ISSN 0976 – 3333

Available Online at www.ijpba.info

International Journal of Pharmaceutical & Biological Archives 2016; 7(2): 1 - 8

REVIEW ARTICLE

Haritaki (*Terminalia chebula* Retz.): A Magic Bullet for Various Remedies

Ran Vijai K. S. Maurya[1]*, Neeraj Kumar[2]

[1]Junior Resident, [2]Professor, Department of Rasa Shastra, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, (U.P), India

Received 18 Oct 2015; Revised 09 Feb 2016; Accepted 11 Mar 2016

ABSTRACT

Haritaki (*Terminalia chebula* Retz.) is one of the most frequently used herbal drug, acts as a foundation and additive natural remedy with mild Colonic cleanse properties. It can be used daily without any ill effects and with great benefits. Ayurveda emphasized its action as *Chakshushya, Dipana, Hridya, Medhya, Sarvadoshprashamana, Rasayana, Anulomana* etc. It has been proven with contemporary studies as antioxidant, antidiabetic, antibacterial, antiviral, antifungal, anticancerous, antiulcer, antimutagenic, wound healing activities etc. In this review, we have collected all possible information of its therapeutic usage in different diseases, which makes this drug a magic bullet.

Key words: *Haritaki, Terminalia chebula, Chebulic myrobalan*, Pharmacological actions.

INTRODUCTION

Haritaki (*Terminalia chebula* Retz.) is an important household drug used in many ayurvedic preparations in the treatment of several diseases. *Haritaki* is held in high esteem in Ayurveda for its properties to prevent and cure diseases. It has been quoted by *Acharya* Charaka that a mother can be contradictory to her child sometimes when she was angry but the *Haritaki* fruit cannot be harmful to a person as a medicine and always acts as a care taker. It is commonly called as *Harad* in Hindi and Black myrobalan, Ink tree (or) Chebulic myrobalan in English. It has enjoyed the prime place among medicinal herbs in India since ancient times. *Haritaki* consists of dried pericarp of mature fruits of *Terminalia chebula* belonging to family Combretaceae. It is moderate to large sized tree found throughout India, chiefly in deciduous forests and areas with light rainfall, but occasionally found in moist forest up to an altitude of 1500 m. It is a moderate sized to a large deciduous tree attaining a height of 25- 30 m. with a cylindrical bole, rounded and spreading branches. Leaf buds, branches, and youngest leaves are covered with soft, shining rust coloured hairs [1, 2]. The fruits ripen from November to March, depending upon the locality, and fall soon after ripening. The dried fruit constitutes one of the most important vegetable tanning materials. The mature fruits are collected during January to April by shaking the trees, and are then dried in thin layers, preferably in shade, and graded for marketing [3]. The fruit contains ellagic acid, gallic acid, chebulinic acid, chebugalic acid, and corilagin. The herb is used as a tonic and deobstruent in hepatic and spleen enlargements and in skin diseases in Ayurvedic system of medicine [4]. This plant is used externally in wound healing, fungal infections, inflammations of the mucous membrane of the mouth, and internally as a rejuvenative, astringent, purgative, stomachic, and laxative. It is useful in asthma, piles, and cough[5,6] It has been reported as antioxidant, antidiabetic, antibacterial, antiviral, antifungal, anticancerous, antiulcer, antimutagenic, wound healing activities etc. It is used to prevent aging and impart longevity and body resistance against disease. It has beneficial effect on all the tissues.

Haritaki at a glance

In Ayurveda seven varieties of *Haritaki* fruits, namely, Vijaya, Rohini, Putana, Amrita, Abhaya, Jivanti, and Chetaki has been described along with its feature, use and place of origin [7].

***Corresponding Author:** Ran Vijai K. S. Maurya, **Email:** rvshakya14@gmail.com

Table 1: Showing various classical varieties of *Haritaki*

S. No	Species Name	Feature	Use	Place of Origin
1	*Vijaya*	Oval	All the diseases	*Vindhya*
2	*Rohini*	Circular	In wounds and Ulcers	*Pratisthanka*
3	*Putana*	Little, very hard	As a dressing	*Sindha*
4	*Amrita*	Thick outer Layer	For purification purpose	*Champa, Bhagalpur*
5	*Abhaya*	Having 5 lines	For eye disorders	*Champa, Bhagalpur*
6	*Jivanti*	Golden color	For all diseases	*Saurastra, Gujarat*
7	*Chetaki – White*	Having 3 lines	For purgation	*Saurastra, Gujarat*
	Chetaki – Black	Having 3 lines	For purgation	*Himachal*

A similar categorization is done by Hooker (1886) who recognizes six varieties under *Terminalis chebula*. However, these varieties do not find a place in recent floras (Gamble 1967, Cooke 1967, Ramaswamy & Razi 1973, Rao & Razi 1981, Yoganarsimhan *et al*, 1982, Saldanha & Nicolson 1976).

Table 2: *Haritaki* used as a *Rasayana* with different *Anupana* prescribed in different seasons [8]

S. No	Seasons	Months	*Anupana*
1	*Varsha*	July-Aug	*Saindhav Lavana*
2	*Sharada*	Sept-Oct	*Sharkara*
3	*Hemanta*	Nov-Dec	*Shunthi*
4	*Shisheera*	Jan-Feb	*Pippali*
5	*Vasanta*	Mar-Apr	*Madhu*
6	*Ghrishma*	May-Jun	*Guda.*

In Ayurveda *Haritaki* to be used with *Sharkara* in *Pitta* disorders, with *Saindhav Lavana* in *Kapha* disorders, with *Ghrita* in *Vata* disorders, with *Guda* in *Sarvaroga* [9].

Phyto-constituents

The fruits of *Haritaki* are rich in tannins (about 32%-34%) and its content varies with geographical distribution [10,11]. The tannins of *Haritaki* are of pyrogallol (hydrolysable) type. A group of researchers found so many components of hydrolysable tannins (gallic acid, chebulagic acid, punicalagin, chebulanin, corilagin, neochebulinic acid, ellagic acid, chebulinic acid, 1,2,3,4,6-penta-O-galloyl- β-D glucose, 1,6-di-o-galloyl-D-glucose, casuarinin, 3,4,6-tri-o-glloyl-D-glucose, terchebulin) from *Haritaki* fruits [12]. Other constituents include phenolics such as chebulinic acid, ellagic acid and anthraquinones. Some of the other minor constituents were polyphenols such as corilagin, galloyl glucose, punicalagin, terflavin A, maslinic acid [13]. Besides, fructose, amino acids, succinic acid, betasitosterol, resin and purgative principle of anthraquinone are also present [14,15]. Flavonol, glycosides, triterpenoids, coumarin conjugated with gallic acids called chebulin as well as other phenolic compounds were also isolated[16-18]. Twelve fatty acids were isolated from Haritaki of which palmitic acid, linoleic acid and oleic acid were main constituents [19].

Table 3: Researches at a glance on *Haritaki*

Pharmacological activity	Type of extract	Laboratory Organism/Animal Used	References
Antioxidant	a) 95% of ethanol extract b) water, methanol & 95% of ethanol extract	Adult male albino rats Fermented products	Suchalata S *et al*., 2009 Chia-lin chang *et al*., 2010
Antibacterial	a) Ethanol extract b) Ether, alcoholic, water extract	a) Ethanol extract b) Ether, alcoholic, water extract	Kannan P *et al*., 2009 Malekzadeh F *et al*., 2001
Antifungal	a) Aqueous, alcoholic, ethyl acetate extract b) 70%of methanol, ethyl acetate, hexane, chloroform extract	*Aspergillus niger*, *Aspergillus flavus*, *Alternaria alternata* etc. *Fusarium oxysporum*, *Phytophthora capsici*, *Fusarium solani* etc	Saheb L Shinde *et al*., 2011 Vivek K *et al*., 2010
Anticancer	70% of methanol	Human(MCF-7), mouse (S115) breast cancer cell lines etc	Saleem A *et al*., 2002
Antiviral	a) Acetone extract b) Aqueous extract	Swine influenza A virus Hepatitis B virus	Hongbo Ma *et al*., 2010 Kim TG *et al*., 2001
Antiulcer	Methanolic extract	Wistar albino male rats	Raju D *et al*., 2009
Antidiabetic	a) Ethanol extract b) chloroform extract	Adult albino male rats Streptozotocin induced diabetic rats	Gandhipuram Periyasamy *et al*., 2006 Rao N.K *et al*., 2006
Wound healing	a) Hydro alcoholic extract b) 90% of ethanol extract	Induced diabetic rats Wistar albino rats	Manish Pal Singh *et al*., 2009 Choudhary GP 2011
Anticonvulsant	Ethanolic, chloroform, Petroleum ether aqueous extract	Rats	Hogade Maheswar G *et al*., 2010
Antimutagenic	a) Chloroform, aqueous extract b) Acetone, aqueous chloroform extract	*Salmonella typhimurium* *Salmonella typhimurium*	Grover IS *et al*., 1992 Kaur S *et al*., 2002
Anticarries	Aqueous extract	*Streptococcus mutans*	Jagtap AG *et al*., 1999
Cardio protective effect	95% of ethanol extract	Adult albino male rats	Suchalata S *et al*., 2005

Radiation protective effect	Aqueous extract	Rats	Jagetia GC *et al*., 2002
Cytotoxic effect	Acetone extract	Cancer cell lines	Kaur S *et al*., 2005
Immunodulatory effect	Alcohol extract	Male wistar rats	Vaibhav Aher *et al*., 2011

PHARMACOLOGICAL ACTIVITY

Antioxidant and free radical scavenging activity:

The leaves bark and fruit of *Haritaki* possessed high antioxidant activity and phenolics were found to be responsible for this activity [20]. Aqueous extract of *Haritaki* inhibited xanthine /xanthine oxidase activity and was also an excellent scavenger of radicals [21]. *Haritaki* in a polyherbal formulation (Aller-7/ NR-A2) inhibited free radical induced hemolysis and also significantly inhibited nitric oxide release from lipopolysaccharide stimulated murine macrophages [22]. Six extracts and four compounds of fruit exhibited antioxidant activity at different magnitudes of potency[23]. Acetone extract has stronger antioxidant activity than alpha-tocopherol and HPLC analysis with diode array detection indicated the presence of hydroxybenzoic acid derivatives, hydroxycinnamic acid derivatives, flavonol aglycones and their glycosides, as main phenolic compounds [24].

Anticarcinogenic activity:

A group of researchers have reported the inhibitory action on cancer cell growth by the phenolics of fruit and found that chebulinic acid, tannic acid and ellagic acid were the most growth inhibitory phenolics of *T. chebula* [25]. Ethanol extract of fruit inhibited cell proliferation and induced cell death in a dose dependent manner in several malignant cell lines including human (MCF-7) and mouse (S115) breast cancer cell line, human osteosarcoma cell line (HOS-1), human prostate cancer cell (PC-3) and a non-tumorigenic immortalized human prostate cell line (PNT1A). Besides, acetone extract of bark and fruit powder of harbors constituents with promising anticarcinogenic activity [26].

Antimutagenic, radioprotective and chemopreventive activity:

Antimutagenic activity of aqueous extract and hydrolyzable tannins from in Salmonella typhimurium has been documented [27]. The administration of aqueous extract of prior to whole body irradiation of mice resulted in a reduction of peroxidation of membrane lipids in the mice liver as well as a decrease in radiation induced damage to DNA. It also protected the human lymphocytes from undergoing the gamma radiation-induced damage to DNA exposed *in vitro* [28] showed chemo-preventive effect on nickel chloride -induced renal oxidative stress, toxicity and cell proliferation response in male Wistar rats [29].

Hepatoprotective activity:

A mixture of chebulic acid (CA) and its minor isomer, neochebulic acid with a ratio of 2:1 isolated from ethanolic extract of fruits showed strong hepatoprotective activity [30]. Ethanol extract was found to prevent the hepatotoxiocity caused by the administration of rifampicin, isoniazid and pyrazinamide (combination) in sub-chronic model (12 weeks) [31]. In a herbal formulation (HP-1) showed hepato protective activity against carbon tetrachloride induced toxicity in rat hepatocytes [32].

Cardioprotective activity:

Haritaki extract pretreatment was found to ameliorate the effect of isoproterenol on lipid peroxide formation and retained the activities of the diagnostic marker enzymes in isoproterenol induced myocardial damage in rats [33]. Its pericarp has also been reported to have cardioprotective activity in isolated frog heart model [34].

Cytoprotective activity:

Gallic acid (GA) and CA were isolated from the extract of the herbal medicine (myrobalan, the fruit of T. chebula) as active principal that blocked the cytotoxic T- lymphocyte- mediated cytotoxicity. Granule exocytosis in response to anti-CD3 stimulation was also blocked by GA and CA at the equivalent concentrations [35]. The ethanolic extract of fruit exhibited a notable cytoprotective effect on the HEK-N/F cells. In addition its extract exhibited significant cytoprotective effect against UV-induced oxidative damage. These observations were attributed to the inhibitory effect of the extract on the age dependent shortening of the telomere length as shown by the Southern Blots of the terminal restriction fragments of DNA extracted from sub-culture passages [36]. It exhibited the development of duodenal ulcers and appeared to exert a cytoprotective effect on the gastric mucosa in vivo[37]. Cytoprotective effect on oxidative stress and inhibitory effect on cellular aging of its fruits have also been documented [38].

Antidiabetic and renoprotective activity:
Haritaki fruits and seeds exhibited dose dependent reduction in blood glucose of streptozotocin induced diabetic rats both in short term and long term study and also had renoprotective activity [39,40].

Antibacterial activity:
Haritaki exhibited antibacterial activity against a number of both Gram-positive and Gram-negative human pathogenic bacteria [41-43]. Ethanedioic acid and ellagic acid isolated from butanol fraction of fruit extract had strong antibacterial activity against intestinal bacteria, *Clostridium perfingens* and *Escherichia coli* [44]. It is effective in inhibiting the urease activity of *Helicobactor pylori*, an ubiquitous bacterium implicated in the development of gastritis, ulcers and stomach cancers [43]. GA and its ethyl ester isolated from ethanolic extract of showed antimicrobial activity against methicillin-resistant *Staphylococcus aureus* (*S. aureus*) [45]. Ripe seeds of also exhibited strong antibacterial activity against *S. aureus*[46]. The aqueous extract of strongly inhibited the growth of Streptococcus mutans, salivary bacteria [47].

Antifungal activity:
An aqueous extract of exhibited antifungal activity against a number of dermatophytes and yeasts [48,49]. It is effective against the pathogenic yeast *Candida albicans* and dermatophytes Epidermophyton, Floccosum, Microsporum gypseum and Trichophyton rubrum [48]. Its inhibitory effect on three dermatophytes (Trichophyton spp.) and three yeasts (Candida spp.) has also been documented [50]. An aqueous extract of galls of showed inhibitory effects on three dermatophytes (Trichophyton spp.) and three yeasts (Candida spp.) [48]. In vitro anticandidal activity of methanol extract of *T. chebula* was observed against clotrimazole resistant *Candida albicans* [51]. Seed extract exhibited antifungal activity against Trichophyton glabrata [48].

Antiviral activity:
Haritaki fruits afforded four immunodeficiency virus type 1 (HIV-1) Integrase inhibitors, GA (I) and three galloyl glucoses (II-IV). Their galloyl moiety plays a major role for inhibition against the 3'-processing of HIV-1 integrase of the compounds [52] has also retroviral reverse transcriptase inhibitory activity [53]. It protects epithelial cells against influenza A virus, supporting its traditional use for aiding in recovery from acute respiratory infections [54].The methanol and aqueous extracts of showed a significant inhibitory activity with on human immunodeficiency virus-1 reverse transcriptase [55]. It also demonstrated the therapeutic activity against herpes simplex virus both in vitro and in vivo tests [56]. These finding prompted a team of Japanese researchers to investigate *Haritaki* effect on human cytomegalovirus (CMV). They found that was effective in inhibiting the replication of human cytomegalovirus in vitro and in an AIDS model with immune suppressed mice and concluded that it may be beneficial for the prevention of CMV diseases and immunocompronised patients [57].

Anti-inflammatory and anti-arthritic activity:
Aqueous extract of dried fruit of *Haritaki* showed anti-inflammatory by inhibiting inducible nitric oxide synthesis [58]. Chebulagic acid from immature seeds of significantly suppressed the onset and progression of collagen induced arthritis in mice [59]. *Haritaki* in a polyherbal formulation (Aller-7) exhibited a dose dependent anti-inflammatory effect against Freund's adjuvant induced arthritis in rats [60].

Adaptogenic and antianaphylactic activities:
Haritaki fruit was one of the six Ayurvedic herbs administered to animals to test their adaptogenic potential. All six traditional rasayana plants were able to aid the animals against a variety of different stressors working in different ways[61]. Besides, animal studies show that when extract of *Haritaki* was administered following induction of anaphylactic shock, the serum histamine levels were reduced, indicating its strong antianaphylactic action [62]. Water soluble fraction of *Haritaki* had a significant increasing effect on anti-dinitrophenyl IgE-induced tumor necrosis factor-alpha production from rat peritoneal mast cells indicating its strong antianaphylactic action [62].

Hypolipidemic and hypocholesterolemic activity:
Hypolipidemic activity of *Haritaki* extract against experimentally induced atherosclerosis has been documented [63]. It also possessed hypocholesterolemic activity against cholesterol [63].

Gastrointestinal motility improving and antiulcerogenic activity:
Although its traditional use as laxative is well established, *Haritaki* fruit has been shown to increase gastric emptying time [64]. This action appeared to be balanced with a protective effect

on the gastrointestinal mucosa, with the improvement in the secretory status of Brunner's gland involved in the protection against duodenal ulcer [65].

Antispasmodic activity:

One of the numerous studies of demonstrated its 'anti-vata' or 'anti-spasmodic' properties by the reduction of abnormal blood pressure as well as intestinal spasms. This confirm its traditional usefulness for spastic colon and other intestinal disorders [66].

Anticaries activity:

The aqueous extract of *Heritage* strongly inhibited the growth, sucrose induced adherence and glucan induced aggregation of Streptococcus mutants. Mouth rinsing with a 10% solution of the extract inhibited the salivary bacterial count and glycolysis of salivary bacteria for up to 90 min post rinsing [47,67].

Wound healing activity:

Topical administration of an alcoholic extract of *Haritaki* leaves on the healing of rat dermal wounds showed that treated wounds healed faster as indicated by improved rates of contraction and decreased period of epithelialization [68].

Purgative property:

Purgative action of an oil fraction from *Haritaki* has been proved [69].

CONCLUSION

Haritaki is one of the most versatile plants having a wide spectrum of pharmacological and medicinal activities. This versatile medicinal plant is the unique source of various types of compounds having diverse chemical structure. Though, it has a number of pharmacological activities due to the presence of various types of bioactive compounds.

ACKNOWLEDGEMENT

The authors are thankful to Dr Vinamra Sharma, Ph.D. scholar and Senior resident, Department of Rasa Shastra, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, U.P., India for their kind support to prepare this manuscript.

REFERENCE

1. Aiyer K.N., Kolammal M. Pharmacognosy of Ayurvedic drugs, Dept. of Pharmacognosy, University of Kerala, Trivandrum,. 1963; 1(7): 102- 105.
2. Padhi M.M. Medicinal plants in geriatric health care, CCRIAS, Dept. of AYUSH, Min. of Health & Family Welfare, Govt. of India, 2008; 39 42.
3. Krishnan K.S. The Wealth of India, Raw Material. 1998; 10: 171.
4. Chopra R. N., Nayar S.L., Chopra I.C. Glossary of Indian Medicinal Plants, CSIR, New Delhi, India. 1956; 104.
5. Shastry JLN, Dravyaguna Vijnan, Chaukhambha Orientalia, Varanasi, Part II, 2005, page 209‑15.
6. Cooke Theodore. Flora of Bombay (pt‑1). Calcutta: Botanical Survey of India; 1967. p. 195‑205.
7. Chunekar KC. Bhavaprakash nighantu. Varanasi: Chaukhamba Bharati Academy; 1999. p. 3.
8. Vaisya R., Editor, Misra B., Commentator, Vidyotani Hindi Commentary, Bhav Prakash Nighantu, 9th Edi., Chaukhamba Sanskrit Sansthan, Varanasi, Haritakyadi Varga 7/34, p. 3-9.
9. Vaisya R., Editor, Misra B., Commentator, Vidyotani Hindi Commentary, Bhav Prakash Nighantu, 9th Edi., Chaukhamba Sanskrit Sansthan, Varanasi, Haritakyadi Varga 7/33, p. 3-9.
10. Kumar A, Lakshman K, Jayaveera K, Satish K, Tripathi SM. Estimation of rutin and quercetin *Terminalia chebula* by HPLC. Int J Aesth Antiag Med 2009; 2(1): 3.
11. Jayaramkumar K. Effect of geographical variation on content of tannic acid, gallic acid, chebulinic acid, and ethyl gallate in *Terminalia chebula* fruits. Nat Prod 2006; 2(3-4): 170-175.
12. Juang LJ, Sheu SJ, Lin TC. Determination of hydrolyzable tannins in the fruit of *Terminalia chebula* by high-performancc liquid chromatography and capillary electrophoresis. J Sep Sci 2004; 27(9): 718-724.
13. Williumson EN. Major herbs of Ayurveda. London: Churchill Livingstone; 2002, p. 299.
14. Tubtimdee C, Shotipruk A. Extraction of phenolics from *Terminalia chebula* Retz. with water-ethanol and water-propylene glycol and sugaring-out concentration of extracts. Sep Puri Tech 2011; 77(3): 339-346.

15. Thakur M, Rana RC, Thakur S. Physiochemical evaluation of *Terminalia chebula* fruits. J Non Timber Forest Prod 2008; 15: 37- 42.
16. Rangsriwong P, Rangkadilok N, Satayavivad J, Goto M, Shotipruk A. Subcritical water extraction of polyphenolic compounds from Terminalia chebula Retz. fruits. Sep Puri Tech 2009; 66: 51-56.
17. Muhammad S, Khan BA, Akhtar N, Mahmood T, Rasul A, Hussain I, *et al*. The morphology, extractions, chemical constituents and uses of *Terminalia chebula*: A review. J Med Plants Res 2012; 6(33): 4772-4775.
18. Yoganarasimhan SN. Medicinal plants of India. Bangalore: Self Publication; 2000, p. 541.
19. Zhang X, Chen C, He S, Ge F. Supercritical-CO2 fluid extraction of the fatty oil in *Terminalia chebula* and GC-MS analysis. Zhong Yao Cai 1997; 20(9): 463 464.
20. Chang CL, Lin CS. Development of antioxidant activity and pattern recognition of *Terminalia chebula* Retzius extracts and its fermented products. HungKuang J 2010; 61: 115-129.
21. Naik GH, Priyadarsini KI, Naik DB, Gangabhagirathi R, Mohan H. Studies on the aqueous extract of *Terminalia chebula* as a potent antioxidant and a probable radioprotector. Phytomedicine 2004; 11(6): 530-538.
22. Mahesh R, Bhuvana S, 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): 358-363.
23. Hazra B, Sarkar R, Biswas S, Mandal N. Comparative study of the antioxidant and reactive oxygen species scavenging properties in the extracts of the fruits of *Terminalia chebula*, *Terminalia belerica* and *Emblica officinalis*. BMC Comp Alter Med 2010; 10: 20.
24. Lee HS, Won NH, Kim KH, Lee H, Jun W, Lee KW. Antioxidant effects of aqueous extract of *Terminalia chebula in vitvo* and *in vitro*. Biol Pharm Bull 2005; 28(9): 1639-1644.
25. Saleem M. Hushum P. Harkonen K, Pihlaja. Inhibition of cancer cell growth by crude extract and phenolics of *Terminalia chebula* fruit. J Ethnopharmacol 2002; 81: 327-336.
26. Reddy DB, Reddy TC, Jyotsna G, Sharan S, Priya N, Lakshmipathi V, *et al*. Chebulagic acid, a COX-LOX dual inhibitor isolated from the fruits of *Terminalia chebula* Retz., induces apoptosis in COLO-205 cell line. J Ethnopharmacol 2009; 124(3): 506-512.
27. Grover IS, Bala S. Antimutagenic activity of *Terminalia chebula* (myroblan) in *Salmonella typhimurium*. Indian J Exp Biol 1992; 30(4): 339-341.
28. Gandhi NM, Nayar CKK. Radiation protection by *Terminalia chebula* some mechanistic aspects. Mol Cell Biochem 2005; 277(1-2): 43-48.
29. Prasad L, Husain Khan T, Jahengir T, Sultana S. Chemomodulatory effect of *Terminalia chebula* against nickel chloride-induced oxidative stress and tumor promotion response in male Wistar rats. J Trace Elem Med Biol 2006; 20(4): 233-239.
30. Lee HS, Jung SH, Yun BS, Lee KW. Isolation of chebulic acid from *Terminalia chebula* Retz. and its antioxidant effect in isolated rat hepatocytes. Arch Toxicol 2007; 31(3): 211-218.
31. Tasduq SS, Singh AK, Salti NK, Gupta DK, Suri K. *Terminalia chebula* fruits prevent liver toxicity caused by sub-chronic administration of refampicin, isoniazid and pyrazinamide (PZA) in combination. Hum Exp Toxicol 2006; 25(3): 11-18.
32. 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; 22(12): 639-645.
33. Suchalatha S, Shyamadevi CS. Protective effect of *Terminalia chebula* against experimental myocardial injury induced by isoproterenol. Indian J Exp Biol 2004; 42(2): 174-178.
34. Reddy VRC. Cardioprotective activity of the fruit of *Terminalia chebula*. Fitoterapia 1990; 61: 517-525.
35. Chang CL, Lin CS, Lai GH, Chen YH, Tuan WC, Hsu CM. Influence of

Terminalia chebula extracts on the effect of PC12 cell growth. J Trad Med 2010; 21(1): 23-30.
36. Minkyun NA, Wan BAE, Kang SS, Min BS, Yoo JK, Yuk OK, et al. Cytoprotective effect on oxidative stress and inhibitory effect on cellular aging of *Terminialia chebula* fruit. Phytother Res 2004; 18: 737-741.
37. 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; 131(3): 567-574.
38. Na M, Bae M, Keng SS, Min BS, Yoo JK, Kamiryo Y, *et al*. Cytoprotective effect on oxidative stress and inhibitory effect on cellular aging of *Terminalia chebula* fruit. Phytother Res 2004; 18(9): 737-741.
39. Kannan VR, Rajasekar GS, Rajesh P, Balasubramanian V, Ramesh N, Solomon EK, *et al*. Anti-diabetic activity on ethanolic extracts of fruits of *Terminalia chebula* Retz. Alloxan induced diabetic rats. Am J Drug Discov Dev 2012; 2: 135-142.
40. 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; 6: 105-115.
41. Khan KH, Jain SK. Regular intake of *Terminalia chebula* can reduce the risk of getting typhoid fever. Adv Biotech 2009; 8(9): 10- 15.
42. Khan KH. The effect of regular intake of *Terminalia chebula* on oxidative stress in mice originated from *Salmonella typhimurium.* EurAsia J BioSci 2009; 3: 113-121.
43. Malckzadeh F, Ehsanifar H, Shahamat N, Levin M, Colwell RR. Antibacterial activity of black myrobalan (*Terminalia chebula* Retz.) against Helicobactor pyroli. Int J Antimicrob Agent 2001; 18(1): 85-88.
44. Kim HG, Cho JH, Jeong EY, Lim JH, Lee SH, Lee HS. Growth inhibitory activity of active component from *Terminalia chebula* fruits against intestinal bacteria. J Food Prot 2006; 69(9): 2205- 2209.
45. Sato Y, Oketani H, Singyouchi K, Ohtsubo T, Kihara M, Shibata H, *et al*. Extraction and purification of effective antimicrobial constituents of *Terminalia chebula* Retz. against methicillin resistant *Staphylococcus aureus*. Bull Pharm Bull 1997; 20(4): 401- 404.
46. Bonjar GH. Antibacterial screening of plants used in Iranian folkloric medicine. Fitoterapia 2004; 75(2): 231-235.
47. Aneja KR, Joshi R. Evaluation of antimicrobial properties of fruit extracts of *Terminalia chebula* against dental caries pathogens. Jundishapur J Microbiol 2009; 2(3): 105-111.
48. Barazani VO, Sathiyomoorthy P, Shalev R, Vardy D, Golan GA. Screening of South-Indian medicinal plants for anti-fungal activity. Phyther Res 2003; 17(9): 1123-1125.
49. Dutta BK, Rahman I, Das TK. Antifungal activity of Indian plant extracts. Mycoses 1998; 41(11-12): 535-536.
50. Mehmood Z, Ahmad I, Mohammad F, Ahmad S. Indian medicinal plants: A potential source of anticandidal Drugs. Pharm Biol 1999; 37(3): 237-242.
51. Bonjar GH. Inhibition of Clotrimazole-resistant *Candida albicans* by plants used in Iranian folkloric medicine. Fitoterapia 2004; 75(1): 74-76.
52. Jeong AHN, Kim CY, Lee JS, Kim TG, Kim SH, Lee CK, *et al*. Inhibition of HIV-1 integrase by galloyl glucoses from *Terminalia chebula* and flovonol glycoside gallates from Euphorbia pekinensis. Plant Med 2002; 68: 457-459.
53. Lee D, Boo K, Woo J, Duan F, Lee K, Kwon T, *et al*. Antibacterial and Anti-viral activities of extracts from *Terminalia chebula* barks. J Korean Soc Appl Biol Chem 2011; 54(2): 295-298.
54. Badmaev V, Nowakowski M. Protection of epithelial cells against influenza A virus by plant derived biological response modifier Ledretan-96. Phytother Res 2000; 44(4): 245-249.
55. Gambari R, Lampronti L. Inhibition of immunodeficiency type-1 virus (HIV 1) life cycle by medicinal plant extracts and plant derived compounds. Adv Phytomed 2006; 2: 299-311.
56. Kurowa M, Nagasaka K, Hirabayashi T, Uyama S, Sato H, Kagiyama T, *et al*.

Efficacy of traditional herbal medicines in combination with acyclovir against Herpes Simplex Virus-1 infection in vitro and *in vitvo*. Antiviral Res 1995; 27 (1-2): 19-37.
57. Yukawa TA, Kurokawa M, Sato S, Yoshida Y, Kageyamer S, Hasegawa T, *et al*. Prophylactic treatment of cytomegalovirus infection with traditional herbs. Antiviral Res 1996; 32(2): 63-70.
58. 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; 78(11): 861-866.
59. Nair V, Singh S, Gupta YK. Anti-arthritic and disease modifying activity of *Terminalia chebula* Retz. in experimental models. J Pharm Pharmacol 2010; 62(12): 1801-1806.
60. 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; 26(1-2): 43-51.
61. Rege NN, Thatte UM, Dahanukar SA. Adaptogenic properties of six Rasayana herbs used in Ayurvedic medicines. Phytother Res 1999; 13: 275-291.
62. Shin TY, Jeong HG, kim DK, Kim SH, Lee JK, Chae BS, et al. Inhibitory action of water soluble fraction of Terminalia chebula on systematic and local anaphylaxis. J Ethnopharmacol 2001; 74: 133-140.
63. Maruthappan V, Shree KS. Hypolipidemic activity of (Terminalia chebula) in atherogenic diet induced hyperlipidemic rats. J Adv Pharm Tech Res 2010; 1: 229-235.
64. Israni DA, Patel KV, Gandhi TR. Anti-hyperlipidemic activity of aqueous extract of *Terminalia chebula* and Gaumutra in high cholesterol diet fed rats. Int J Pharm Sci 2010; 1(1): 48-59.
65. 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; 49(3): 262-268.
66. Seyyed AM, Ali V, Mohammad KGN, Peyman M. Spasmogenic activity of the seed of *Terminalia chebula* Retz in rat small intestine: In vivo and *in vitro* studies. Malays J Med Sci 2011; 18(3): 18-26.
67. Carounanidy U, Satyanarayanan R, Velmurugan A. Use of an aqueous extract of *Terminalia chebula* as an anticaries agent: a clinical study. Indian J Dent Res 2007; 18(4): 152-156.
68. 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 Comp Alter Med 2011; 11: 1-9.
69. Vani T, Rajani M, Sarkar S, Shishoo CJ. Antioxidant properties of ayurvedic formulation triphala and its constituents. Int J Pharmacog 1997; 35: 313-317.