to develop new drugs.

Keywords: Terminalia; Traditional medicine; Pharmacological activities; Haritaki plant

INTRODUCTION

Medicinal plants have long been used and considered around the world. Many of them are known today as the source of drug production. Many others have not yet been sufficiently studied. Therefore, the study and research of medicinal plants used in traditional medicine and their various effects in the treatment of some diseases can help produce new drugs (Benzie and Wachtel-Galor, 2011; Petrovska, 2012; Zhang et al., 2019).

Some characteristics of medicinal plant leads to their usage as an antibacterial agent to treat gastroenteritis and diarrhea (Salimikia et al., 2020). In another study, a list of medicinal plants used as hepatoprotective agents in Shahrekord was investigate.

They demonstrated tables that provide a good basis for more scientific use of medicinal plants and make products with higher efficacy and less harms (Abbasi et al., 2019). Additionally, these plants are used as treatment of viral diseases, due to much lower side effects than other treatments. Nazarian and Rafieian explained effective medicinal plants to treat Hepatitis B that Terminalia Chebula is one of them (Samani and Kopaei, 2018). Terminalia is one of the most widely used medicinal plants in traditional medicine in different parts of the world consisting of 250 species. Since many of these species have been used in a variety of Asian medicinal systems, their biological characteristics have been well studied.

Address for correspondence: Akram Alizadeh, Department of tissue engineering and applied cell sciences, Semnan University of medical sciences, Semnan, Iran, Email: alizadehbio@gmail.com

Received date: 12 August 2022

Accepted: 14 September, 2022

Published: 07 October, 2022

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: pnrjournal@gmail.com

How to cite this article: Altememy D, Alizadeh A, Ghasemi S, Current Medical Applications of Terminalia Chebula: An Overview ., J Pharm Negative Results 2022;13(4):183-192

Access this article online

Quick Response Code:



Website:

www.pnrjournal.com

DOI:

10.47750/pnr.2022.13.04.023

Most of the prescription drugs used to treat diseases nowadays are essentially isolated from plants and/or are semi-synthetic analogues of phytochemicals. Based on the estimates, almost 25% of all drugs used are of plant origin. *T. chebula* is a plant used in traditional medicine all over the world (Cock, 2015a). One of the main sources of therapeutic agents for illness treatments is medicinal plants like *Terminalia* (Amalraj and Gopi, 2017). Different therapeutic properties for *Terminalia* species have been reported until now. Today, species of *Terminalia* are being tested in studies that were used in traditional drug systems in the past (Cock, 2015a).

T. chebula, commonly known as black-or chebulic myrobalan, is a species of *Terminalia*. This plant can be found in South Asia from India and Nepal east to southwest China (Yunnan), and south to Sri Lanka, Malaysia, and Vietnam. It is a popular plant in Traditional Chinese medicine, Tibetan medicine, Ayurveda and Traditional Iranian Medicine. It also has some other names like Halela or Halileh in Persian, Harad, and Hara in Hindi, Hardi in Gujrati, Hirda in Marathi, Haritaki in Sanskrit and Bengali, Karaka in Telegu, Kadukkai in Tamil and Chebulik myrobalan in English (Bag *et al.*, 2013a; Gupta, 2012a; Rathinamoorthy and Thilagavathi, 2014a). Since there are many different types of phytoconstituents in *T. chebula*, it has several medicinal effects. A number of chemical constituents have been isolated from the plant extract, including a coumarin conjugated with gallic acids called chebulin, ellagic acid, 2,4-chebulyl-D-glucopyranose, arjunglucoside I, arjungenin and the chebulosides I and II (Tewari *et al.*, 2017), chebulinic acid (a phenolic acid compound isolated from the ripe fruits) (Lee *et al.*, 2007), gallic acid, ethyl gallate (Saleem *et al.*, 2002), punicalagin, terflavin A, terchebin, luteolin (Lee *et al.*, 2010), Luteic acid (isolated from the bark) (Nierenstein and Potter, 1945), and tannic acid (Chang and Lin, 2012; Upadhyay *et al.*, 2014). Moreover, among the compounds in Haritaki, phenolic carboxylic compounds, phenols, terpenoids and triterpene saponins, flavonoids can be mentioned (Ali and Khan, 2009).

The fruit of the tree possesses various health benefits and has been used as a traditional medicine against various human diseases (Bag *et al.*, 2013a).

This review was prepared to gather published information on pharmacological uses and polyherbal formulation of *Terminalia chebula*.

BOTANICAL DESCRIPTION

T. chebula tree is 15-24 m high. The leaves are oval or elliptical in shape and have a large pair of large glands at the top of the petiole. In addition, terminal spikes are found in yellowish-white flowers, and they blossom in May-June. The fruits appear in July-December. Additionally, they are green and yellowish grey when they are unripe and ripe, respectively (Babita *et al.*, 2011a; Bag *et al.*, 2013b).

CLASSIFICATION BASED ON THE SIZE OF THE FRUIT

(A) Survariharade – They are large, dense, and heavy with about 2 inches long. They are yellowish-brown after being cut with yellowish or darkish brown, pulp and stone. (B) Rangariharade- They are smaller, less wrinkled, and less furrowed than the above variety; it is about one inch long; the epidermis is yellow. When it is cut, it presents a yellow dried pulp a stone. The pulp is less astringent than that of Survariharade. (C) Balaharade – In comparison with the two previous groups, this category is smaller and has a deep brown or black color with a highly wrinkled, dark, or brown epidermis. Additionally, the pulp is dark and homogenous; there is no stone. (D) Java harade- These are the smallest groups, while other characters are similar to those of Balaharade (Rathinamoorthy and Thilagavathi, 2014b).

CLASSIFICATION ACCORDING TO THE SHAPE

(A) Vijaya- it has an alabu shape. It is used in all diseases and can be found in Vindhya Mountains.

(B) Rohini- it has a round shape and is used in Vrana. This shape has been seen in Zansi and other states of India.

(C) Pootana- it has small size, thin mesocarp with a giant seed, externally used; habitat: Sind.

(D) Amirtha- Mesocarp is more used for Shodhana Karma habituation.

(E) Abhay- The fruit has five ribs used in eye diseases; habitat: Champaranya, Himalaya.

(F) Jeevantee- The fruit is golden yellow and is used in all conditions; habitat: Himalaya.

(G) Chetak- The fruit has three ribs and is used as purgative (Rathinamoorthy and Thilagavathi, 2014b).

CLASSIFICATION ACCORDING TO THE GROWTH OF THE FRUIT

When the size is like cumin seed, it is called Halileh – Zira.

When the size is like raw corn, it is called Halileh – Javi.

When the size is like a raisin, it is called Halileh – Zangi.

When the fruit is greenish-yellow and somewhat rigid, it is called Halileh – Chini,

When it is totally mature, it is called Halileh – Asfer.

When the fruit is fully matured, it is called Halileh – Kabul (Rathinamoorthy and Thilagavathi, 2014b).

PHARMACOLOGICAL AND THERAPEUTIC USES

T. chebula is called “The king of medicines” or “Mother of medicine” in Tibet because of its power to mend with a wide spectrum of pharmacological properties. For example: hypolipidemic, antibacterial, antifungal, antiviral, anti-anaphylactic, anti-mutagenic, and gastrointestinal motility ameliorating and anti-ulcerogenic properties. Other

properties include hepatoprotective, cardioprotective, antidiabetic, retinoprotective, antiarthritic, wound recuperating, neuroprotective, immunomodulatory, and anti-fertility activities.

T. chebula is routinely used as a conventional pharmaceutical prescription to treat a few disorders such as asthma, sore throat, spewing, hiccough, diarrhea, dysentery, gastroenteritis, wound infections, skin diseases, candidiasis, and urinary tract infections (Bag *et al.*, 2013b; Gupta, 2012b). The different pharmacological properties of this plant and its impact on treating various diseases can be seen in table 1.

Neuroprotective Activity

The neuroprotective activity of methanol and water extracts of *T. chebula* against H₂O₂-induced poisonous quality toward the PC12 cell line has been demonstrated. Additionally, the plant is a potential candidate for improving H₂O₂-induced neurodegenerative diseases (Chang and Lin, 2012). In a study, the positive effects of hydroalcoholic fruit extract of *T. chebula* on seizures, seizure-induced cognitive impairment, and oxidative stress in rats were reported (Kumar *et al.*, 2018a).

T.Chebula And Alzheimer's Disease

Medicinal plants have regained their importance in treating diseases and disorders, particularly in treating psychiatric and neurological disorders. This plant has therapeutic properties and contains various biochemicals such as; hydrolysable tannins, phenolic compounds, and flavonoids (Afshari *et al.*, 2016a; Sarker *et al.*, 2011a).

Alzheimer's disease (AD) is a chronic neurodegenerative disease. This illness usually starts slowly and worsens over time. A hypothesis about AD is the deficiency of acetylcholine in the synaptic cleft of the cerebral cortex that causes memory disorders. The ache is located on the postsynaptic membrane. Hydrolysis of acetylcholine can terminate signal transmission. The inhibition of acetylcholinesterase could result in the accumulation of acetylcholine in the synaptic cleft in AD and lead to neurotransmission. Gallotannin, Tannic acid, Gallic acid, Ellagic acid in the extract of *T. chebula*, have been reported to have anticholinesterase properties. Anti-inflammatory properties of *T. chebula* in different experimental systems have been shown that could be attributed to Chebulagic acid, Ellagic acid, Gallic acid, and Ellagitannins. It has a major role in oxidative stress in the pathogenesis of AD. We can conclude that this herb is effective in preventing the progression of AD (Afshari *et al.*, 2016b).

Hepatoprotective Activity

T. chebula extract is displayed to impede hepatotoxicity caused by the administration of rifampicin (RIF), isoniazid (INH), and pyrazinamide (PZA) (combination). The ethanolic extract of *T. chebula* fruit has hepatoprotective

activity, known as chebulic and neo chebulic acid, which is able to decrease the cytotoxicity of tert-butyl hydroperoxide (t-BHP)-induced cell in confined rodent hepatocyte experimental analysis (Suchalatha and Shyamala Devi, 2004).

T.Chebula And Hemorrhoid

Hemorrhoid is a widespread anorectal disorder. This is the symptomatic enlargement and abnormally downward displacement of anal cushions. It becomes a disease when is swelling or inflamed. Steroids and flavonoids are used in modern medicine for the treatment of hemorrhoids. Some reports have revealed the positive effects of flavonoids in treating hemorrhoids in Iranian traditional medicine. Anti-bleeding effects of flavonoids and anti-inflammatory effects of *T. chebula* are impressive in Iranian traditional medicine to treat hemorrhoids (Rahimi and Abdollahi, 2013a). In a study this plant was used in hemorrhoid treatment compared with placebo capsules. The study showed that after four weeks, the herbal intervention (*T. chebula*) had more positive effects in different variables (pain, constipation, hemorrhoids mass size, and hemorrhoids hemorrhage) and could be a good supplement for the treatment of hemorrhoids (Andarkhor *et al.*, 2019).

Use As An Astringent

Extract of *T. chebula* is used as an astringent, digestive, antiseptic, alterative, laxative, diuretic, and carminative (Muhammad, 2012a; Patel *et al.*, 2020).

Cardioprotective Activity

Cardioprotective impact of ethanolic extract of *T. chebula* fruit was observed in rodents, in which isoproterenol was used to damage cardiac muscles. Moreover, it can enhance the isoproterenol effect on lipid peroxide formation and the protective effects of enzyme markers in rodents (rats).

It has also been declared that isolated frog heart model has cardioprotective activity (Bag *et al.*, 2013b; Chang and Lin, 2012; Suchalatha and Shyamala Devi, 2004). Some patients with type 2 diabetes are faced with cardiovascular risk, and using *T. chebula* can minimize the cardiovascular risk factors compared to placebo (Pingali *et al.*, 2020).

Hypolipidemic/ Hypocholesterolemic Activity

Based on the previous studies, *T. chebula* has an essential decrease in total cholesterol and triglycerides (Rathinamoorthy and Thilagavathi, 2014b).

Antidiabetic And Ophthalmic Problems

T. chebula extract in rats has been shown a dose-dependent effect on diabetes mellitus. Furthermore, observable retinoprotective activity was also exhibited in *T. chebula*-treated rats (Bag *et al.*, 2013b; Gupta, 2012b). Singh *et al.* investigated the antidiabetic and wound healing activity of methanolic extract of the seeds of *T. chebula*. They observed this feature by effective stimulation of insulin secretion (Singh *et al.*, 2017). The effect of *T. chebula* hydro-ethanolic

extract in an herbal combination with two other materials was evaluated in streptozotocin (STZ)-induced diabetic rats. This herbal combination acted as an antidiabetic, antioxidant, and hypolipidemic agent (Sotoudeh *et al.*, 2019a).

Myrobalan is helpful in visual acuity and drainage from the eyes. It is a good eye tonic. This plant is used for epiphora and eye-burning when soaked in rosewater (Jokar *et al.*, 2016a).

Antifungal Activity

A liquid extract of *T. chebula* demonstrated an antifungal property against various dermatophytes, including *Epidermophyton*, *Floccosum*, *Tricophytonrubrum*, and *Microsporumgypseum* yeasts, e.g., *Candida albicans*. Aqueous, alcoholic, and ethyl acetate extract of *T. chebula* leaves were effective against five pathogenic fungi including *Helminthosporium tetramera*, *Alternaria brassicicola*, *A. alternate*, *A. niger*, and *Aspergillus flavus* (Bag *et al.*, 2013b; Gupta, 2012b).

The antifungal property of *T. chebula* was compared to gold standard amphotericin B (control) against *Candida albicans*. The results showed that higher concentrations of *T. chebula* had higher antifungal activity (Manipal *et al.*, 2019).

Antiviral Activity

Since acetone extract of *T. chebula* has low cost, convenient preparation, and strong impact, it is used to treat pandemic swine Flu A infection. Gallic acid and three galloyl glucoses are four human HIV-type 1 integrase inhibitors of *T. chebula*. Galloyl had a significant role in the 3'-processing inhibition of HIV-1 integrase (Gupta, 2012b).

Antimicrobial Activities

T. chebula has been shown antibacterial activities against gram-positive and gram-negative bacteria such as *Pseudomonas aeruginosa* ATCC 27853, *Salmonella typhi* SSFP 4S, *S. aureus* ATCC 25923, *Staphylococcus epidermidis* MTCC 3615, and *Bacillus subtilis* MTCC 441 (Gupta, 2012b).

Additionally, *T. chebula* is highly effective against *H. pylori*. *H. pylori* is responsible for stomach cancer, gastric ulcers, and gastritis. The aqueous extract of *T. chebula* forcefully inhibited the growth of *Streptococcus mutans* (Aneja and Joshi, 2009). Spraying *T. chebula* has inhibitory effects against bacteria such as strain X-100 of the bacterium *Xanthomonas campestris*, *Klebsiella* (Agrawal *et al.*, 2010), and *Shigella* intestinal bacteria (Khan and Jain, 2009; Kim *et al.*, 2006). Alcoholic extract of *T. chebula* has a powerful antibiotics activity against multidrug-resistant *Escherichia coli* (Gupta, 2012b). Additionally, in a study *P. mirabilis*, *K. pneumonia*, *A. baylyi*, and *P. aeruginosa* were used to show the growth inhibitory activity of *T. chebula* fruit extracts alone and in combination with conventional antibiotics (Mandeville and Cock, 2018). This property of *T. chebula*

was used in combination with recycled polyesters to expand the range of their application because of increasing antibacterial activities (Lee *et al.*, 2020). Additionally, *in vitro* antibacterial activity of ethyl acetate extract of *T. chebula* was shown compared to standard amoxicillin for treatment of subclinical mastitis in three breeds of cattle in India (Kher *et al.*, 2019).

The antibacterial activity of *T. chebula* fruit extract was applied in combination with silver nanoparticles (AgNPs) to treat various diseases. The preliminary bioactivity evaluations demonstrated that the bio-conjugation of AgNPs, using *T. chebula* fruit extract, significantly enhanced the antibacterial potentials of the latter. The higher sensitivity of *B. subtilis* compared to *P. aeruginosa* in antibacterial activity of the as-prepared AgNPs was explained (Ankegowda *et al.*, 2020).

The antimicrobial activity of *T. chebula* against the following organisms has been studied by the disk diffusion method: *Bacillus subtilis*, *S. aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Staphylococcus flexinaria*, and *Pseudomonas aeruginosa* (Rathinamoorthy and Thilagavathi, 2014b). Two main ingredients of *T. chebula* against methicillin-resistant *S. aureus* with antimicrobial activity include Gallic acid and ethyl ester (Chattopadhyay and Bhattacharyya, 2007). *T. Chebula* can be used in combination with other materials to improve antimicrobial activities; for example, in the biogenic synthesis of silver palladium bimetallic nanoparticles (AgPd NPs). The disc diffusion method results showed AgPd NPs antibacterial activity against gram-positive bacterial strains like MRSA 11, MRSA 56, and gram-negative bacterial strain *P. aeruginosa* compared to the positive control (Sivamaruthi *et al.*, 2019).

Anticancer Properties

Cancer is an irregular growth of cells that develops and spreads through uncontrolled cell division. Cancer is not one disease but a group of more than one hundred disorders distinction (Chavan *et al.*, 2013). Healthy growth and development of cells depend on the fine-tuning of inhibitory and excitatory pathways. Proto-oncogenes and tumor suppressor genes control the cell cycle. Another common feature of many cancers is the chromosomal instability correlated with oxidative stress (Cock, 2015a; Hanahan and Weinberg, 2000a). Oxidative stress leads to genetic instability and creates new tumors.

Consuming high levels of antioxidant species of *Terminalia chebula* block genetic instability and, therefore, blocks tumorigenesis, which might be effective in cancer treatment (Cock, 2015b).

Triphala has been prepared from Amalaki (*Embilca officinalis*), Haritaki (*Terminalia chebula*), and Bibhitaki (*Terminalia bellirica*). Various cancer cell lines such as thymic lymphoma cells, human breast cancer, human prostate cancer, and human pancreatic cancers are affected by cytotoxic effects of Triphala (Cock, 2015b; Singh *et al.*, 2001).

T. chebula has been applied in lung cancer. Antiproliferative activity of *T. chebula* was studied by MTT (a colorimetric assay for assessing cell metabolic activity) methods to study human lung cancer and mouse lung cancer cell lines. The evidence indicated that *T. chebula* acted by regulating the Bcl-2 family protein-mediated mitochondrial pathway. The investigation of the antiproliferative effect of *T. chebula* on breast cancer cell line (MCF-7) and normal breast epithelial cells (MCF-10a) was conducted. The changes in body weight, along with other tumor parameters such as tumor incidence, tumor volume, serum biochemical parameters, histopathological findings of breast tissue, tumor burden, and tumor weight were measured. The antioxidant activity of the plant extract was related to its use against cancer treatment (Henry *et al.*, 2020). Ethanolic extract of *T. chebula* displayed cytotoxic effects on MCF-7 cells. The anticancer activity of ethanolic extract of *T. chebula* fruits in breast cancer (MCF-7) cell lines has been shown (Priscilla, 2013; Sarker *et al.*, 2011b).

Investigations have shown that Gallic acid (GA) in *T. chebula* is the key factor in suppressing esophageal carcinoma growth. GA molecular mechanism showed a decrease in Ki-67 expression and promotion in cell apoptosis associated with the inhabitation of the Hippo pathway (Sun and Wang, 2020). *T. chebula* as a natural agent is a suitable candidate for further investigation in the treatment and cancer prevention (Wang *et al.*, 2015).

Anaphylactic Effect

Following the induction of anaphylactic shock, the extract of *T. chebula* reduced the serum histamine level showing an intense anti-anaphylactic activity (Babita *et al.*, 2011b). The water solvent part of *T. chebula* had a significantly increasing impact on anti-dinitrophenyl IgE-induced TNF α generation from rat peritoneal mast cells showing a strong antianaphylactic activity (Bag *et al.*, 2013b).

Antimutagenic And Antiproliferative Activities

Studies have shown that phytochemicals in acetone extract of *T. chebula* have antimutagenic and anticarcinogenic properties. Additionally, to examine the growth of several malignant cell lines, including human (MCF-7) and mouse (S115) breast cancer cell lines, a human osteosarcoma cell line (HOS-1), a human prostate cancer cell line (PC3), and a non-tumorigenic, immortalized human prostate cell line (PNT1A) using assays for proliferation (3H-thymidine incorporation and coulter counting), cell viability (ATP determination) and cell death (flow cytometry and Hoechst DNA staining), the methanolic extract of *T. chebula* was used. The extract decreased cell viability, inhibited cell proliferation, and induced cell death in a dose-dependent manner in all cell lines. The ability of potent dual inhibition against COX and 5-LOX in ethanolic fruit extract of *T. chebula*, chebulagic acid has also been demonstrated. It also showed antiproliferative activity against HCT-15, COLO-205, MDA-MB-231, DU-145, and K562 cell lines (Gupta, 2012b). In a study, the dried fruits of *T. chebula* were powdered and extracted with 95% ethanol. The

antimutagenic activity was determined by the Ames test using TA98 and TA100 strains of *Salmonella typhimurium*. Gallic acid and ellagic acid are two major compounds of the ethyl acetate portion, which may be responsible for potent antimutagenic activity (Singamaneni *et al.*, 2019).

Antioxidant Activity

Aqueous extract of *Terminalia chebula* acts as an antioxidant agent. In as much as it can protect the cellular organelles from the radiation actuated harm, it may be considered a likely radioprotector (Rathinamoorthy and Thilagavathi, 2014b). The results indicated that triethyl chebulate was a potent antioxidant and free-radical scavenger, which might contribute to the anti-oxidative ability of *T. chebula*. Because of the presence of the enzymatic and non-enzymatic antioxidants in *T. belerica* and *T. chebula*, the aqueous extracts of both plants have antioxidant properties. They can have anti-microbial properties in various diseases, too (Gupta, 2012b).

Moreover, regarding the studies, the dried fruit of *T. chebula* has antioxidant activities. The antioxidant activities of neutral polysaccharide, isolated by ion-exchange chromatography, were determined using free radical scavenging (DPPH and superoxide) and FRAP assays. The results suggested that an amylopectin-type polysaccharide (TFP-a) could be used as a potential natural antioxidant (Jeong *et al.*, 2019). Exposure to diazinon, a synthetic insecticide, caused liver dysfunction, and weakened the antioxidant system. Regarding previous studies, antioxidants can protect cell membrane integrity and decrease enzyme leakage through free radical scavenging activities. The presence of flavonoids and other compounds in *T. chebula* extract has protective effects on diazinon-induced liver injury (Ahmadi-Naji *et al.*, 2017). In another study, the specific phenolic compositions of *T. chebula* led to the identification of rutin, catechin, caffeic acid, gallic acid, ellagic acid, epicatechin, and quercetin as antioxidant compounds. This composition was determined by high-performance liquid chromatography (Sabir *et al.*, 2020).

Cellular Aging Effect

T. chebula and *T. arjuna* with a high voluminosity of phenolic ingredients showed strong antioxidant and anti-senescence properties (Afshari *et al.*, 2016b). Ethanol extract of *T. chebula* demonstrated a significant inhibitory effect on cellular senescence (Muhammad, 2012a).

Immunomodulatory Effect

Results also indicated the immunomodulatory effects of *T. chebula* by increasing the concentrations of antioxidant enzymes, GSH, and proliferation of T and B cells as immune cells (Rathinamoorthy and Thilagavathi, 2014b).

Antiarthritic Activity

According to the studies, this plant is an effective agent in the treatment of rheumatoid arthritis. A significant inhibition of joint swelling was observed in hydroalcoholic extract of *T.*

chebula compared with control in both formaldehyde-induced and CFA-induced arthritis (Gupta, 2012b).

Anti-Inflammatory Activity

T. chebula plant possesses gallic acid which is one of the main endogenous phenolic acids with anti-inflammatory properties (Hsu *et al.*, 2007; Muhammad, 2012a). This plant showed anti-inflammatory properties by regulating nitrite and TNF- α production, iNOS, COX-2 levels, and translocation of NF- κ B protein on RAW 264.7 cells (Shendge *et al.*, 2020). Additionally, the positive effect of the chloroform extract of *T. chebula* in NO secretion reduction has been reported. The inhibition activity in COX2, IL-1 β , IL-6, and TNF- α expressions were confirmed. Based on the results, *T. chebula* could be used as a reliable anti-inflammatory candidate herb in addition to the many chemical compounds available in the medical markets (Farhan *et al.*, 2020).

Wound Healing

The survey revealed that *T. chebula* has a significant impact on wound healing. Topical management of alcoholic extract of *T. chebula* on skin wounds in rats is restored quickly *in vivo*. *T. chebula* could stimulate fibroblasts; therefore the synthesis of glycosaminoglycans and collagen deposition increases and accelerates wound healing significantly (Sawant *et al.*, 2013).

Dermatologic And Cosmetic Uses

The extract of *T. chebula* is used as a depigmenting ingredient in cosmetics. It has been shown that methanol extract of *T. chebula* can be an inhibitor of the melanin (Jin *et al.*, 2006; Muhammad, 2012b). Myrobalan improves pallidness, diminishes greying of the hair, and acts as a hair tonic. It is also useful in the treatment of leprosy (Jokar *et al.*, 2016b).

Dental And Oral Cavity

The plant improves the gums and teeth and is useful in oral ulcers treatment (Jokar *et al.*, 2016a). Moreover, the ethanol extracts of *T. chebula* helps prevent periodontal disease induced by dental plaque bacteria (Sars-cov- *et al.*, 2020).

Anticaries Activity

Acetone, ethanol, methanol extract of *T. chebula* have powerful effects on dental caries. Hence, they have been considered as antimicrobial agents against dental caries (Bag *et al.*, 2013b). Rinsing the mouth with a 10% the extract can inhibit the glycolysis of salivary bacteria for up to 90 minutes (Sawant *et al.*, 2013).

In a research, different medicinal plants have shown anticaries effects against *S. mutans* glucosyltransferases (gtf). Regarding the final result of kinetic analysis, *T. chebula* had considerable inhibitory action (Mandava *et al.*, 2019).

Antifertility Activity

The oral administration of *T. chebula*'s bark began histological modifications in seminiferous tubules of the cured mice. Fructose levels in seminal vesicles and sialic acid in epididymal have significantly decreased in comparison with control. The sperm parameters of all the mice extracts-treated groups showed a significant reduction compared to controls. The results suggest the adverse effects of aqueous bark extract of *T. chebula* on the male reproductive system (Gupta, 2012b).

Miscellaneous Uses

In the Unani system it is utilized as a blood purifier. The pulp of the fruit was used as pills, dysentery, chronic diarrhea, constipation, flatulence, asthma, urinary disorder, vomiting, hiccup, intestinal parasites, ascites, and enlarged spleen and liver. Both leaves and fruits of *T. chebula* are also utilized as mordant (Muhammad, 2012a).

Traditional Medicine Values

In traditional medicine, in Unani, Ayurveda, and homeopathic medicine, the fruit of *T. chebula* has been used to treat geriatric diseases to improve memory and brain functions. This plant is used in anti-aging therapies, enhancing memory and brain function. The yellow color of the fruit indicates that it is ripe. If the yellow fruit dries, it hardens and is known as yellow myrobalan (Afshari *et al.*, 2016b).

The most important sources of information, reference books, regarding Halileh (*T. chebula*) in TIM (Traditional Iran Medicine) are as follows: The Avicenna's Canon, At-Tibbieh, Axirazam, Sharhe-Asbab, Al-Alaieh, Al-Igraz, Kholasat-Al-Hekmaa, Akbari medicine, and Al-Mabahis (Jokar *et al.*, 2016a).

T. chebula is one of the most important plants in traditional medicine. Myrobalan is called Halileh in TIM textbooks in Farsi, Ah-halilaj in Arabic, and Harharu in Hindi (Jokar *et al.*, 2016a). The following uses are the most important ones indicated in traditional medicine:

Psychological Uses

According to the TIM sources reports, memory retention and brain activity is strengthened by myrobalan. It is reported to have healing properties for bewilderment, headache, melancholy, depression, obsession, amnesia, facial paralysis, anthropophobia, vertigo, and insomnia (Jokar *et al.*, 2016a).

In a study, the anti-amnesic effect of *T. chebula* extract (TCE) in mice induced by scopolamine was studied. TCE reduced hippocampal acetylcholinesterase activities and increased acetyltransferase and acetylcholine levels in the scopolamine-induced model. Also, the suppression of scopolamine-induced oxidative damage is done by TCE treatment with the ease of increasing levels of reactive oxygen species, nitric oxide, and malondialdehyde (Kim *et al.*, 2018).

Hepatic, splenic, and urinary effects

The liver tonic of myrobalan is applicable in liver temperament moderating and generalized swelling treatment and spleen pain, as a diuretic, and treat polypus (Jokar *et al.*, 2016a).

Cardiopulmonary Effects

Myrobalan is useful in heart refreshing, heart palpitations, and tachycardia treatment (Jokar *et al.*, 2016a).

Gastrointestinal Effects

T. chebula has been used to treat human peptic ulcers and gastritis. *T. chebula* has a strong depletive impact and increases gastric emptying time. The balance of this action, which is done with a defensive effect on the gastrointestinal mucosa, leads to an improvement in the secretory status of Brunner's gland. This gland is effective in the preservation against duodenal ulcer (Safavi *et al.*, 2016). Myrobalan tonic causes disgorging controlling, diarrhea stomach moisture absorption, and stomach retention and appetite enhancement (Jokar *et al.*, 2016a).

Other Effects

Opening the blockage of the bile and preventing the evolution and development of burning black bile are other effects of using myrobalan. It is effective in combined fever treatment, diluting humor, and laxative to dry dampness as a humor solvent, for joint pain and to boil humor relief (Jokar *et al.*, 2016a).

TERMINALIA CHEBULA AND AVAILABLE DRUGS IN THE MARKET

As already mentioned, Triphala has historically been used to relieve constipation. Triphala has triggered the death of cancer cells and significantly decreased the size of the tumors (Kumar, 2014). The drugs produced from this plant are known as Haritaki and Triphala in foreign countries and Hemolax in Iran. One of the three compounds in Triphala, Haritaki (*T. chebula*), is considered to be one of the best herbs for balancing Vata dosha. It is protecting the body's natural cleansing process. It is effective in gradually removing accumulated natural toxins in the GIT (gastrointestinal tract). Rejuvenating the skin strengthens the tissues and supports the proper function of the colon, lungs, liver, and spleen. Haritaki has been used in the past as a treatment for all Vata-related imbalances. Haritaki is highly respected in India as it is believed to increase energy, intelligence, and consciousness.

CONCLUSION

The studies of *T. chebula*, as a medicinal plant in traditional medicine, led to an increase in information about its various characteristics and effects on the treatment of some diseases in the production of new drugs. *T. chebula* (Haritaki) is one of the most important medicinal plants used in Ayurveda,

Chinese, Tibetan, and Iranian medicines because of having some pharmacological properties. *T. chebula* is known as the mother of medicine. It has a biodiversity of both nutritional and medicinal components. Triphala as an herbal remedy plays a vital role in treating various diseases. Medicinal plants have regained popularity among scientists in many countries. There is an urgent need to investigate its phytoconstituents and biological activities to develop an effective, safe, and cheap herbal product.

This article provides information about the various properties of the plant in Indian and Iranian traditional medicine and other regions worldwide; such information can be used to prepare and develop new herbal medicines.

Acknowledgment

The authors would like to thank the Shahrekord University of Medical Sciences and Semnan University of Medical Sciences for their supports.

Authors' Contribution

AA contributed to designing the study, performed data collection, DA manuscript preparation. SG supervised and edited the manuscript. The final version of the manuscript was confirmed by all authors.

Conflict Of Interest

Authors declare no conflict of interests.

Ethical Consideration

No ethical approval was required for this review article.

Funding/Support

This research did not receive any specific grant from funding agencies in the public, commercial, or profit sectors. There has been no financial support for this work.

REFERENCES

- Abbasi, N., Rafieian-Kopaei, M., Karami, N., Ghanadi, K., 2019. An Ethnobotanical Study of Hepatoprotective Herbs from Shahrekord, Chaharmahal and Bakhtiari Province, Southwest of Iran. *Egypt. J. Vet. Sci.* 50, 129–134. <https://doi.org/10.21608/ejvs.2019.13946.1089>
- Afshari, A.R., Sadeghnia, H.R., Mollazadeh, H., 2016a. A Review on Potential Mechanisms of Terminalia chebula in Alzheimer's Disease. *Adv. Pharmacol. Sci.* <https://doi.org/10.1155/2016/8964849>
- Afshari, A.R., Sadeghnia, H.R., Mollazadeh, H., 2016b. A Review on Potential Mechanisms of Terminalia chebula in Alzheimer's Disease. *Adv. Pharmacol. Sci.* <https://doi.org/10.1155/2016/8964849>
- Agrawal, A., Gupta, A., Choudhary, N.K., Wadhwa, S., Dave, K., 2010. Antibacterial Activity of Hydroalcoholic Extract of Terminalia chebula Retz . on Different Gram-positive and Gram-negative Bacteria. *Pharmacogn. Rev.* 1, 485–488.
- Ahmadi-Naji, R., Heidarian, E., Ghatreh-Samani, K., 2017. Evaluation of the effects of the hydroalcoholic extract of Terminalia chebula fruits on diazinon-induced liver toxicity and oxidative stress in rats. *Avicenna J. phytomedicine* 7, 454–466. <https://doi.org/10.22038/ajp.2017.21401.1807>
- Ali, Z., Khan, I., 2009. Chemical Constituents of Terminalia chebula. *Planta Med.* 75, 112–127. <https://doi.org/10.1055/s-2009-1216479>

- Amalraj, A., Gopi, S., 2017. Medicinal properties of Terminalia arjuna (Roxb.) Wight & Arn.: A review. *J. Tradit. Complement. Med.* 7, 65–78. <https://doi.org/10.1016/j.jtcme.2016.02.003>
- Andarkhor, P., Sadeghi, A., Khodadoost, M., Kamalinejad, M., Gachkar, L., Abdi, S., Zargar, A., 2019. Effects of Terminalia chebula Retz. in treatment of hemorrhoids: A double – blind randomized placebo – controlled clinical trial. *Eur. J. Integr. Med.* 30, 100935. <https://doi.org/10.1016/j.eujim.2019.100935>
- Aneja, K.R., Joshi, R., 2009. Evaluation of antimicrobial properties of fruit extracts of terminalia chebula against dental caries pathogens. *Jundishapur J. Microbiol.* 2, 105–111.
- Ankegowda, V.M., Kollur, S.P., Prasad, S.K., Pradeep, S., Dhramashekara, C., Jain, A.S., Prasad, A., Srinivasa, C., Sridhara Setty, P.B., Gopinath, S.M., S, R.P., Bahkali, A.H., Syed, A., Shivamallu, C., 2020. Phyto-Mediated Synthesis of Silver Nanoparticles Using Terminalia chebula Fruit Extract and Evaluation of Its Cytotoxic and Antimicrobial Potential. *Molecules* 25, 5042. <https://doi.org/10.3390/molecules25215042>
- Babita, Y., Rani, K.S., Sulochana, B., Mamta, S., 2011a. A Perspective Study of Haritaki. *Int. J. Res. Ayurveda Pharmacy) Consult. Cent. Counc. Res. Ayurvedic Sci.* 2, 1466–1470.
- Babita, Y., Rani, K.S., Sulochana, B., Mamta, S., 2011b. A PERSPECTIVE STUDY OF HARITAKI. *Int. J. Res. Ayurveda Pharmacy) Consult. Cent. Counc. Res. Ayurvedic Sci.*
- Bag, A., Bhattacharyya, S.K., Chattopadhyay, R.R., 2013a. The development of Terminalia chebula Retz. (Combretaceae) in clinical research. *Asian Pac. J. Trop. Biomed.* 3, 244–252. [https://doi.org/10.1016/S2221-1691\(13\)60059-3](https://doi.org/10.1016/S2221-1691(13)60059-3)
- Bag, A., Bhattacharyya, S.K., Chattopadhyay, R.R., 2013b. The development of Terminalia chebula Retz. (Combretaceae) in clinical research. *Asian Pac. J. Trop. Biomed.* [https://doi.org/10.1016/S2221-1691\(13\)60059-3](https://doi.org/10.1016/S2221-1691(13)60059-3)
- Benzie, I.F.F., Wachtel-Galor, S., 2011. Herbal medicine: Biomolecular and clinical aspects: Second edition. *Herb. Med. Biomol. Clin. Asp.* Second Ed. 1–464.
- Chang, C.L., Lin, C.S., 2012. Phytochemical composition, antioxidant activity, and neuroprotective effect of Terminalia chebula Retzius extracts. *Evidence-based Complement. Altern. Med.* 2012. <https://doi.org/10.1155/2012/125247>
- Chattopadhyay, R.R., Bhattacharyya, S.K., 2007. Plant Review Terminalia chebula: An update. *Pharmacogn. Rev.* 1, 151–156.
- Chavan, S.S., Damale, M.G., Shamkuwar, P.B., Pawar, D.P., 2013. Traditional Medicinal Plants for Anticancer Activity. *Int J Curr Pharm Res* 5, 50–54.
- Cock, I.E., 2015a. The medicinal properties and phytochemistry of plants of the genus Terminalia (Combretaceae). *Inflammopharmacology.* <https://doi.org/10.1007/s10787-015-0246-z>
- Cock, I.E., 2015b. The medicinal properties and phytochemistry of plants of the genus Terminalia (Combretaceae). *Inflammopharmacology.* <https://doi.org/10.1007/s10787-015-0246-z>
- Farhan, M.M., Turkey, S.A., Nadhim, M.H., 2020. Anti-Inflammatory and gene expression studies of terminalia chebula extracts against interleukins and TNF. *Eur. J. Mol. Clin. Med.* 7, 229–237. <https://doi.org/10.31838/ejmcm.07.02.37>
- Gupta, P.C., 2012a. Biological and pharmacological properties of Terminalia chebula Retz. (haritaki)- an overview. *Int. J. Pharm. Pharm. Sci.*
- Gupta, P.C., 2012b. Biological and pharmacological properties of Terminalia chebula Retz. (haritaki)- an overview. *Int. J. Pharm. Pharm. Sci.*
- Hanahan, D., Weinberg, R.A., 2000a. The hallmarks of cancer. *Cell.* [https://doi.org/10.1016/S0092-8674\(00\)81683-9](https://doi.org/10.1016/S0092-8674(00)81683-9)
- Hanahan, D., Weinberg, R.A., 2000b. The hallmarks of cancer. *Cell.* [https://doi.org/10.1016/S0092-8674\(00\)81683-9](https://doi.org/10.1016/S0092-8674(00)81683-9)
- Henry, D.P., Ranjan, J., Murugan, R.K., Sivanantham, A., Alagumuthu, M., 2020. Exploration of anti-breast cancer effects of Terminalia chebula extract on DMBA-induced mammary carcinoma in Sprague Dawley rats. *Futur. J. Pharm. Sci.* 6, 108. <https://doi.org/10.1186/s43094-020-00124-z>
- Hsu, F.L., Yang, L.M., Chang, S.F., Wang, L.H., Hsu, C.Y., Liu, P.C., Lin, S.J., 2007. Biotransformation of gallic acid by Beauveria sulfurescens ATCC 7159. *Appl. Microbiol. Biotechnol.* 74, 659–666. <https://doi.org/10.1007/s00253-006-0692-z>
- Jeong, H.K., Lee, D., Kim, H.P., Baek, S.H., 2019. Structure analysis and antioxidant activities of an amylopectin-type polysaccharide isolated from dried fruits of Terminalia chebula. *Carbohydr. Polym.* 211, 100–108. <https://doi.org/10.1016/j.carbpol.2019.01.097>
- Jin, Y.Z., Li, G.H., Ahn, S.Y., Row, K.H., Kim, E.K., 2006. Extraction and purification of depigmenting agents from Chinese plants. *Chem. Res. Chinese Univ.* 22, 162–167. [https://doi.org/10.1016/S1005-9040\(06\)60067-6](https://doi.org/10.1016/S1005-9040(06)60067-6)
- Jokar, A., Masoomi, F., Sadeghpour, O., Nassiri-Toosi, M., Hamed, S., 2016a. Potential therapeutic applications for Terminalia chebula in Iranian traditional medicine. *J. Tradit. Chin. Med.* [https://doi.org/10.1016/s0254-6272\(16\)30035-8](https://doi.org/10.1016/s0254-6272(16)30035-8)
- Jokar, A., Masoomi, F., Sadeghpour, O., Nassiri-Toosi, M., Hamed, S., 2016b. Potential therapeutic applications for Terminalia chebula in Iranian traditional medicine. *J. Tradit. Chin. Med.* [https://doi.org/10.1016/s0254-6272\(16\)30035-8](https://doi.org/10.1016/s0254-6272(16)30035-8)
- Khan, K.H., Jain, S.K., 2009. Regular intake of Terminalia chebula can reduce the risk of getting typhoid fever. *Adv. Biotech.* 8, 10–15.
- Kher, M.N., Sheth, N.R., Bhatt, V.D., 2019. In Vitro Antibacterial Evaluation of Terminalia chebula as an Alternative of Antibiotics against Bovine Subclinical Mastitis. *Anim. Biotechnol.* 30, 151–158. <https://doi.org/10.1080/10495398.2018.1451752>
- Kim, H.G., Cho, J.H., Jeong, E.Y., Lim, J.H., Lee, S.H., Lee, H.S., 2006. Growth-inhibiting activity of active component isolated from Terminalia chebula fruits against intestinal bacteria. *J. Food Prot.* 69, 2205–2209. <https://doi.org/10.4315/0362-028X-69.9.2205>
- Kim, M.S., Lee, D.Y., Lee, J., Kim, H.W., Sung, S.H., Han, J.S., Jeon, W.K., 2018. Terminalia chebula extract prevents scopolamine-induced amnesia via cholinergic modulation and anti-oxidative effects in mice. *BMC Complement. Altern. Med.* 18, 136. <https://doi.org/10.1186/s12906-018-2212-y>
- Kumar, A., 2014. A review of traditional anticancer nano-medicine : triphala. *Pharma Innov. J.* 3, 60–66.
- Kumar, R., Arora, R., Agarwal, A., Gupta, Y.K., 2018a. Protective effect of Terminalia chebula against seizures, seizure-induced cognitive impairment and oxidative stress in experimental models of seizures in rats. *J. Ethnopharmacol.* 215, 124–131. <https://doi.org/10.1016/j.jep.2017.12.008>
- Kumar, R., Arora, R., Agarwal, A., Gupta, Y.K., 2018b. Protective effect of Terminalia chebula against seizures, seizure-induced cognitive impairment and oxidative stress in experimental models of seizures in rats. *J. Ethnopharmacol.* 215, 124–131.
- Lee, H.S., Jung, S.H., Yun, B.S., Lee, K.W., 2007. Isolation of chebulic acid from Terminalia chebula Retz. and its antioxidant effect in isolated rat hepatocytes. *Arch. Toxicol.* 81, 211–218. <https://doi.org/10.1007/s00204-006-0139-4>
- Lee, H.S., Koo, Y.C., Suh, H.J., Kim, K.Y., Lee, K.W., 2010. Preventive effects of chebulic acid isolated from Terminalia chebula on advanced glycation endproduct-induced endothelial cell dysfunction. *J. Ethnopharmacol.* 131, 567–574. <https://doi.org/10.1016/j.jep.2010.07.039>
- Lee, J.H., Jung, J.S., Kim, S.H., 2020. Dyeing and antibacterial properties of chemically recycled PET thermal-bonded nonwovens dyed with Terminalia chebula dye. *Polymers (Basel).* 12, 1675. <https://doi.org/10.3390/POLYM12081675>
- Mandava, K., Batchu, U.R., Kakulavaram, S., Repally, S., Chennuri, I., Bedarakota, S., Sunkara, N., 2019. Design and study of anticaries effect of different medicinal plants against S.mutans glucosyltransferase. *BMC Complement. Altern. Med.* 19, 197. <https://doi.org/10.1186/s12906-019-2608-3>
- Mandeville, A., Cock, I.E., 2018. Terminalia chebula Retz. Fruit Extracts Inhibit Bacterial Triggers of Some Autoimmune Diseases and Potentiate the Activity of Tetracycline. *Indian J. Microbiol.* 58, 496–506. <https://doi.org/10.1007/s12088-018-0754-9>

- Manipal, S., Fathima, L., Hussain, S.T., Venkat, R., 2019. Efficacy of anti-bacterial and anti-fungal action on four medicinal plants extract the a.Arabica, t.chebula, a.indica, and v.vinifera against streptococcus mutans and candida albicans-an in-vitro study. *Int. J. Res. Pharm. Sci.* 10, 3121–3126. <https://doi.org/10.26452/ijrps.v10i4.1608>
- Muhammad, S., 2012a. The morphology, extractions, chemical constituents and uses of Terminalia chebula: A review. *J. Med. Plants Res.* <https://doi.org/10.5897/jmpr11.1339>
- Muhammad, S., 2012b. The morphology, extractions, chemical constituents and uses of Terminalia chebula: A review. *J. Med. Plants Res.* <https://doi.org/10.5897/jmpr11.1339>
- Nierenstein, M., Potter, J., 1945. The distribution of myrobalanin. *Biochem. J.* 39, 390–392. <https://doi.org/10.1042/bj0390390>
- Patel, S., Patil, S., Parvatikar, P., 2020. Analysis of the phytochemical profile of Terminalia chebula fruit extract with antioxidative and anti-inflammatory activity on breast cancer cell line. *BLDE Univ. J. Heal. Sci.* 5, 29. <https://doi.org/10.4103/2468-838x.303768>
- Petrovska, B.B., 2012. Historical review of medicinal plants' usage. *Pharmacogn. Rev.* 6, 1–5. <https://doi.org/10.4103/0973-7847.95849>
- Pingali, U., Sukumaran, D., Nutralapati, C., 2020. Effect of an aqueous extract of Terminalia chebula on endothelial dysfunction, systemic inflammation, and lipid profile in type 2 diabetes mellitus: A randomized double-blind, placebo-controlled clinical study. *Phyther. Res.* 34, 3226–3235. <https://doi.org/10.1002/ptr.6771>
- Priscilla, D., 2013. Jasmine. Assessing the potential of the ethanolic extracts of Terminalia chebula against breast cancer. *World J. Pharm. Pharm. Sci.* 2, 5702–5708.
- Rahimi, R., Abdollahi, M., 2013a. Evidence-based review of medicinal plants used for the treatment of hemorrhoids. *Int. J. Pharmacol.* 9, 1–11. <https://doi.org/10.3923/ijp.2013.1.11>
- Rahimi, R., Abdollahi, M., 2013b. Evidence-based review of medicinal plants used for the treatment of hemorrhoids. *Int. J. Pharmacol.* 9, 1–11.
- Rathinamoorthy, R., Thilagavathi, G., 2014a. Terminalia chebula - Review on pharmacological and biochemical studies. *Int. J. PharmTech Res.* 6, 97–116.
- Rathinamoorthy, R., Thilagavathi, G., 2014b. Terminalia chebula - Review on pharmacological and biochemical studies. *Int. J. PharmTech Res.*
- Sabir, S.M., Abbas, S.R., Shahida, S., Khan, M.F., 2020. In-Vitro antioxidant, anti-lipid peroxidative activities and In-Silico study of Terminalia chebula bioactive compounds. *Clin. Phytoscience* 6, 83. <https://doi.org/10.1186/s40816-020-00233-5>
- Safavi, M., Shams-Ardakani, M.R., Sadat, Seyedbagheri, M., Foroumadi, A., 2016. The Efficacy of Iranian Traditional and Folk Medicinal Plants for Some Gastrointestinal Disorders. *Tradit. Integr. Med.* 3–17.
- Saleem, A., Husheem, M., Härkönen, P., Pihlaja, K., 2002. Inhibition of cancer cell growth by crude extract and the phenolics of Terminalia chebula retz. fruit. *J. Ethnopharmacol.* 81, 327–336. [https://doi.org/10.1016/S0378-8741\(02\)00099-5](https://doi.org/10.1016/S0378-8741(02)00099-5)
- Salimikia, I., Bahmani, M., Abbaszadeh, S., Rafieian-Kopaei, M., Nazer, M.R., 2020. Campylobacter: A Review of New Promising Remedies with Medicinal Plants and Natural Antioxidants. *Mini-Reviews Med. Chem.* 20, 1462–1474. <https://doi.org/10.2174/1389557520666200117141641>
- Samani, Z.N., Kopaei, M.R., 2018. Effective Medicinal Plants in Treating Hepatitis B. *Int. J. Pharm. Sci. Res.* 9.
- Sarker, S., Seraj, S., Sattar, M.M., Haq, W.M., Chowdhury, M.H., Ahmad, I., Jahan, R., Jamal, F., Rahmatullah, M., 2011a. Medicinal plants used by folk medicinal practitioners of six villages in Thakurgaon District, Bangladesh. *Am. J. Sustain. Agric.*
- Sarker, S., Seraj, S., Sattar, M.M., Haq, W.M., Chowdhury, M.H., Ahmad, I., Jahan, R., Jamal, F., Rahmatullah, M., 2011b. Medicinal plants used by folk medicinal practitioners of six villages in Thakurgaon District, Bangladesh. *Am. J. Sustain. Agric.* 5, 332–343.
- Sars-cov-, C.S.V., Hussain, I., Amjad, N., Khan, B.A., Awan, S.B., Hussain, N., 2020. Broad Antimicrobial Effects of Terminalia chebula : A Useful Candidate for its Broad Antimicrobial Effects of Terminalia chebula : A Useful Candidate for its Clinical Studies Verses SARS-CoV-2.
- Sawant, R., Binorkar, S. V., Bhojar, M., Gangasagre, N.S., 2013. Phyto-constituents bio-efficacy and phytopharmacological activities of terminalia chebula-A review. *Int J Ayu Alt Med* 1, 1–11.
- Shendge, A.K., Sarkar, R., Mandal, N., 2020. Potent anti-inflammatory Terminalia chebula fruit showed in vitro anticancer activity on lung and breast carcinoma cells through the regulation of Bax/Bcl-2 and caspase-cascade pathways. *J. Food Biochem.* 44, e13521. <https://doi.org/10.1111/jfbc.13521>
- Singamaneni, V., Dokuparthi, S.K., Banerjee, N., Kumar, A., Chakrabarti, T., 2019. Phytochemical Investigation and Antimutagenic Potential of Ethanolic Extracts of Emblica officinalis, Terminalia chebula and Terminalia bellirica. *Nat. Prod. J.* 10, 488–494. <https://doi.org/10.2174/2210315509666190618101140>
- Singh, A., Srivastav, R., Pandey, A., 2017. Protective Role of Terminalia chebula in Streptozotocin-induced Diabetic Mice for Wound Healing Activity. *Br. J. Med. Med. Res.* 22, 1–8. <https://doi.org/10.9734/bjmmr/2017/33137>
- Singh, S., Farhan Asad, S., Ahmad, A., Khan, N.U., Hadi, S.M., 2001. Oxidative DNA damage by capsaicin and dihydrocapsaicin in the presence of Cu(II). *Cancer Lett.* 169, 139–146. [https://doi.org/10.1016/S0304-3835\(01\)00544-4](https://doi.org/10.1016/S0304-3835(01)00544-4)
- Sivamaruthi, B.S., Ramkumar, V.S., Archunan, G., Chaiyasut, C., Suganthi, N., 2019. Biogenic synthesis of silver palladium bimetallic nanoparticles from fruit extract of Terminalia chebula – In vitro evaluation of anticancer and antimicrobial activity. *J. Drug Deliv. Sci. Technol.* 51, 139–151. <https://doi.org/10.1016/j.jddst.2019.02.024>
- Sotoudeh, R., Hadjzadeh, M.-A.-R., Gholamnezhad, Z., Aghaei, A., 2019a. The anti-diabetic and antioxidant effects of a combination of Commiphora mukul, Commiphora myrrha and Terminalia chebula in diabetic rats. *Avicenna J. phytomedicine* 9, 454–464. <https://doi.org/10.22038/ajp.2019.12721>
- Sotoudeh, R., Hadjzadeh, M.-A.-R., Gholamnezhad, Z., Aghaei, A., 2019b. The anti-diabetic and antioxidant effects of a combination of Commiphora mukul, Commiphora myrrha and Terminalia chebula in diabetic rats. *Avicenna J. phytomedicine* 9, 454–464.
- Suchalatha, S., Shyamala Devi, C.S., 2004. Protective effect of Terminalia chebula against experimental myocardial injury induced by isoproterenol. *Indian J. Exp. Biol.* 42, 174–178.
- Sun, G.L., Wang, D., 2020. Gallic acid from Terminalia chebula inhibited the growth of esophageal carcinoma cells by suppressing the Hippo signal pathway. *Iran. J. Basic Med. Sci.* 23, 1401–1408. <https://doi.org/10.22038/ijbms.2020.42283.9982>
- Tewari, D., Mocan, A., Parvanov, E.D., Sah, A.N., Nabavi, S.M., Huminiecki, L., Ma, Z.F., Lee, Y.Y., Horbanczuk, J.O., Atanasov, A.G., 2017. Corrigendum to: Ethnopharmacological Approaches for Therapy of Jaundice: Part II. Highly Used Plant Species from Acanthaceae, Euphorbiaceae, Asteraceae, Combretaceae, and Fabaceae Families [Front. Pharmacol. 8, (2017), (519)] doi: 10.3389/fphar.2017.00519. *Front. Pharmacol.* 8, 519. <https://doi.org/10.3389/fphar.2017.00519>
- Upadhyay, A., Aghari, P., Singh, D.K., 2014. A review on the pharmacological aspects of Terminalia chebula. *Int. J. Pharmacol.* 10, 289–298. <https://doi.org/10.3923/ijp.2014.289.298>
- Wang, M., Yang, L., Ji, M., Zhao, P., Sun, P., Bai, R., Tian, Y., Su, L., Li, C., 2015. Aqueous extract of Terminalia chebula induces apoptosis in lung cancer cells via a mechanism involving mitochondria-mediated pathways. *Brazilian Arch. Biol. Technol.* 58, 208–215. <https://doi.org/10.1590/S1516-8913201400202>
- Zhang, X.R., Kaunda, J.S., Zhu, H.T., Wang, D., Yang, C.R., Zhang, Y.J., 2019. The Genus Terminalia (Combretaceae): An Ethnopharmacological, Phytochemical and Pharmacological Review. *Nat. Products Bioprospect.* 9, 357–392. <https://doi.org/10.1007/s13659-019-00222-3>

Table 1: Various pharmacological properties of *T. chebula*

Property	Application	Reference
Neuroprotective	Useable in seizures, seizure-induced cognitive impairment, and oxidative stress	(Kumar et al., 2018b)
Hepatoprotective	Having a decrease in cytotoxicity of tert-butyl hydroperoxide (t-BHP)-induced cell in confined rodent hepatocyte experimental analysis.	(Suchalatha and Shyamala Devi, 2004)
Cardioprotective	Minimizing the risk factors of cardiovascular compared to placebo in type 2 diabetes patients	(Singh et al., 2017)
Antidiabetic and retinoprotective	Having antidiabetic and wound healing activity effectively stimulate the secretion of insulin	(Sotoudeh et al., 2019b)
Hypolipidemic/ Hypocholesterolemic	Has an essential decrease in total cholesterol and triglycerides	(Rathinamoorthy and Thilagavathi, 2014b)
Antifungal	Effective against five pathogenic fungi such as; <i>Alternaria brassicicola</i> , <i>Aspergillus flavus</i> , <i>A. alternate</i> , <i>A. niger</i> , and <i>Helminthosporium tetramera</i>	(Bag et al., 2013b; Gupta, 2012b)
Antiviral	Treat pandemic swine Flu, had a major role in the inhibition of HIV-1 integrase	(Gupta, 2012b)
Antibacterial	Highly effective against <i>Salmonella typhi</i> SSFP 4S, <i>Staphylococcus epidermidis</i> MTCC 3615, <i>S. aureus</i> ATCC 25923, <i>Bacillus subtilis</i> MTCC 441 and <i>Pseudomonas aeruginosa</i> ATCC 27853	(Gupta, 2012b)
Antimicrobial	Antimicrobial activity against <i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Escherichia coli</i> , <i>Staphylococcus flexinaria</i> , and <i>Pseudomonas aeruginosa</i> by the disk diffusion method:	3
Anticaries	Has a powerful effect on dental caries	1
Antimutagenic and antiproliferative	Including promising antimutagenic and anticarcinogenic phytochemicals, Cancer cell viability reduction, Cell proliferation inhibition, and cell death induction in a dose-dependent manner	(Gupta, 2012b)
Antioxidant	Protect the cellular organelles from the radiation actuated harm, a strong antioxidant and free-radical scavenger	(Gupta, 2012b; Rathinamoorthy and Thilagavathi, 2014b)
Antiarthritic	As a disease-modifying agent in the treatment of rheumatoid arthritis	(Gupta, 2012b)
Antifertility	Having the adverse effects on the reproductive system	(Gupta, 2012b)
Immunomodulatory	Increasing the concentrations of antioxidant enzymes, GSH, and proliferation of T and B cells as immune cells	(Rathinamoorthy and Thilagavathi, 2014b)
Anaphylactic	Reduces the serum histamine level showing a strong anti-anaphylactic activity	(Babita et al., 2011b)
Wound healing	Stimulate fibroblasts; therefore, the synthesis of glycosaminoglycans and collagen deposition increase and it accelerates wound healing significantly	(Mandava et al., 2019)
Anticancer	Is a suitable candidate for further investigation in the treatment and cancer prevention (lung, breast, prostate, and human pancreatic)	(Hanahan and Weinberg, 2000b; Priscilla, 2013; Wang et al., 2015)
Alzheimer	Having anti cholinesterase properties and preventing the progression of Alzheimer	(Rahimi and Abdollahi, 2013b)
Hemorrhoid	Positive effects in different hemorrhoids' variables (pain, constipation, hemorrhoids mass size, and hemorrhoids hemorrhage)	(Muhammad, 2012a)