

PHARMACOLOGICAL AND THERAPEUTIC POTENTIAL OF *TERMINALIA
CHEBULA* RETZIUS – A CRITICAL REVIEW

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ABSTRACT

The use of plants and plant products as medicines could be traced from the beginning of human civilization. Rigveda written between 4500 - 1600 has the earliest mention of medicinal use of plants in Hindu culture. A large proportion of the world population, especially in the developing countries relies mainly on the herbs as a cheap resource of medicinal drug. *Terminalia chebula* Retz. (TC) belongs to the family Combretaceae is one of the most important medicinal plants used in all streams of traditional medicines. TC has a wide range of medicinal properties and is an important ingredient of *Triphala*, a versatile formulation used effectively in various diseases. In Ayurveda TC is a key drug used for rejuvenation with mild laxative effect. TC possesses antioxidant, hepatoprotective, antibacterial, antiviral, antidermatophytic, antimutagenic, Ach inhibition, hypoglycaemic, hypolipidemic, antiulcer activities. Besides it has least adverse effect with no toxicity. Present article is an endeavour to review pharmacological and therapeutic potential of various extracts and isolated phytoconstituents of *Terminalia chebula* to enhance our knowledge.

Keywords: *Terminalia chebula* Retz, human civilization, isolated phytoconstituents, hepatoprotective.

INTRODUCTION

Terminalia chebula Retzius (*T. chebula*), commonly known as Chebulic myroblans in English and *Harad* in Hindi. As it eradicates all illnesses its nomenclature in Sanskrit is *Haritaki*.^[1] The genus *Terminalia* is the second largest genus in the family Combretaceae which is found in India, Southeast Asia, Africa and Egypt and other subtropical and tropical regions of the world up to an altitude of 1500m.^[2] The family Combretaceae is comprised of 20 genera and about 475 species.^[3] Of these, about 200 belong to the genus *Terminalia*, making it the second largest genus of the family after *Combretum*.^[4] Species of *Terminalia* vary greatly in morphology, anatomy and karyotype evidence.^[5,6]

It has been used extensively in Ayurved, Siddha, Unani, Tibetan, Thai medical practice. Many studies demonstrating the evidence of its versatile pharmacological activities have been reported till date.

Present article is an endeavour to review the evidence of therapeutic uses of *Terminalia chebula* in nut shell

METHOD

The data available in various databases has been collected in the period of August 2016 to November 2016 which was further critically reviewed. The compiled information has been systematically studied and categorized in different headings and commented.

RESULTS

Types of *Terminalia Chebula*

In **Ayurvedic** literature *Terminalia Chebula* has been mentioned in *Brihatrayee* viz. Charak, Susruta and Vagbhatt main classics but its varieties have first time been described by *Nighantus*. These varieties have diverse in habitat, identification criteria, therapeutic uses as mentioned in following table.^[7]

Sr. No.	Types	Habitat	Identification from Fruit shape	Therapeutic uses
1.	Vijaya	Vindhya	Gourd shaped	All disease, purificationary measures & preparation of malt
2.	Rohini	Sindh	Round shaped	Internal use & Wounds
3.	Putana	Vindhya	Proportionately bigger stone	External application
4.	Amrita	Champa(Madhyapradesh)	Fleshy	Purgative

5.	Abhaya	Champa(Madhyapradesh)	Has 5 ridges	Eye disease
6.	Jivanti	Saurashtra	Golden in colour	Oleation theory
7.	Chetaki	Himalaya	Has 3 ridges	Purgative

In **Tibetan** health science literature also *Terminalia Chebula* has been classified as per the seven types on the basis of characteristics, therapeutic uses eTC.^[8]

Types: - 1] *Rnam par rgyal ba (Vijaya)*, 2] *Bum gyi mgrin*, 3] *Gso byed*, 4] *Bdud rtsi* (Amrita), 5] *Jigsmed(Abhaya)*, 6] *Phel byed*, 7] *Skam po*.

Identification:- *Rnam par rgyal ba (Vijaya)* is characterized by closed lips and a fine neck, *Gser mdog (Knaka Varna)* is of golden color, round shaped, and contains five or eight ridges (Wrinkles). *Sa Chen (Mamsala)* is fleshy. *Bigs byed (Vindkya)* is black and stoneless, and *Snung (Suksma)* has many wrinkles.

Therapeutic Uses: -In Tibetan literature the therapeutic uses are mentioned as per part of plant. Roots for bone, Stem for muscles, Bark for skin, Branches for vascular system, leaves for visceral and fruit for vital organs related diseases.

In contemporary science Brandis has identified two principal varieties as Ordinary variety and Tomentose form (Possibly *T. gangetica*).^[9] Botanically two more species have been found which are *Terminalia citrina* Roxb found in Assam and Bengal and *T. pallida* in South India.^[10]

Currently three types of *Terminalia chebula* (TC) are available. 1) Large, 2) Small & 3) Yellow. The large variety is fully matured whereas small is an immature fruit before development of seed and if the fruits are collected after complete development of seed but not of the fruit it is a yellow variety of TC.^[11]

Analytical studies related to *Terminalia Chebula*

Several analytical studies have been reported the methods of detection and isolation of markers of TC. A high performance liquid chromatography method coupled with diode array detection was developed by Anil Mahajan *et al.* to determine simultaneously seven different marker from *Terminalia chebula* with excellent resolution, precision and recovery. These markers are gallic acid, methyl gallate, ethyl gallate, ellagic acid, chebulagic acid, chebulinic acid, penta-*O*-galloyl- β -D-glucose.^[12] Another studies have reported isolation of fourteen hydrolyzable tannins from TC.^[13,14] Further Lih-Jeng Juang, Shuenn-Jyi Sheu *et al.* by optimizing the pH values, buffer composition and buffer concentration of the eluent or carrier, the tannins and related compounds successfully determined from *T. chebula* by HPLC within 80 min and by MEKC within 40 min.^[15] Isolation of 2,4-chebulyl- β -D-glucopyranose a new natural product having anticancer activity by chromatographic fractionation of the extract of TC has been reported.^[16] Besides a new triterpene, 2 α -

hydroxymicromeric acid and two known compounds, maslinic acid and 2 α -hydroxyursolic acid have been isolated from *Terminalia chebula* leaves.^[17]

The tannin content in TC is found to be 30-32 %.1,2 and are divided into hydrolyzable tannins and flavonoid-derived condensed tannins. The hydrolyzable tannins can be further categorized into gallotannins and ellagitannins. which can be categorized into four groups: 1) phenolcarboxylic acids eg. gallic acid, ellagic acid and chebulic acid; 2) gallotannins eg. 1,6-di-*O*-galloyl- β -D-glucose, 3,4,6-tri-*O*-galloyl- β -D-glucose and 1,2,3,4,6-penta-*O*-galloyl- β -D-glucose; 3) ellagitannins eg punicalagin, casuarinin, corilagin and terchebulin; 4) others eg. chebulanin, neochebulinic acid, chebulagic acid and chebulinic acid. Using spectroscopic methods and chemical evidence the structures can be explained.^[18,19] An analytical study demonstrated that the water extract of TC afforded the greatest yield and total phenolic and tannin content whereas methanol extract yielded the greatest total triterpenoid content.^[20] Moreover the fruit of TC could be an important source of dietary supplement. The edible fruit tissue of the TC contained 10.3 and 14.5 times more vitamin C and protein, respectively when compared with commercial apples. 100 g of the raw fruit fulfils the minimum Recommended Dietary Allowance (RDA) for Se, K, Mn, Fe and Cu. Besides TC fruit contains aspartic acid, glutamic acid, arginine, proline and lysine 39.6, 8.6, 6.7, 6.4 and 5.0%, respectively, of the total amino acids.^[21]

Traditional therapeutic uses of *Terminalia Chebula*

In Ayurved the fruit of TC (*Haritaki*) is used both externally as well as internally for medicinal purposes. Externally, the paste of fruit is used effectively on the mouth ulcers & piles. It also hastens the healing of chronic wounds and ulcers. A fine powder of *Haritaki* is used as a tooth powder to strengthen the gums. Specific vehicle (Anupan) has been quoted in classics to achieve rejuvenating effect of *Terminalia chebula* in accordance to the season. In *Varsa ritu* (July- August), it should be taken with rock salt, in *Sharad ritu* (September-October) with sugar, in *Hemanta ritu* (November- December) with sunthi, in *Shishira ritu* (January-February) with pippali, in *Vasanta ritu* (March-April) with honey and in *Grishma ritu* (May-June) with jiggery.^[22] Regular consumption of *Haritaki* powder fried in ghee along with a meal having adequate ghee, promotes longevity and boosts energy. *Vagbhata* subscribed *Haritaki* for the wide range of diseases like common gastrointestinal ailments, tumours, ascites, piles, enlargement of liver and spleen, worms, colitis. Classics have described the different therapeutic uses of *Haritaki* as per the method of consumption of the fruit. If the bark of *Haritaki* is consumed by chewing it improves digestion whereas if rubbed on stone and then consumed it will show

purgative effect. But if it is consumed after steaming it causes constipation and intake of fried *Haritaki* leads to balance of all the humours of the body. *Haritaki* if consumed in meals enhances intellect, physical strength and power of senses, eliminates bodily waste material. The combination of different drugs affect the effect of *Haritaki* like if consumed with Rock salt (*Siandhav*), sugar and (*ghrita*) balances the vitiation of *Kapha*, *Pitta* and *Vata dosha* respectively whereas if consumed with jiggery will cure all the illnesses of body.^[23] It is most useful in all the group of disorders resulted from excess in growth of body tissues (*Santarpanjanya vikar*).^[24] Moreover it is one of the ingredients of *Triphala*, a versatile preparation used in Ayurveda, with combination of other two herbs *Terminalia bellerica* & *Emblica officinalis*.

Classics have also quoted few precautionary measures for the prescription of *Haritaki*. TC should be carefully used by lean individuals, in severe weakness, excessively dry condition of body, emaciated person due to fast, mental depression, pitta conditions and in pregnancy.

Pharmacological activities

Critical literature review disclosed that *Terminalia chebula* possess wide range of pharmacological activities. Besides a toxicity study revealed no mortality in mice in the doses used up to 2gm/kg ensures the safety of TC for therapeutic purpose.^[25] Numerous experimental and clinical studies reported for its evidence have been compiled as follows.

Antioxidant activity

TC is a potent and cheap natural source of antioxidant. Many reports have confirmed the antioxidant activity of TC which have been compiled as follows.

In an experimental study 6 extracts and 4 pure compounds of *T. chebula* demonstrated antioxidant activity at different magnitudes of potency. The antioxidant activity of them was noted from different pathways and was suggested to be specific in some term.^[26] In another experiment *t*-BHP was employed to induce acute oxidative stress in rat hepatocytes & in Vitro. Two distinctive pathways are involved in the metabolism of *t*-BHP in hepatocytes. The first employs the initiation of lipid peroxidation^[27] while the second results in NADPH oxidation. The *in vitro* experiment showed that TC extract could quench DPPH free radicals and reflected in increased cell viability in rat hepatocytes exhibiting antioxidative property. The significant effectiveness of pretreatment and subsequent removal of the TC extract prior to *t*-BHP treatment indicated that TC exerted its protective activity intracellularly, rather than extracellularly by reacting with *t*-BHP in the culture medium.^[28] Further the phenolics of TC prevent nickel chloride-induced oxidative stress by decreasing LPO, restoring the activity of glutathione- S-transferase,

glutathione reductase, and glutathione peroxidase.^[29] The aqueous extract of *Terminalia chebula* showed potential antioxidant activity against γ -radiation-induced lipid peroxidation in rat liver microsomes and damage to superoxide dismutase enzyme in rat liver mitochondria. In the same study the antimutagenic activity of the TC extract was exhibited with the inhibition of γ -radiation-induced strand breaks formation in plasmid pBR322 DNA. The extract also inhibits xanthine/xanthine oxidase activity and is an excellent scavenger of DPPH radicals^[30] An experiment revealed that the methanol extract of TC fruit found to be better hydroxyl and superoxide radical scavengers than standard mannitol & quercetin when compared with *T. bellerica* and *E. officinalis*.^[31] Also *T. chebula* is proved to be a powerful antioxidant than butylated hydroxy toluene, butylated hydroxy anisole^[32] and α -tocopherol.^[33] MinKyun Na, KiHwan Bae *et al* claimed that *T. chebula* extract may have inhibitory effect on the age-dependent shortening of the telomere resulted in inhibition of oxidative stress.^[34] The preventive effects of aqueous extract of *Terminalia chebula* on oxidative and antioxidative status in liver and kidney of aged rats compared to young albino rats has been evaluated. The results of the study based on various oxidative stress marker demonstrated that aqueous extract of TC inhibits the development of age-induced damages by providing protection against oxidative stress.^[35] The methanol, aqueous and ethanol extract showed good antioxidant activity based on the horseradish peroxidase-luminol-hydrogen peroxide (H_2O_2) assay, cupric sulfate-Phen-Vc- H_2O_2 & luminol- H_2O_2 assays and Pyrogallol-luminol assay respectively.^[21] The 70% methanolic extract of TC showed reducing power and iron chelating activity. Eventually it can reduce the toxic level of iron in iron overloaded mice and hence protect liver from oxidative stress and fibrosis.^[36] The methanolic extract of *Terminalia chebula*, *Terminalia bellerica*, *Emblica officinalis* and their combination 'Triphala' were found to inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals in vitro.^[37] Similarly T. Vani, M. Rajani *et al* further confirms these findings.^[38]

Hepatoprotective activity

Few research studies have been claimed the hepatoprotective potential of *Terminalia chebula* as follows. A mixture of chebolic acid and its minor isomer, neochebolic acid isolated from TC exhibited the protection of rat hepatocytes against toxicity induced by *tert*-butyl hydroperoxide (*t*-BHP)- on the basis of cell cytotoxicity, intracellular reactive oxygen species level, and the ratio of GSSH to the over total GSH.^[39] In another experimental study the hepato- reno protective effect of silymarin and *Terminalia chebula* against acetaminophen induced toxicity in rats was evaluated. The results revealed that post treatment with silymarin and *T. chebula* has significantly reversed the alterations of hepato- reno markers and offered better protection.^[40] The aqueous extract of *Triphala*, Ayurvedic formulation of which *Terminalia chebula* is one of the ingredient

have showed significant inhibition of acute liver toxicity induced by acetaminophen in mice. The researcher claimed that the effect may be due to its antioxidant & TNF- α lowering properties of extract.^[41] Another herbal formulation HP-1 containing *Terminalia chebula* along with other herbs viz. *Phyllanthus niruri*, *Terminalia bellerica*, *Phyllanthus emblica* and *Tinospora cordifolia* has been tested for hepatoprotective activity against carbon tetrachloride (CCl₄) induced toxicity. Silymarin and antioxidants viz. ascorbic acid, β -carotene and tocopherol were used for comparison. The study showed that HP-1 is a potential hepatoprotective. TC restores the anti-oxidative enzymes and suppressed the formation of the superoxide anion radical exhibiting its antioxidant activity as well.^[42]

Antibacterial Activity

T. chebula dry fruit possesses a potential broad spectrum of antimicrobial activity against different types of pathogens. The *T. chebula* fruit extract was highly effective against *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus subtilis* and *Pseudomonas aeruginosa*.^[43] Besides aqueous extracts of TC contain a heat stable agents which showed significant antibacterial activity against *Helicobacter pylori* and had a minimum inhibitory concentration and minimum bacteriocidal concentration of 125 and 150 mg/l, respectively.^[44] The gallic acid and ethyl ester, isolated from ethyl alcohol extract of fruits of *T. chebula* have been proved for antibacterial activity against methicillin-resistant *Staphylococcus*.^[45] The methanolic leaf extract of *T. chebula* considered to be as equally potent as the most effective antibiotics, such as ciprofloxacin, gentamycin, kanamycin, ofloxacin and cephalixin when compared to aqueous extract.^[46]

Antiviral Activity

Anti-cytomegalovirus (CMV) activity in vitro and in vivo was noted by aqueous extract of *Terminalia chebula* in immunosuppressed mice.^[47] A multicomponent herbal formula Ledretan-96 containing TC as one of the ingredient showed protective activity against cytopathic effects caused by influenza A virus on epithelial tissue culture cell line. It has been noted that out of the 23 components tested, only one *Terminalia chebula*, showed a significant protective effect. In addition, the complete formula maintained antiviral activity at a higher therapeutic index than the *Terminalia chebula* extract alone.^[48]

Anti-dermatophytic effect

An aqueous extract of *Terminalia chebula* showed inhibitory effects on three dermatophytes (*Trichophyton* spp.) and three yeasts (*Candida* spp.). An aqueous extract of *T. chebula* showed pronounced inhibitory effects than ethanol extracts indicating the tannins are the plausible candidates for the anti-dermatophytic effects of *T. chebula*.^[49]

Anticancer activity

A 70% methanol extract of *Terminalia chebula* fruit, was found to be effective on growth in several malignant cell lines including a human (MCF-7) and mouse (S115) breast cancer cell line, a human osteosarcoma cell line (HOS-1), a human prostate cancer cell line (PC-3) and a non-tumorigenic, immortalized human prostate cell line (PNT1A). In all cell lines studied, the extract decreased cell viability, inhibited cell proliferation, and induced cell death in a dose dependent manner.^[19] Chebulagic acid fractionated by ethanolic extract of the fruits of *Terminalia chebula* is found to be a COX-2 and 5-LOX dual inhibitor. COX and 5-LOX are the key enzymes involved in inflammation and carcinogenesis. It also showed anti-proliferative activity against HCT-15, COLO-205, MDA-MB-231, DU-145 and K562 cell lines and induces apoptosis in COLO-205 cells.^[50] Both the above said studies underlines the anticancer attribute of TC.

Antimutagenic Activity

The tannin fraction of TC extract reported to be highly significant against S9-dependent mutagen, 2AF. However, *chebula* tannins were partly effective against NPD mutagen but not at all effective against mutagen 4NQNO.^[51] An aqueous extract of TC reduced NPD as well as 2-AF induced revertant significantly in strains of *Salmonella typhimurium*. The experiment also noted that autoclaving of the aqueous extract reduces the insignificant inhibitory effect.^[52] The chloroform and acetone extracts of *Triphala* showed inhibition of mutagenicity induced by direct and S9-dependent mutagens in TA98 and TA100 tester strains of *Salmonella typhimurium*.^[53]

Acetylcholine inhibition activity

Acetylcholinesterase inhibitors have been extensively used for the symptomatic treatment of Alzheimer's disease. The phytochemical isolated from TC named 1,2,3,4,6-penta-*O*-galloyl- β -D-glucose showed significant acetylcholinesterase and butyrylcholinesterase inhibitory effects comparable with Tacrine.^[54] The aqueous extract of *T. chebula* showed highest efficacy to inhibit acetylcholinesterase when tested in comparison with other herbs viz. *Terminalia bellerica*, and *Emblca officinalis* and *Triphala*.^[55]

Hypolipidemic activity

In atherogenic diet induced hyperlipidaemic model, the rats receiving treatment with TC showed significant reduction in total cholesterol, triglycerides, total protein and elevation of high density lipoprotein cholesterol showing significant hypolipidemic activity.^[56] In an experimental study including rabbits *Terminalia chebula* showed significantly lowers cholesterolaemia and cholesterol content of aorta and liver. No increased excretion of cholesterol is found during study hence the action might be mediated through enzymic degradation of cholesterol in the liver or elsewhere.^[57]

Hypoglycemic activity

The ethanolic extract of TC fruit has potential hypoglycemic action in STZ induced diabetic rats. The hypoglycemic effect was found to be more effective than standard therapeutic drug Glibenclamide.^[58] Further in another short term and long term study the chloroform extract of *T. chebula* produced dose-dependent reduction in blood glucose of diabetic rats comparable with standard drug, Glibenclamide. The results indicate a prolonged action of TC in reduction of blood glucose probably mediated through enhanced secretion of insulin from the β -cells of Langerhans or through extra pancreatic mechanism. Significant reno-protective activity is also observed in *T. chebula* treated rats.^[59] In another animal study methanolic extract of *Terminalia chebula*, *Terminalia belerica*, *Embllica officinalis* and their combination 'Triphala' were found to reduce the blood sugar level significantly within 4 h comparable to standard control.^[60]

Antiulcer Activity

The hydro-alcoholic extract of *Terminalia chebula* showed significant reduction in lesion index, total affected area and percentage of lesion in the aspirin, ethanol and cold restraint stress-induced ulcer models. Similarly, the extract increased mucus production in aspirin and ethanol-induced ulcer models. Also *T. chebula* extract showed antisecretory activity in pylorus ligated model, which lead to a reduction in the gastric juice volume, free acidity, total acidity, and significantly increased gastric pH.^[61]

Wound healing activity

The effects of topical administration of an alcohol extract of the leaves of *Terminalia chebula* found to be effective with improved rates of contraction and decreased period of epithelialization. Biochemical studies revealed a significant increase in total protein, DNA and collagen contents in the granulation tissues of treated wounds. The tensile strength of tissues from extract treated incision wounds increased by about 40%. In addition, *T. chebula* possessed antimicrobial activity against *Staphylococcus aureus* and *Klebsiella* providing antibacterial protection.^[62]

Anticaries agent

The mouth rinsing with aqueous extract of *Terminalia chebula* strongly inhibited the growth, sucrose induced adherence and glucan induced aggregation of *Streptococcus mutans* in the saliva samples up to 3 h after rinsing and glycolysis of salivary bacteria for up to 90 min post rinsing as well.^[63]

Myocardial protection

Myocardial infarction, the most dreaded sequel among ischemic heart diseases, is invariably followed by several biochemical alterations. *T. chebula* extract pretreatment was found to ameliorate the effect of isoproterenol on myocardial damage and retained the activities of the

altered diagnostic marker enzymes and hence display cardioprotective effect.^[64]

Antinociceptive Activity

The ethanol extract TC is exhibited antinociceptive effect claimed to be contributed to triterpenoids present in TC and may be partially related to the cholecystokinin receptor pathways.^[26]

Antianaphylaxis Activity

The aqueous fraction of *Terminalia chebula* showed inhibition of 48/80-induced anaphylaxis in local as well as systemic level. The effect is pronounced in pre-treatment when compared with post induction of anaphylactogen. The serum histamine release levels from rat peritoneal mast cells were reduced in a dose-dependent manner.^[65]

Effect of TC on NF- κ B

Nuclear factor kappa-light chain-enhancer of activated B cells (NF- κ B) is responsible for the expression of numerous genes involved in cell survival, proliferation, angiogenesis, inflammation, invasion and metastasis, among other processes. Treatment with TC extract inhibited NF- κ B activity and protected against I κ B α degradation and strongly suppressed I κ B α phosphorylation in Jurkat-NF- κ B-RE-*bla* cells. In addition, the TC extract downregulated certain NF- κ B regulated genes, including *IL-8* and *MCP-1*, in Jurkat-NF- κ B-RE-*bla* cells. Moreover, gallic acid was identified from the TC extract demonstrating its ability to inhibit NF- κ B activity in Jurkat-NF- κ B-RE-*bla* cells.^[66]

Effect of TC on Bronchial Asthma

An Ayurvedic clinical study has been reported evaluating two Ayurvedic formulations on bronchial asthma (*Tamak shvasa*) viz. *Shvasaharaleha* and *Vasaharitakiavaleha*. The results of the study indicate that the *Vasa Haritaki avaleha* containing *Terminalia chebula* provided better relief than *Shvasahara Leha* in *Tamaka Shvasa*.^[67]

DISCUSSION

Terminalia chebula, a medicinal herb native of tropical and sub-tropical region of glob. TC has been always in main stream herbal entity in Indian and Unani system of medicine. It has a very eminent place in all the traditional systems of medicine. The important markers identified in TC are gallic acid, methyl gallate, ethyl gallate, ellagic acid, chebulagic acid, chebulinic acid, penta-*O*-galloyl- β -D-glucose, Also 2,4-chebulyl- β -D-glucopyranose a triterpene, 2 α -hydroxymicromeric acid and maslinic acid and 2 α -hydroxyursolic acid have been isolated from *Terminalia chebula leaves*. Moreover TC has been proved as a rich source of protein, vitamin C and important amino acids. Besides Se, K, Mn, Fe and Cu are available in adequate quantity to fulfil minimum recommended dietary allowance. Different analytical methods have been reported for identification and isolation of chemical constituents. TC is an essential

ingredient of *Triphala*, a widely-used formulation in Ayurved. TC is a mild purgative and successfully used as a rejuvenating agent. TC in combination of different vehicle may be used versatilely for different therapeutic purpose. The toxicity study revealed that large dose like 2gm/kg in mice did not cause any mortality establishing its safety profile.

Numerous *in vitro*, *vivo* and clinical studies acknowledged TC as an important natural agent for many medical illnesses. The most pharmacological activities demonstrated by TC are claimed due to the antioxidant potential of TC. Oxidative stress is an important process identified as a cause for many diseases. Reactive oxygen species (ROS) such as superoxide radicals, hydroxyl radicals, iron-oxygen complexes, hydrogen peroxide and lipid peroxides are generated by several oxidative reactions.^[68] Although up to some extent ROS helps the immune system to clean harmful microorganisms, excessive ROS may react with biological molecules like DNA, proteins and phospholipids, leading to oxidative damage in tissue and eventually causes free radical-related diseases such as inflammation, heart disease, diabetes, gout, cancer etc.^[69] Antioxidants inhibits the propagation of the oxidizing chain reaction and thereby prevents the oxidation of essential biological macromolecules and convert excessive ROS into non-toxic compounds. An imbalance between the amount of ROS and 'antioxidant' enzymes leads to ill health.^[70-71] TC with its fractions are proved to be potent antioxidant and eventually cures many diseases with the complications. Few studies have been reported hepatoprotective activity of TC against *tert*-butyl hydroperoxide (*t*-BHP), acetaminophen, carbon tetrachloride CCl₄. Researcher have claimed the antioxidant potential of TC for the hepatoprotective effect. TC also possess antibacterial and antiviral activity. The antibacterial effect has been exhibited against the microorganism viz. *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Helicobacter pylori* and methicillin-resistant *Staphylococcus*. Methanolic extract of *T. chebula* are superior to aqueous extract in terms of antimicrobial effect. Two plausible reasons accounting for the higher antibacterial activity of methanolic extracts claimed as: 1) the nature of biological active components like alkaloids, flavonoids, essential oil, terpenoids etc., which may be enhanced in the presence of methanol; 2) the stronger extraction capacity of methanol may have produced a greater number of active constituents responsible for antibacterial activity.⁴⁷ The antiviral effect was seen against Cytomegalo virus and Influenza A virus. Moreover, it has exhibited anti-dermatocytic effect with inhibition of dermatophytes and yeasts. Anticancer activity of TC has been noted in various malignant cell lines with antiproliferative activity, decreased cell viability and induced cell death. Various markers present in TC extracts have shown anti-mutagenic effect against many mutagens. Amongst the ingredients of *Triphala*,

TC have exhibited highest acetylcholinesterase inhibition effect and may be used in the treatment of Alzheimer. TC also lowers the cholesterolemia without influencing serum triglyceride levels, euglobulin clot lysis time or platelet adhesiveness. TC showed more effective hypoglycemic activity in STZ induced diabetic animals than standard therapeutic drug Glibenclamide. TC have also demonstrated antiulcer activity in gastric mucosal layer and dermal wounds as well. In addition, it is antimicrobial preventing possibility of infection to exposed wound. TC showed anticaries activity by affecting the growth of bacteria. TC found to provide myocardial protection against isoproterenol induced myocardial damage. It is well known that the cholecystokinin receptor has antagonist effect on nociception and ethanol extract TC have good affinity for CCK receptor.^[72] Hence an antinociceptive activity has been demonstrated by TC. Pre-treatment of TC extract showed a pronounced protection in local and systemic anaphylaxis. Also an Ayurvedic formulation containing TC have exhibited better relief in patients suffering from bronchial asthma as compared to another formulation.

CONCLUSION

Terminalia chebula is a novel medicinal herb used from ages in the Indian, Tibetan and Unani system medicine. TC may be used as an important source for discovery of new and potential drug molecules in contemporary health science.

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