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Therapeutic & Phytochemical Profiling of *Terminalia chebula* Retz. (Harad): A Review

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Abstract
Terminalia chebula Retz., belonging to the Combretaceae family, is very important medicinal plant found throughout India and other subtropical and tropicals regions of the world. It can exhibit various kinds of pharmacological activities due to presence of various kinds of phytoconstituents such as gallic acid, methyl gallate, ethyl gallate, ellagic acid, chebulagic acid, chebulinic acid, penta-*O*-galloyl-*β*-D-glucose and many others. Owing to significant health benefits exerted by *T. chebula*, it is known as 'King of Medicines' in Tibet and is used as conventional medicine for household remedy against many ailments. It is reported to possess anticancer, antimicrobial, antioxidant, antiviral, cardiotonic, antidiabetic, immunomodulatory, memory‐enhancing, and anti‐inflammatory activities. So the main aim of current review article is to focus on the various therapeutical potentials of *T. chebula* and on the various phytochemicals present in its various parts that are responsible for such action.

Keywords: *Terminalia chebula* Retz., medicinal plants, therapeutic potential, phytochemicals

Introduction
Medicinal plants are part and parcel of human society since the beginning of civilization. Developing as well as developed world both are attracted towards herbal system of medicines due to economic issues and negligible side effects respectively. Human interest for utilization of medicinal and aromatic plants for cure and prevention of various ailments is revived in recent times due to general belief that green medicine is healthier than synthetic product [1].
Terminalia chebula Retz. is commonly known as Harad (in Hindi), Chebulic myrobalan (in English) and Hritaki (in Sanskrit). It belongs to the family Combretaceae and found throughout India and other countries having tropical and subtropical environment. It is popular traditional medicine of Unani, Ayurveda and Homeopathic medicinal systems. Owing to various pharmacological activities, it is known as "King of medicines" in Tibet and list top in Ayurvedic Materia Medica.

Fig 1: *Terminalia chebula* fruits

It is used to treat numerous disease symptoms such as tumors, intermittent fever, rheumatism, paralysis, memory loss, diabetes, neurological disorders, hepatomegaly, constipation [2, 3]. It is reported to possess various medicinal properties such as antioxidant, antidiabetic, antimicrobial, anti-inflammatory, antimutagentic, antiproliferative, cardioprotective, antiarthritic, hepatoprotective, preventing, gastrointestinal motility and wound healing activity [4].

Photochemical profiling of *T. chebula*

As there is correlation between nature engineered secondary metabolites and pharmaceutical activity, various known or unknown phytoconstituents from harad can be potent agents for discovery of noval drugs. Total phyto-constituents of *Terminalia chebula* are hydrolysable tannins (which may vary from 20-50%) and they are responsible for pharmacological activities. various kinds of phytochemials are shown in table 2, 3, 4, 5 & 6 [5].

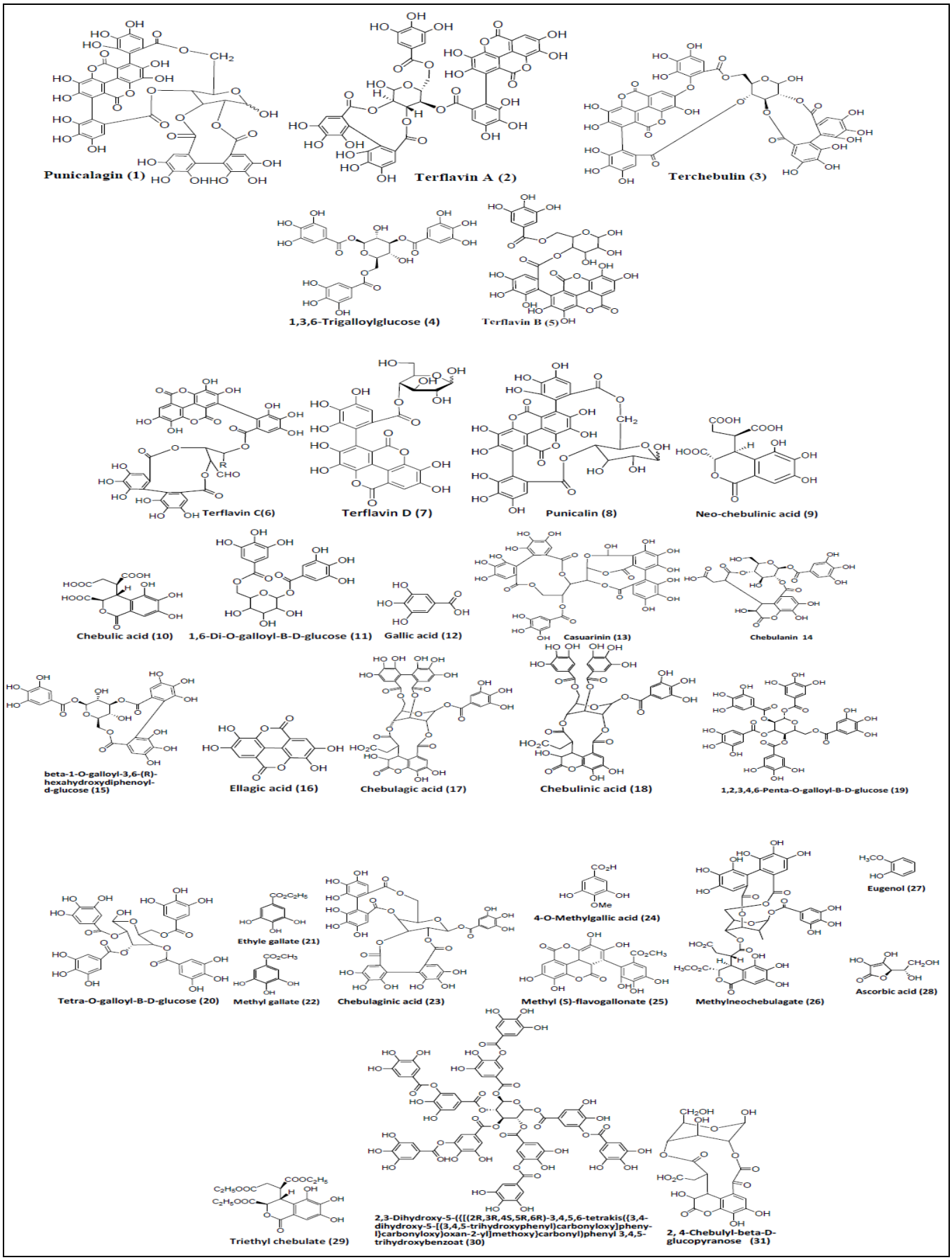

Fig 2: Structure of chemical constituents (Tannins) of *Terminalia chebula* [5]

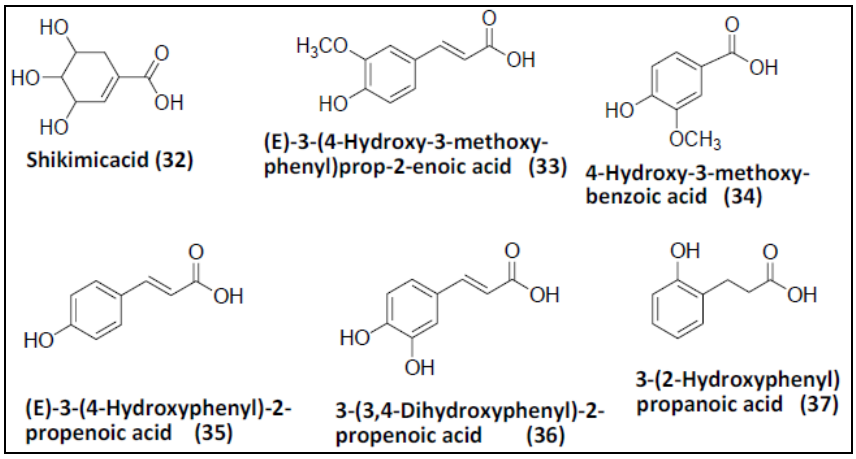

Fig 3: Structure of some phenolic carboxylic compounds from *Terminalia chebula* [5]

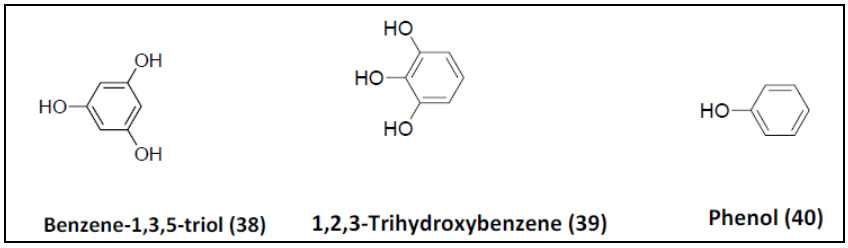

Fig 4: Structure of some phenolic compounds from *Terminalia chebula* [5]

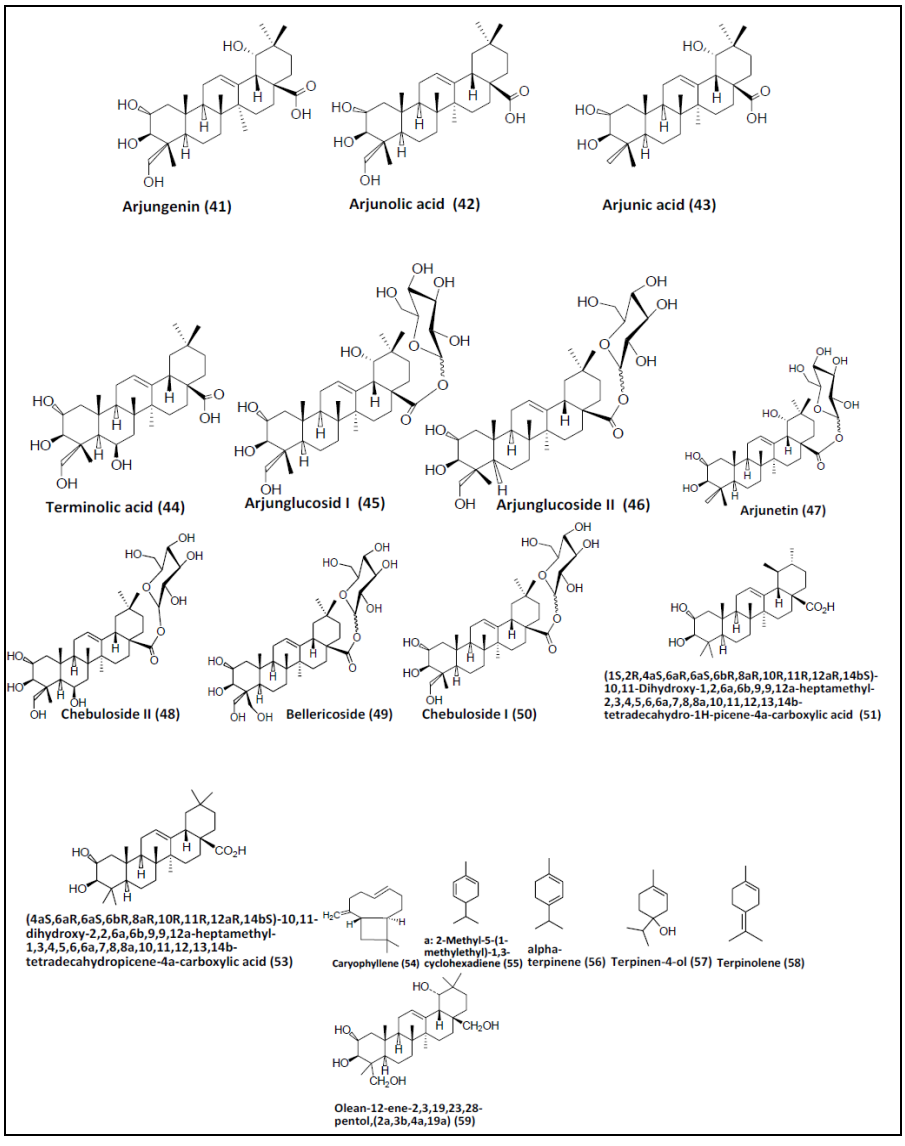

Fig 5: Structure of Terpenoids and Triterpene Saponins from *Terminalia chebula* [5]

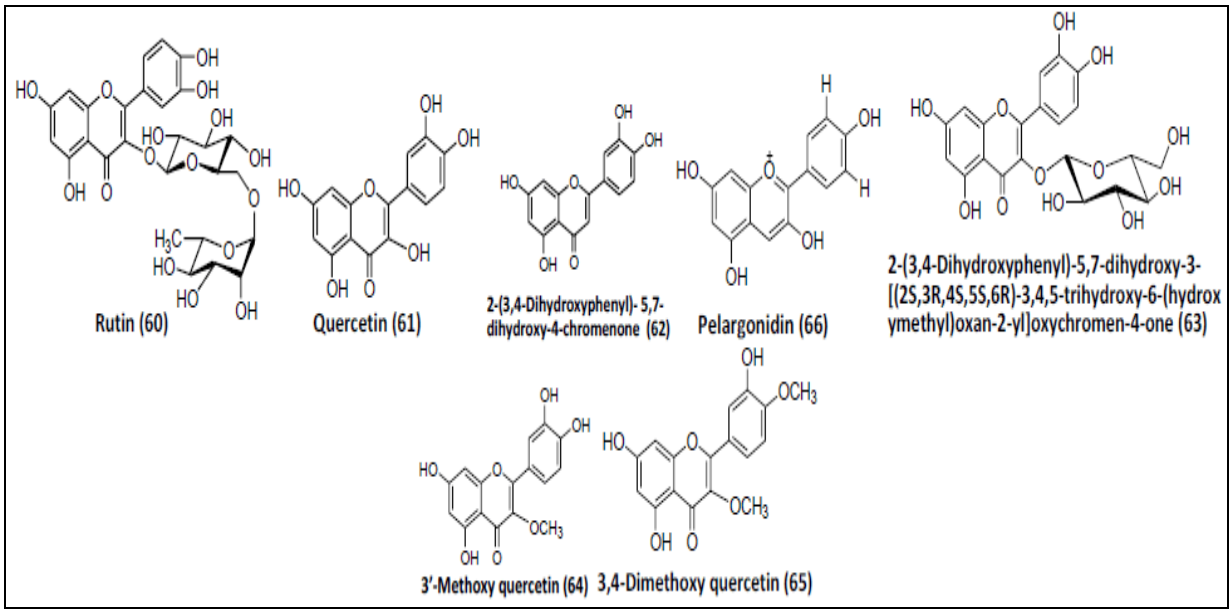

Fig 6: Structure of Flavonoids from *T. chebula* [5]

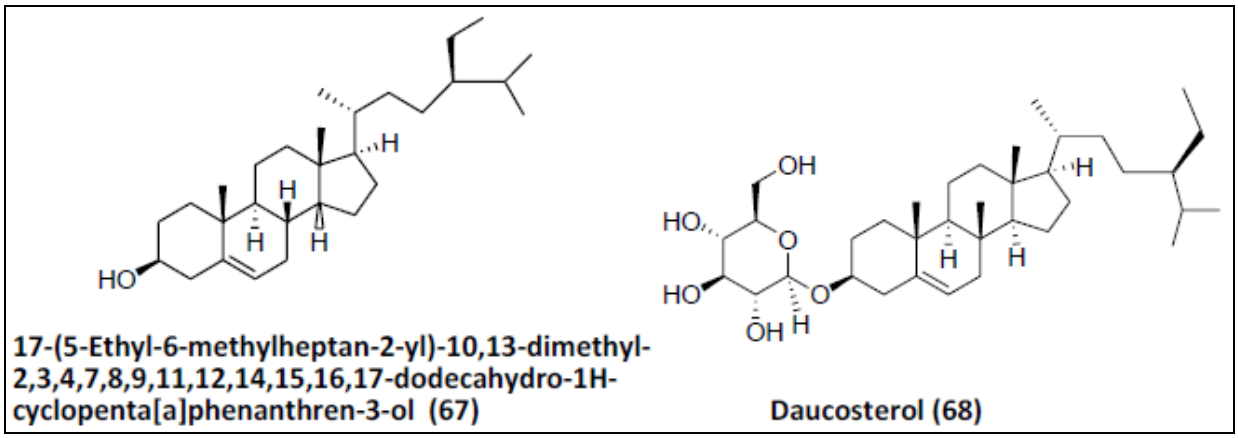

Fig 7: Structure of sterols from *T. chebula* [5]

Traditional uses of *Terminalia chebula*

- 'Triphala' is commonly used herbal preparation of three fruits from *T. chebula*, *T. bellerica*, *E. officinalis*, and is used as laxative in chronic constipation, detoxifying agent of the colon, food digestive problems (poor digestion and assimilation) and rejuvenator of the body [6]. Triphala is also known to stimulate appetite and is useful in treating cancer and detoxification. Triphala is considered as the most versatile of all herbal formulations and is prescribed as a cardiotonic and for Candida infection [7].
- It is used in Thai traditional medicine as a carminative, astringent and expectorant [8].
- It is one of top listed plant in Ayurvedic materia medica for the treatment of asthma, bleeding piles, sore throat, vomiting and gout [9].
- It is used as anti-hemorrhagic agent by providing defence against bleeding.
- Its powder is used for cleansing of teeth and is believed to make gums and teeth stronger.
- Harad fruit and sugar together are used for treatment of opthalmia, skin infections and edema.
- The pulp of the fruit is given in piles, chronic diarrhea, dysentery, flatulence, asthma, urinary disorder, vomiting, hiccup, intestinal worms and enlarged spleen and liver [10].
- The word mordant has been consequent from Latin word "modere" which means to nibble, as it nibbles the surface of a substrate and helps to fix a dye on the substrate. The leaves and fruits of *T. chebula* are also used as mordant [11].
- In allopathy, *T. chebula* extract is used as an astringent [10].

Therapeutic activities of *Terminalia chebula* parts

1. Antioxidant activity

Oxidative stress is due to imbalance between the rate of free radicles formation and rate of free radicals scavenging. These free radicals are mainly responsible for the tissue damage, mutation in genetic material and many degenerative diseases [12]. To counteract these ROSs in human body, various kinds of synthetic drugs are used which can scavenge free radicals formed during metabolism in human body [13]. But now-a-days natural antioxidants from plants are replacing synthetic drugs due to their negligible side effects [14]. As it is well documented that phenolics and flavonoids are responsible for antioxidant ability of plants, so we can infer that antioxidant capacity of plant extracts is directly proportional to the amount of phenolics and number of hydroxyl group on each molecule. Cheng *et al.* (2003) reported that *T. chebula* fruit extracts in water, methanol and 95% ethanol possessed high amount of total phenolic, total triterpenoids and total tannin content [15].

Naik *et al.* (2004) reported the aptitude of the *T. chebula* fruit extract in deactivating 1, 1-diphenyl-2-picrylhydrazyl (DPPH)

radicals. The decrease in DPPH absorption in the presence of varying concentration (3.5 to 23 µg/ml) of the extract has been monitored and it can be seen that the absorbance due to DPPH decreases continuously up to 23 µg/ml [16].

In vitro antioxidant and reactive oxygen species scavenging activities of *Terminalia chebula*, *Terminalia belerica* and *Emblica officinalis* fruit extracts was evaluated by Hazra *et al.* (2010). They found that the flavonoid content follows the order *T. chebula* > *E. officinalis* > *T. belerica* whereas the phenolic content follows the order *E. officinalis* > *T. belerica* > *T. chebula* [17].

Studies by Chen *et al*. (2011) have shown that *Terminalia chebula* is an excellent anti-oxidant. In a study, 6 extracts and 4 pure compounds of *Terminalia chebula* exhibited *in-vitro* antioxidant properties of anti-lipid peroxidation, anti-superoxide radical formation and DPPH activities at different concentration. The results demonstrated that tri-ethyl-chebulate was a strong antioxidant and free-radical scavenger, which might contribute to the anti-oxidative ability of *Terminalia chebula* [18].

Walia *et al.* (2011) studied the antioxidant efficacy and phenolic content of two chloroform extracts of fruits of *Terminalia chebula* prepared by maceration and sequential method and observed that the chloroform extract prepared by maceration method has low phenolic content as compared to chloroform extract prepared by sequential method [19].

Studies carried out by Arya *et al.* (2012) showed that methanolic extracts of *T. chebula* leaves have high Total Phenolic Content (266.16 mg GAE/g extract), Total Flavonoid Content (29.31 mg Quercetin/g extract), Total Tannin Content (8.36 Catechin/g extract) and good DPPH scavenging capacity (DPPH IC_{50} = 11.6 µg/mL) [20].

Tariq and Reyaz (2013) was studied the photochemical analysis of *Terminalia chebula* plant extracts of leaves, fruits, seed, stem and roots. The phenol content was maximum in roots (72.46 mg/gdw) followed by seeds, leaves, stem and fruits. The sugar content was highest in leaves (7.12 mg/gdw) followed by fruits, stem, root and seed. The protein content was maximum in fruits (44.40 mg/dgw) followed by seeds, leaves, stem and roots [21].

Guleria *et al*. (2016) evaluated the amount of the total phenolic, flavonoid and antioxidant activity in ethanolic extract of fruit and leaves of *Terminalia chebula* from Himachal Pradesh. Qualitative phytochemicals analysis of ethanolic extract of fruit and leaves revealed the presence of phenols, tannins, carbohydrates, glycosides, saponin, phytosteriods and flavonoids. Phenolic content of ethanolic extract of fruit (242.3±5.09 mg/g gallic acid equivalents) was higher than that of leaves (162.4±4.31 mg/g gallic acid equivalents); whereas ethanolic extract of leaves (157.75 ± 3.88 mg/g rutin equivalents) possess higher amount of flavonoids content as compared to that of fruits (126.45±5.58 mg/g rutin equivalents). DPPH activity of ethanolic extract of fruits (IC50-6.5 µg/ml) was more than that of leaves (IC50-7.034 µg/ml) [22].

Venkatesan *et al*. (2017) found that different kinds of phytochemicals (proteins, carbohydrates, vitamin C, tannins, flavonoids and phenolic compounds) were present in various concentrations in all methanolic and acetone extracts of *T. chebula* bark. They also reported that highest quantity of both primary and secondary metabolites was noticed in acetone extract such as, phenol 159.51 ± 0.86 µg/mg GAE, tannin 151.89 ± 1.92 µg/mg TAE, flavonoid 117.56 ± 0.60 µg/mg CE, flavonol 73.26 ± 0.33 µg/mg RU, carbohydrate 154.67 ± 0.59 GE, ascorbic acid 134.97 ± 0.41 µg/mg AAE and protein 76.00 ± 2.00 µg/mg BSAE followed by methanol extract [23].

Saha *et al.* evaluated The polyphenolic extract of *T. chebula* fruits for antioxidant activity by determining the reducing power, total antioxidant capacity, DPPH radical concentration (IC_{50} 14 µg/mL), nitric oxide radical concentration (IC_{50} 30.51 µg/mL) and hydrogen peroxide scavenging activity (IC_{50} 265.53 µg/mL) under *in vitro* conditions. They studied that the extract had significant reducing capacity and nitric oxide scavenging activity. It also scavenged hydrogen peroxide-induced radicals. The activity of the extract might be due to the total polyphenolic content. The antioxidant activity of the extract was significantly higher than the standard ascorbic acid, and its activity is concentration-dependent [24]. It is concluded that a polyphenolic-rich fraction of *T. chebula* fruits is a potential source of natural antioxidants.

2. Anti-inflammatory activity

Anti-inflammatory effect of fruit extract of *T. chebula* on cultured RAW 264.7 cell lines was determined by COX/LOX assay. Cyclooxygenases (COX-2) and 5-lipoxygensases (5-LOX) are key marker enzymes for the diseases with impaired arachidonic acid metabolism [25, 26]. In this attempt to isolate a natural product with COX-LOX dual inhibition, it was identified *Terminalia chebula* as a potential source. Preliminary studies with the methanolic fruit extract of *T. chebula* showed potent inhibition of COX-2 and 5-LOX with IC50 values of 50.54 and 100.254µg/ml respectively [27].

3. Anticancer activity

Growth of several malignant cell lines such as 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) was significantly inhibited by 70 % methanolic extract of *Terminalia chebula* fruit. In all cell lines studied, the extract decreased cell viability, inhibited cell proliferation, and induced cell death in a dose dependent manner [28]. 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 [29]. Several other studies including above clearly indicates that fruits of *T. chebula* exhibits significant anti-cancer potential.

Anti-bacterial activity

Medicinal plants are important source for discover a new antimicrobial agents with significant activity against infective microbes. Venkatesan *et al.* studied the *in vitro* antibacterial potential in various solvent extracts of *Terminalia chebula* bark and found out that Acetone extract expressed significant high antibacterial activity against *S. typhi* (15 mm) [23].

Ponnusamy *et al.* studied the antibacterial activity of ethanolic extract of *T. chebula* fruit against clinically important strains of bacteria by using disc diffusion method. They found out that *T. chebula* extract was highly effective against *Salmonella typhi* SSFP 4S, *Staphylococcus epidermidis* MTCC 3615, *Staphylococcus aureus* ATCC 25923, *Bacillus subtilis* MTCC 441and *Pseudomonas aeruginosa* ATCC 27853. These results indicated that *T. chebula* dry fruit possesses a potential broad spectrum antimicrobial activity [30].

Hypoglycemic activity

T. chebula fruit 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 [31]. Similarly ethanolic extracts of harad fruits exhibited appreciable amount of anti-diabetic activity on Alloxan induced diabetic rats [32].

Conclusion

Terminalia chebula is very good source of diverse kinds of phytochemicals that can be used for development of novel drugs. It may be inferred from current review article that harad is very potent medicinal plant for medicinal purposes due to versatile pharmacological activities associated with it.

References

1. Philipson JD. Plants as a Source of Valuable Products. In. Secondary Products from Plant Tissue Culture, Charlwood BV and MJ Rhodes (Eds.) Clarendon Press, Oxford, 1990, 1-22.
2. Nadkarni KM. Indian Materia Madica, Popular Prakashan Pvt. Ltd, Bombay 1976, 1202-11.
3. Kirtikar KR, Basu BD. *Terminalia chebula.* In: Indian Medicinal Plants, Lolit Mohan Basu Publication, and Allahabad, India, 1935, 1020-23.
4. Bag A, Bhattacharyya SK, Chattopadhyay RR. The development of *Terminalia chebula* Retz. (Combretaceae) in clinical research. Asian Pac J Trop Biomed. 2013; 3(3):244-52.
5. Riaz M, Khan O, Sherkheli MA. Chemical constituents of *Terminalia chebula*. Nat Prod Ind J. 2017; 13(2):112.
6. Gupta PC. Biological and pharmacological properties of *Terminalia chebula* Retz. (Haritaki). Int J Pharm Pharm Sci. 2012; 4:62-68.
7. Kaur S, Michael H. The *in vitro* cytotoxic and apoptotic activity of Triphala-an Indian herbal drug. J Ethnopharmacol. 2005; 97:15-20.
8. Panunto W, Jaijoy K. Acute and chronic toxicity studies of the water extract from dried fruits of Terminalia chebula Rezt. In rats. IJARNP. 2011; 3:36-43.
9. Aneja KR, Joshi R. Evaluation of antimicrobial properties of fruit extracts of Terminalia chebula against dental caries pathogens. Jundishapur J Microbio. 2009; 2:105-111.
10. Thomas J, Joy PP, Mathew G, Skaria S, Duethi BP, Joseph TS. Agronomic practices for aromatic and medicinal plant, Directorate of arecanut and spices Development India. Calicut, Kerala, India, 2000, 124-128.
11. Kumar JK, Sinha AK. Resurgence of Natural Colorants. Natural Product Lett. 2004; 18:59-84.
12. Halliwell B, Gutteridge JM. Free Radicals in Biology and Medicine. Oxford University Press, Oxford, 1998.
13. Yazdanparast V, Ardestani A. *In vitro* antioxidant and free radical scavenging activity of *Cyperus rotundus*. J. Med. Food. 2007; 10:667-674.
14. Yazdanparast R, Bahramikias S, Ardestani A. *Nasturtium oficinale* reduces oxidative stress and enhances antioxidant capacity in hypercholesterolaemic rats. Chem. Biol. Interact. 2008; 172:176-184.
15. Cheng HY, Lin TC, Yu KH, Yang CM, Lin CC. Antioxidant and free radical scavenging activities of *Terminalia chebula*. Biological and Pharmaceutical Bulletin. 2003; 26(9):1331-1335.
16. 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; 11:530-538.
17. 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 Complementary and alternative Medicine. 2010; 10:20.
18. Chen X, Sun F, Ma L, Wang J, Qin H, Du G. *In vitro* evaluation on the antioxidant capacity of tri-ethylchebulate, an aglycone from *Terminalia chebula* Retz fruit. Indian Journal of Pharmacol. 2011; 43(3):6.
19. Walia H, Kumar S, Arora S. Comparative analysis of antioxidant and phenolic content of chloroform extract/fraction of *Terminalia chebula*. Journal of Basic and Clinical Pharmacy. 2011; 2(3):143-149.
20. Arya A, Nyamathulla S, Noordin MI, Mohd MH. Antioxidant & hypoglycemic activities of leaf extracts of three popular *Terminalia* species. E-Journal of Chemistry 2012; 9(2):883-892.
21. Tariq AL, Reyaz AL. Quantitative phytochemical analysis of traditionally used medicinal plant *Terminalia chebula*. International research Journal of Biotechnology. 2013; 4(5):101-105.
22. Guleria S, Dev K, Khosla PK. Comparative analysis of phytochemicals and antioxidant activities of fruit and leaves of *Terminalia chebula* from Himachal Pradesh. International Journal of Biology, Pharmacy and Allied Sciences. 2016; 5(6):1195-1206.
23. Venkatesan A, Kathirvel A, Prakash S, Sujatha V. Antioxidant, antibacterial activities and identification of bioactive compounds from *Terminalia chebula* bark extracts. Free Radicals and Antioxidants. 2017; 7(1):43-49.
24. Saha S, Verma RJ. Antioxidant activity of polyphenolic extract of *Terminalia chebula* Retzius fruits. Journal of Taibah University for Science. 2016; 10: 805-812.
25. Pelletier MJ, Lajeunesse D, Reboul P, Pelletier JP. Therapeutic role of dual inhibitors of 5-LOX and COX, selective and non-selective nonsteroidal anti-inflammatory drugs. Ann Rheum Dis. 2003; 62:501-509.
26. Goossens L, Pommery N, Hénichart JP. COX-2/5-LOX dual acting anti-inflammatory drugs in cancer chemotherapy. Curr Top Med Chem. 2007; 7:283-296.
27. Rani AA, Jeeva S, Punitha MJS. Anti Oxidant, Anti-Inflammatory, Antiproliferative And Apoptotic Properties Of *Terminalia Chebula* (Fruit) Towards Raw 264.7 And Oral KB Cell Lines. International Journal of Applied and Pure Science and Agriculture. 2016; 2(5):90-100.
28. Anonymous. The Wealth of India. Raw Materials, CSIR, New Delhi, India. 1976; 10:168-70.
29. Reddy DB, Reddy TCM, Sharan JS, Priya VN, Reddanna PL. Chebulagic acid, a COX–LOX dual inhibitor isolated from the fruits of *Terminalia chebula* Retz., induces apoptosis in COLO-205 cell line. Journal of Ethnopharmacology. 2009; 124:506-512.
30. Ponnusamy K, Ramadevi SR, Waheeta Hopper. Antibacterial activity of *Terminalia chebula* Retz fruit extract. African Journal of Microbiology Research. 2009; 3(4):180-184.
31. 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.

32. Kannan VR, Rajasekar GS, Rajesh P, Balasubramanian V, Ramesh N, Solomon EK. 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.