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Bioequivalence & Bioavailability International Journal
ISSN: 2578-4803

Ethnopharmacological Review of *Terminalia chebula*

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Review Article

Volume 3 Issue 1

Received Date: December 01, 2018

Published Date: January 04, 2019

DOI: 10.23880/beba-16000135

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Abstract

Terminalia chebula, traditionally regarded as universal panacea, is known for its pleiotropic effects, including the effects on oxidative stress, malignant tumor growth, wound healing, and insulin sensitivity in Type 2 diabetes. In India and Southeast Asia the fruit is used as a popular folk medicine for antitussive, diuretic, homeostatic, laxative and cardiotonic treatments. In the fruits of *T. chebula* three hydrolyzable tannins chebulinic acid, chebulagic acid and 1, 3, 6-tri-O-galloyl-ß-D-glucose could be determined by RP-HPLC. The contents of the first two substances were interrelated with the varieties. Experimental studies presented by different article show important action of substance present in fruit pulp *Terminalia chebula*, Antibacterial activity Test showed a broad spectrum of antibacterial activity with an inhibition zone size of 11 to 27 mm, against all the test bacteria. There was a synergistic action of the crude extracts with broad spectrum antibiotic like tetracycline and other pulp extract also act on viral disease In vitro they may inhibited the replication of human cytomegalovirus growth. Antioxidant activity of *T. chebula* fruit pulp well established, The aqueous extract of *T. chebula* fruit pulp was tested for its cytoprotective activity. Show, the cultured rat primary hepatocytes and rat whole livers the extract reversed an oxidative injury; caused by tert-butyl hydroperoxide and lactate dehydrogenase leakage significantly. Pharmacological effects, includes against anaphylactic shock, Antispasmodic activity, Gastrointestinal activity, Cardiotonic activity etc.

Keywords: Ethnopharmacological; Gastrointestinal; Cardiotonic; Elliptic; Botanical

Introduction

Medicinal plants are the one of the many sources of emerging drug and they establish main component of human society from the dawn of civilization to diseases and have been considered valuable source of unique phyto constituents which are used extensively in the development of drugs against various diseases. *Terminalia chebula*a kinds of trees, very large, up to 40 m high, rarely shrubs; the branches and stem often in tiers. They grow in sunny forests and thickets, tree native to North East India and Indo-Burma region. The tree yields a

fruit which has an abrasive seed but a fleshy pulp [1]. The plant is highly regarded in Ayurvedic and Tibetan medicine. The seed, called "Harda" or Kala Namak in Hindi, is also used in Indian cooking. Leaves are alternate or subopposite, the leaf blades are elliptic, both surfaces are glabrous or adpressed villous, at least when young. The base is obtuse-rounded or cuneate, the apex mucronate, the lateral veins appear in 6 - 12 pairs. The inflorescences stand axillary or terminal with numerous flowers. The flowers smell slightly fragrant; the calyx tube is distally cupular, 2.5 - 3.5 mm long with five lobes, mucronate to aristate. The fruits seem ovoid or ellipsoid, five ridged, becoming deeply winkled when dry, blackish-brown when ripe, 2 - 4.5 x 1.2 x 2.5 mm tall. The flowers appear May-June, the fruits July-December. *Terminalia chebula* has been extensively used in ayurveda, unani and homoeopathic system. The Sanskrit name for *Terminalia chebula* is 'Haritaki' which means yellowish dye (harita) that contains the god Siva (Hari, i.e. the Himalayas) and it is known to cure (harayet) all the diseases [2]. In Sanskrit 'Haritaki' is also known as 'Abhaya' which refers to the 'fearlessness', as it provides in the face of the disease. In Indian mythology, this plant has been known to be originated from the drops of ambrosia (Amrita) which fell on the earth when Indra was drinking it [3]. *Terminalia chebula* (Combretaceae) is medium to large-sized tree distributed throughout tropical and subtropical Asia, including China and Tibet. This tree is wild in the forests of Northern India, Uttar Pradesh, Bengal, Southern Maharashtra, Tamil Nadu and Karnataka. The fruit is used medicinally [4]. It is considered to be a rasayana (with literal meaning: Path (ayana) of the Juice (rasa), or Elixir vitae) for Vata, balances tridoshas (loosely translated to three energetic forces in the body), enhances digestion (dipanapachana), sharpens the senses (medhyam), displays alterative (medicinal substance that acts gradually to nourish and improve the system), astringent, expectorant, anti-inflammatory, anodyne, cardiotonic, laxative, antiseptic and antiemetic properties. Seven different types of fruits are recognized (i.e. vijaya, rohini, putana, amrita, abhaya, jivanti and chetaki), based on the region of harvestation, as well as its colour and shape [5-8].

Plant parts used the fruits, the bark, and the leaves

Plant Botanical and Demographical Detail: It consists of dried fruit, root, bark of plant knows as *Terminalia chebula.*

a. Geographical Source: Dhaka, Bangladesh.
b. Family: Combretaceae
c. Common name: Haritaki
d. Synonyms:

- **China:** Zhang-Qin-Ge, Hezi
- **Germany:** Myrobalane
- **Bengali:** Haritaki
- **Hindi:** Harre, Harad, Harar
- **Malayalam :** Katukka
- **Marathi :** Hirda, Haritaki, Harda, Hireda
- **Punjabi**: Hakeka, Harar
- **Tamil**: Ammai, Amutam, Aritaki, Pethiyam, Varikkai
- **Telugu**: Karakkaya;
- **Urdu:** Halela.

Names of the fruit:

a. English: Myrobalan, black myrobalan, black chebulic, chebulic myrobalan, medicinal
b. Terminalia fruit French: Myrobalan indien
c. Chin.: Hezi Tibet: Harra, harro
d. Hindi: Har Tamil: Kadah kai German: Myrobalane African vernacular names of the fruit:
e. Fulde: Wake Hausa: Banshe
f. Pharm. definition: Fructus Chebulae

Traditional Uses

In India the fruits are available in markets. They are used as a mild laxative and as an adstringent against wounds and abscesses. In the dental care dried powder is applied against stomatitis and against ulcers of the gum. The plant is used as an antidote against bites of snakes, finally [9]. In India and Southeast Asia the fruit is used as a popular folk medicine for antitussive, diuretic, homeostatic, laxative and cardiotonic treatments. In China the drug is a remedy against a sore throat and cough, against long during diarrhoea connected with a prolapsed rectum. In Tibet the dried fruit is used against ulcers and dysentery [10].

Constituents in the Fruits

Characteristic compounds are tannins, triterpenes, saponines and mucous substances. The tannins are esters of different phenol-carbonic acids. Chebulinic acid is a dimer, tergallic acid a trimere, and terchebulinic acid a tetramere of the gallic acid being connected with glucose. After hydrolysis the free monomers can be analysed. The total phenolic contents of *T. arjuna, T. bellerica*, *T. chebula* and *T. muelleri* leaves, bark and fruits are 72.0 - 167.2 mg/g. Plant derived medicines and alkaloid are part of the Indian traditional health care system. Therefore a concentrated extract of *T. chebula* was tested in dental care.

A mouth rinse of 10 % was prepared by dilution with sterile distilled water and was assessed by testing 50

salivary samples collected from people with high risk of caries and dental infection .Salivary pH, buffering capacity, other microbial activity and infection were assayed before rinsing, immediately after, 10 min, 30 min, and 1hr after rinsing. There was an increase in the pH and buffering capacity and decrease in microbial count. The aqueous extract of *T. chebula* fruit pulp extract used as mouth rinse seems to be an effective anticaries agent. **Toxicity dose** In mice > 3 g/kg lethal [11-14].

In the **fruits** of *T. chebula* three hydrolyzable tannins chebulinic acid, chebulagic acid and 1, 3, 6-tri-O-galloyl-ß-D-glucose could be determined by RP-HPLC. The contents of the first two substances were interrelated with the varieties. They seem to be suitable for evaluation for the quality assessment of the drug and for the differentiation of the varieties [15,16]. Further hydrolysable tannins were castalagin, ellagic acid, flavogallonic acid, punilagin, terchebulin. In the **fruits** of *T. chebula* fourteen tannins could be separated by HPLC, combined with Capillary Electrophoresis [17]. The **kernels** of the fruits contain 49 % fatty oil. Its fatty acid composition is quite similar to that of conventional oils. Palmitic acid, linolic acid and oleic acid are the main constituents. Their yield can be raised with supercritical CO_2 extraction [18]. In Brazil the fruits of T. catappa, named castanhola, are included in the national biodiesel program [15]. In New Delhi, India the fruits of *T. chebula* are used for the production of tannase.

Results of Phytochemical Analysis of Fruit Pulp

Phytochemical analysis shows some of the important finding of fruit constituent.

Phytochemicals	(EEFTC) + / -
Phytosterols	+
Triterpenoids	+
Saponins	-
Alkaloids	-
Carbohydrates	+
Flavanoids	-
Lactones	-
Phenolic Compounds & Tannins	+
Proteins	-
Glycosides	+
Fixed Oils And Fatty Acid	-
(+) Presence, (-) Absence.	
EEFTC: Ethanolic Extract of Fruits of *Terminalia chebula.*	

Table 1: Phytochemical analysis of EEFTC [19].

Experimental Studies

After extensively review the experimental studies presented by different article show important action of substance present in fruit pulp *Terminalia chebula*.

Antibacterial Activity

The ethanolic extracts of *T. chebula* fruits pulp constituent were tested for its activity against methicillin-resistant and methicillin-sensitive Staphylococcus aureus strains from clinical isolates. Test showed a broad spectrum of antibacterial activity with an inhibition zone size of 11 to 27 mm, against all the test bacteria. There was a synergistic action of the crude extracts with broad spectrum antibiotic like tetracycline and other. Thin-layer chromatography Shows that phenols and flavonoids as major active compounds [20]. In another experiment with gallic acid and its ethyl ester could be verified on the basis of spectroscopic evidence [21]. Ether and alcohol extracts of *T. chebula* fruit were tested against H. pylori in an agar diffusion test. The water extract had a MIC value of 125 mg/L and a value MBC of 150 mg/L. fruit powder, incorporated in agar gave higher MIC and MBC values (150 and 175 mg/l). The water extract *T. chebula* fruit inhibited the activity of urease at a concentration of 1 -2.5 mg/L [22]. The aqueous extract of *T. chebula* found antagonise the growth, the sucrose induced adherence and the glucan-induced aggregation of Streptococcus mutans. Mouth rinsing with a 10 % solution of the *T. chebula* significantly reduced the total bacterial counts and the total streptococcal counts in the saliva samples. Mouthwash solution inhibited glycolysis of salivary bacteria for up to 90 min after rinsing [23].

Antiviral Activity

Hot water extracts of *T. chebula* fruit were examined for anticytomegalovirus activity in vitro and in vivo. In vitro they may inhibited the replication of human cytomegalovirus growth. In vivo they were tested in an infection model on immune compromised mice. The fruit herbal extract was orally administered to the mice treated with 50 mg/kg cyclosporine for one day before the intraperitoneal infection against standard. The efficacy was evaluated by the reduction of the virulent yield in the lung infection. The *T. chebula* extract fruit pulp significantly suppressed the virus yields in the lungs of the treated mice compared with the water treated animals. Article is concluded that the water extracts can be beneficial for the prophylaxis from cytomegalovirus in immunocompromised patients [23]. The extract of *T. chebula* showed a strong anti-HSV-1 activity in combination with acyclovir and antiviral drug it seems like drug herb synergism. on higher doses, corresponding

to the human use it limited the development of skin lesions and prolonged the mean survival times of infected mice compared with both acyclovir and with the mice treated alone with the herbal extract ($p<0.01$ and $p<0.05$). Reduction of virus yields in the skin and brain stronger than acyclovir alone. It exhibited a stronger anti-HSV-1 activity in the brains than in the skin, in contrast to acyclovir treatment alone. The combination was no toxic to mice and maybe safer for human use.

Antimutagenic Activity

Tannin fractions and gallic acid from the dried fruit pulp of *T. chebula* were evaluated for their antimutagenic potential. They all were highly significantly active against S9-dependent mutagen 2AF. The effect corresponds with the nature of the fractions; and the monomeric gallic acid efficacy was the least effective [24]. The water extract of *T. chebula* fruits pulp inhibited the direct acting mutagens sodium azide and 4-nitro-o-phenylendiamine in the strains TA100, TA1535, TA97a, TA98 of Salmonella typhi murium and S9-dependent mutagen 2-aminofluoren in TA97, TA98 and TA100 strains and many other strains [25]. In the VITOTOX Test for detection of DNA damages in prokaryotic and eucaryotic cells fruit extracts from *T. chebula* were not genotoxic. This result is consistent with another Ames Test. But in the COMET assay shown that increased DNA damages with a content above 500 ppm.

Anticancer Activity

In human malignant cell lines a 70 % methanolic extract of *T. chebula* fruits pulp shown decreased the cell viability, inhibited the cell proliferation and induced the cell death in a dose-dependent manner. In lower concentrations minimal apoptosis was induced, but at higher dose concentrations necrosis was the major mechanism of the cell death. The following IC50 values could be revealed: Chebulinic acid: 53.2+/-0.16 µM, tannic acid 59.0+/-0.19 µM, ellagic acid 78.5+/-0.24 µM, respectively [26].

Antioxidant and Cytoprotective Effects

The aqueous extract of *T. chebula* fruit pulp was tested for its cytoprotective activity. Show, the cultured rat primary hepatocytes and rat whole livers the extract reversed an oxidative injury; caused by tert-butyl hydroperoxide and lactate dehydrogenase leakage significantly. meanwhile in vivo pre-treatment with 500 or 1000 mg 5 day before; a single dose of 0.01 mM/kg i.p. is significantly lowered the serum levels of the hepatic enzyme markers aspartate aminotransferase and alanine transferase and reduced the indicators of oxidative stress in the liver, such as glutathione disulfide content and lipid peroxidation in a graded dose dependent manner . The histopathological examination of the rat livers showed a reduction of liver lesions and repaired necrosis. The authors speculate that the extract has the possibility of preventing the oxidative damages in living systems. The aqueous extract of *T. chebula* was tested for its antioxidant activity after exposure of gamma radiation in rat liver microsomes and mitochondria. It inhibits xanthine oxidase activity. It is a big scavenger of DPPH radicals. An HPLC analysis showed the presence of ascorbate, gallic acid and ellagic acid. The extract seems to be able to protect cell organelles from radio-induced damages [27,28]. The water extract of *T. chebula* fruit pulp was tested for its radio protective ability and, free radical neutralizing ability was comparable to that of ascorbate (100 µM) 93.5% and gallic acid (100 µM) 91.5%, both. It has ability to protect the plasmid DNA pBR322 from the radiation-induced strand breaks. The administration of 80 mg/kg i.p. prior to whole body irradiation of mice (4 Gray) reduced the peroxidation of lipids membrane in the mice liver from radiation-induced DNA damages [28,29]. Human lymphocytes also were not subjected to DNA damages exposed in vitro by 2 Gray. In preparations of liver microsomes, of mitochondria and of R.B.C from Wistar rats, arjunic acid revealed as a strong antioxidant and as a free radical scavenger more potent than ascorbic acid .Triphala, a ayurvedic combination of equal proportion of the plants *T. chebula, T. bellerica* and Emblica officinalis is extensively used in the Indian medicinal system ayush. The extracts alone, or combined, were verified for their inhibition activity of lipid peroxidation and scavenging hydroxyl and superoxide radicals in vitro. The 50% inhibition of lipid peroxidation, induced by Fe2+/ascorbate were 85.5, 27, 74, and 69 µg/mL. The concentrations required for inhibition of hydroxyl radical scavenging were 165, 71, 155.5, and 12.5 µg/mL. The oral administration of the fruits extracts (100 mg/kg) reduced the blood sugar level in normal and alloxan (120 mg/kg) induced diabetic rats model significantly within 4 h. A continued daily administration sustained the effect. Toxicity assays with mouse fibroblasts showed IC50 values =/> 1500 mµg/mL. The integrity of human erythrocyte membranes was not addressed at these IC50 values [30,31].

Pharmacological Effects

Activity against Anaphylactic Shock

The effect of the water constitution soluble fraction of a portioned methanol extract from *T. chebula* fruit pulp was tested in an anaphylactic shock of rat model in vivo.

The results were tested by the death of rats (200-300 g) and ICR mice (20-30 g).

Doses of 0.01-1.0 g/kg of the fruit extract, administered 1 h before the experiment inhibit the anaphylactic shock with 100 %. Administration after 5-10 min decreased the mortality was dose-dependently. Oral application reduced the subcutaneous anaphylaxis with 63.5 +/-7.8 %. From the rat estimation of mast cells the release of histamine was hindered in a dose dependent manner [31].

Antispasmodic Activity

Crude extract of *T. bellerica* fruit caused the relaxation of spontaneous contractions in the isolated rabbit smooth muscle jejunum at a concentration of 0.1 - 3.0 mg/mL and guinea pig ileum preparation it produced a parallel rightward shift of acetylcholine curves. On rodents, it has got the ability to protect against castor oil-induced diarrhoea and carbachol-mediated bronchoconstriction [32].

The authors expressed that the extract possesses a combination of anticholinergic and Ca2+ - antagonistic effects which may explain its folkloristic use [33].

Gastrointestinal Activity

In the Indian medicine system *T. chebula* is a commonly used agent for improving gastrointestinal motility. With Charles Foster rats gastric emptying was measured.

Rats given *T. chebula* (100 mg/kg/day) increased their gastric emptying with 86.57+/-6.65 % ($p<0.01$) compared with normal rats (51.6+/-7.79 %). From this study *T. chebula* can serve as an alternative to prokinetic drugs available today [34].

Immunosuppressive Effects

Gallic acid and chebulagic acid, isolated from fruit pulp of *T. chebula* inhibited the killing activity of CD8 and CTL clones at IC50 values of 30 and 50 μM, respectively. Granule exocytose in response to anti-CD3 stimulation was also blocked by both substances at the equivalent dose depended concentrations. Chebulagic acid from immature seeds of *T. chebula* is a potent suppressor of the T cell activity [35].

In DBA/1J mice model of arthritis subcutaneous immunization with bovine type II collagen on days 0 and 21. Chebulagic acid was administered i.p for 3 weeks, either as prophylaxis (10 or 20 mg/kg) before disease onset or as a therapy (20mg/kg) after disease onset. In both the prophylactic and either in the therapeutic model, all clinical score, like serum levels of total and anticollagen IgG and levels of interleukin-10 and interleukin-6 were significantly reduced.

Serum levels of the transforming growth factor beta were markedly increased. The number of the granulocytes was reduced, but the proportion of CD4+, CD25+ T cells was greater in the knee joints of the treated with chebulagic acid in mice [35]. Authors expressed that chebulagic acid significantly suppressed the onset and progression the disease inmice.

Cardiotonic Activity

Whole fruit pulp of *T. chebula* is claimed to be useful in the treatment of heart diseases. Different extracts from the dried pulp without kernels have been tried on isolated frog hearts, therefore. For each fruit extract ten-to fifteen experiments were performed, the results are the average of them.

All extracts exhibited cardioprotective activity. The benzene and chloroform extracts showed a moderate cardioprotective activity, though at high doses because they were not completely soluble in the experimental Ringer solution. Ethylacetate, butanone, butanol and other aqueous extracts exerted fairly potent cardioprotective activities. These all given easily dispersible solution, produced dose dependent positive inotropic effects and an increase in the cardiac output. There was no appreciable change in the heart rate. Propranolol could not inhibit the activity of the rabbit heart. Extracts are being tested here stimulated the isolated perfusion frog heart without inducing depression. Chebulin, isolated from the fruit of *T. chebula* was found to depress the isolated perfusion thus the cardiotonic effects of the various extracts appear to be due to some principles present in them [28]. The fruit of *T. chebula* is claimed to be useful against other maladies especially against heart diseases. They are integrated into the composition of many indigenous remedies. Besides the known effects of extracts on isolated frog hearts in this investigation of extracts are applied on (Na+, K+ and Mg2+) ATPases of a whole homogenate prepared from the ventricular portion of the frog heart. Extracts exerted the following inhibition: Butanolic extract solution of 13.5% and 57.4% with doses of 0.5 and 1.0mg Aqueous extract 31.22%, 40.68%, and 49.18% with doses of 0.1, 0.5, and 1.0mg. The inhibition of the ATPase receptor system with the dose of 1mg is enormous. It is more important than

caused by ouabain, which is a specific inhibitor of this ATPase [35].

In rats with isoprotenerol (200 mg/kg) induced myocardial damage an ethanolic extract of *T. chebula* fruits pulp (500 mg/kg) was tested for MI. The level of lipid peroxidase enzyme increased significantly in the serum and the heart. The activity of the myocardial marker enzymes decreased with a concomitant increase in the activity of the serum level. The myocardial necrosis was confirmed by histopathological examination. Pre-treatment with the extract ameliorated the effect of isoprotenerol on the lipid peroxide formation and retained the activities of the diagnostic marker enzymes [36].

Activity Against Intoxication of Cardiac Tissue with Arsenic

Arsenic is a harmful metalloid and is ubiquitous in many environments. Animal study on Mice orally administered 10 mg $NaAsO_2$ for two days accumulated the toxin in the cardiac tissue and reduced the cardiac antioxidant enzymes, namely superoxide dismutase, catalase, Glutathione-S-transferase, glutathione reductase, and glutathione peroxidase. The gift of arsenic increased the total cholesterol level and reduced the high density lipoprotein cholesterol content in the sera. Arjunolic acid, given at a dose of 20 mg/kg for 4 days prior to the intoxication, protected the cardiac tissue from the arsenic-induced oxidative impairment and prevented the hyperlipidemia [37].

Antioxidative Activity against Hepatoxicity

A purified chemical compound, containing chebulic acid and its optical isomer neochebulic acid with a ratio of 2:1 was isolated from the ethanolic extract of *T. chebula* fruits by consecutive extraction. The components were verified by spectroscopic analysis, NMR and MS instrument analysis. These compounds shown in vitro a free radical scavenging activity in isolated rat hepatocytes and a ferric reducing activity. The treatment of infected hepatocytes of the rat with chebulic acid significantly reduced the tert-butyl hydroperoxide (t-BHP)-induced cell cytotoxicity, the intracellular reactive oxygen species level and the ratio of GSSH oxidized form of glutathione (GSH) to the over total GSH (GSH + GSSH) (4.42 %), as compared to that with t-BHT alone (8.33 %) [38].

An ethanolic (95 %) extract of *T. chebula* fruits able to prevent the hepatotoxicity caused by antituberculotic drug like rifampicin, isoniacid and pyracinamide within 12 weeks. Chebuloside was the marker of the extract are the hepatoprotective effect can be attributed to this substance, because of its antioxidative and membrane stabilizing property [38].

Evaluation

In *T. chebula* and its related plants tannins are the main biologically active substances. They are present in different molecular forms, like dimers, tetramers and polymers, depending from the mode of extraction. In aqueous or ethanolic extracts the lower molecules are prevalent. From a medicinal view most of them bring good results. They are effective against bacteria, viruses, parasites and cancer cells. They protect animals and organs with their antioxidant property. They are nearly not toxic. But because there are no dosages known for the use in humans, they cannot be recommended for the internal use with humans.

Conclusion

Terminalia chebula is a potential herbal drug that has plethora of pharmacological actions as evident from this review, however, many other in-vivo and in-vitro researches are still needed to explore its molecular mechanism of action or any other pharmacological action which are still addressed in future.

References

1. Gupta P (2012) Biological and pharmacological properties of *Terminalia chebula Retz*. (haritaki)- An overview: Int J Pharm Pharmac Sci 2(4): 2.

2. Ajayi IA, Ajibade O, Oderinde RA (2011) Preliminary Phytochemical Analysis of some Plant Seeds. Res J Chem S 1(3): 58-62.

3. Das B (1991) *Materia Medica of Ayurveda.* (B Jain Publisher, New Delhi) 8.

4. Srikanthmurthy KR (2000) *Bhavaprakasha of Bhavamishr.* (Krishnanda Academy, Varanasi) 160.

5. Varrier PS (1996) *Indian Medicinal Plants: A Compendium of 500 species.* Edited by Warrier PK, Nambiar VPK and Ramankutty C. Hyderabad: Orient Longman 5: 263.

6. Jagtap AG, Karkera SG (1999) Potential of the aqueous extract of *Terminalia chebula*as an anticaries agent. J Ethnopharmacol 68(1-3): 299-306.

7. Ahmad I, Mehmood Z, Mohammad F (1998) Screening of some Indian medicinal plants for their antimicrobial properties. J Ethnopharmacol 62(2): 183-193.

8. Sato Y, Oketani H, Singyouchi K, Ohtsubo T, Kihara M, et al. (1997) Extraction and purification of effective antimicrobial constituents of *Terminalia chebula* RETS against methicillin-resistant Staphylococcus aureus. Biol Pharm Bull 20(4): 401-404.

9. http://www.toddcaldecott.com/index.php/herbs/learning-herbs/361-haritaki

10. Balunas MJ, Kinghorn AD (2005) Drug discovery from medicinal plants. Life Sci 78(5): 431-441.

11. Bajpai M, Pande A, Tewari SK, Prakash D (2005) Phenolic contents and antioxidant activity of some food and medicinal plants. Int J Food Sc Nutr 56(4): 287-291.

12. Bhattacharya S, Chaudhuri SR, Chattopadhyay S (2007) Healing properties of some Indian medicinal plants against indomethacin-induced gastric ulcerations of rats. Clin Biochem Nutr 41(2): 106-114.

13. Carounanidi U, Satyanaranyanan R, Velmurugan A (2007) Use of an aqueous extract of *Terminalia chebula*as an anticaries agent: A clinical study Indian. J Dent Res 18(4): 152-156.

14. Ding G, Lu YR, Ji CR, Liu YZ (2001) Analysis of tannins in fructus Chebulae and its confusion varieties HPCE. Yao Xue Xue Bao 36(4): 292-295.

15. Shuaibu MN, Wuyep PA, Yanagi T, Hirayama K, Tanaka T, et al. (2008) The use of microfluorometric method for activity-guided isolation of antiplasmodial compounds from plant extracts. Parasitol Res 102(4): 1119-1127.

16. Dos Santos IC, de Carvalho SH, Solleti JI, Ferreira de La Salles W, Teixeira da Silva de La Salles K, et al. (2008) Studies of *Terminalia catappa* oil: Characterization and biodiesel production. Bioresour Techno 99(14): 6545-6549.

17. Atawodi SE, Ameh DA, Ibrahim S, Andrew JN, Nzelibe HC, et al. (2002) Indigenous knowledge system for treatment of trypanosomiasis in Kaduna state of Nigeria. J Ethnopharmacol 79(2): 279-282.

18. Zhang X, Chen C, He S, Ge F (1997) Supercritical CO_2 extraction of the fatty oil in *Terminalia chebula* and GC-MS analysis. Zhong Yao Cai 20(9): 463-464.

19. Manohar VR, Chandrashekar R, Rao SN (2012) Phytochemical Analysis of Ethanolic Extract of Fruits of *Terminalia chebula*(EEFTC), Drug Invention Today 4(10): 491-493.

20. Aquil F, Khan MS, Owais M, Ahmad I (2005) Effect of certain bioactive plant extract on clinical isolates of ß-lactamase producing methicillin resistant Staphylococcus aureus. J Basic Microbiol 45(2): 106-114.

21. Malekzadeh F, Ehsanifar H, Shahamat M Levin M, Colwell RR (2001) Antibacterial activity of black myrobalan (*Terminalia chebula*) against Helicobacter pylori. Int J Antimicrob Agents 18(1): 85-88.

22. Lee SI, Hyun PM, Kim SH, Kim KS, Lee SK, et al. (2005) Suppression of the onset and progression of collagen-induced arthritis by chebulagic acid screened from a natural product library. Arthritis Rheum 52(1): 345-53.

23. Kaur S, Grover IS, Singh M, Kaur S (1998) Antimutagenicity of hydrolysable tannins from *Terminalia chebula*in Salmonella typhimurium. Mutat Res 419(1-3): 169-179.

24. Grover IS, Bala S (1992) Antimutagenic activity of *Terminalia chebula* (myrobalan) in Salmonella typhimurium. Ind J Exp Biol 30(4): 339-341.

25. Saleem A, Husheem M, Härkönen P, Pihlaja K (2002) Inhibition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula* fruit. J Ethnopharmacol 81(3): 327-336.

26. Naik GH, Priyadarsini KI, Naik DB Gangabhagirathi R, Mohan H (2004) Studies on the aqueous extract of *Terminalia chebula*as a potent antioxidant and a probable radioprotector. Phytomedicine 11(6): 530-538.

27. Reddy VRC, Kumari SVR, Reddy BM, Azeem MA, Prabhakar MC, et al. (1990) Cardiotonic activity of the fruits of *Terminalia chebula*. Fitoterapia 41(6): 517-525.

28. Saxena M, Faridi U, Mishra R, Gupta MM, Darokar MP, et al. (2007) Cytotoxic agents from *Terminalia arjuna.* Planta Med 73(14): 1486-1490.

29. Saxena S, Saxena RK (2004) Statistical optimization of tannase production from Penicillium variable using fruits (*Chebulic myrobalan*) of *Terminalia chebula*. Biotechnol Appl Biochem 39(1): 99-106.

30. Murali YK, Anand P, Tandon V, Singh R, Chandra R, et al. (2007) Long-term effects of *Terminalia chebula* on hyperglycemia and associated hyperlipidemia, tissue glycogen content and in vitro release of insulin in streptozotocin induced diabetic rats. Exp Clin Endocrinol Diabetes 115(10): 641-646.

31. Shin TY, Jeong HJ, Kim DK, Kim SH, Lee JK, et al. (2001) Inhibitory action of water soluble fraction of *Terminalia chebula* on systemic and local anaphylaxis. J Ethnopharmacol 74(2): 133-140.

32. Gilani AH, Khan AU, Ali T, Ajmal S (2008) Mechanisms underlying the antipasmodic and bronchodilatory properties of *Terminalia bellerica* fruit. J Ethnopharmacol 116(3): 528-538.

33. Tamhane MD, Thorat SP, Rege NN, Dahanukar SA (1997) Effect of oral administration of *Terminalia chebula* on gastric emptying: an experimental study. J Postgrad Med 43(1): 12-13.

34. Hamada S, Kataoka T, Woo JT, Yamada A, Yoshida T, et al. (1997) Immunsuppressive effects of gallic acid and chebulagic acid on CTL-mediated cytotoxicity. Biol Pharm Bull 20(9): 1017-1019.

35. Azeem MA, Madhava Reddy B, Appa Rhao AVN (1992) Effect of *Terminalia chebula* extracts on frog heart muscle (Na^+, K^+, Mg^{++}) ATPase activity Fitoterapia 43(4): 300-303.

36. Suchalatha S, Shyamala Devi CS (2004) Protective effect of *Terminalia chebula* against experimental myocardial injury induced by isoproterenol. Indian J Exp Biol 42(2): 174-178.

37. Manna P, Sinha M, Sil PC (2008) Arsenic-induced oxidative myocardial injury: Protective role of arjunolic acid. Arch Toxicol 82(3): 137-149.

38. Sun FY, Chen XP, Wang JH (2008) Arjunic acid, a strong free radical scavenger from *Terminalia arjuna*. Am J Chin Med 36(1): 197-207.