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REVIEW ARTICLE

Antimicrobial Evaluation of *Terminalia chebula* Retz.

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ABSTRACT

Medicinal plants are valuable source of human society to combat diseases from the down of civilization. *Terminalia chebula* Retz. is called" King of Medicine' in Tibet and is always listed at the top of the list of "Ayurvedic Meteria Medica" because of its extraordinary power of healing. The whole plant possesses high medicinal value and traditionally used for worldwide emphasis to search for herbal new antimicrobials from natural sources. As the global scenario is now changing towards the use of non toxic plant products having traditional medicinal use, a drug development programme should be undertaken to develop modern drugs with the compounds isolated from *T.chebula* effective against different types of diseases. The present review mainly highlights on the antimicrobial effectiveness of *T. chebula* against multiple drug resistant pathogens in various mild to dreadful diseases.

Keywords: Antimicrobials, Ailment, Resistance and Diseases.

1. INTRODUCTION

India is sitting on a gold mine of well-recorded and traditional well practiced knowledge of herbal medicine [1]. The World Health Organization reported that 80% of the world population relies chiefly on traditional medicines involving the use of plant extracts or their active constituents [2]. It has been estimated that in developed countries such as United States, plant drugs constitute as much as 25% of the total drugs, while in fast developing countries such as China and India, the contribution is as much as 80%. Thus, the economic importance of medicinal plants is much more in countries like India than in rest of the World. In the last few decades, the field of herbal medicine is getting popularized in both developed and developing countries [3]. This is because the herbal medicines are cheap, and has natural origin with higher safety margins and lesser or no side effects [4, 5].

Plants have formed the basis of sophisticated traditional medicine systems that have given rise to some important drugs still in use today [6, 7]. Of the 2,50,000 higher plant species on earth, more than 80,000 are medicinal. However, only 7000 - 7500 species are used for their medicinal values by traditional communities. Numerous studies have been conducted with various plants, screening antimicrobial activity as well as for the discovery of novel antimicrobial chemotherapeutic agents [8, 9, 10]. In view of increasing resistance to existing antimicrobial agents, herbal drugs are being looked as very important source for discovery of new agents for treating various ailments related to bacterial infections [11].

Terminalia chebula is a well known plant used in ayuvedic traditional medicine for their effectiveness against wide range of diseases due to the advantage of the diversity of secondary metabolites responsible for their curing property. Despite the existence of potent antibacterial agents, the appearance of resistant or multi-resistant strains imposes the need for a permanent search and development of new drugs [12]. *Terminalia chebula* (Haritaki) is one of the most important medicinal plants used in medicines of ayurveda, siddha, unani and homeopathy because of having a number of pharmacological properties [13]. [14] has reported that, tannin content of *T. chebula* largely depends on its geographic location and the chief components of tannins are chebulic acid, chebulinic acid, chebulagic acid, gallic acid, corilagin and ellagic acid. From the authors knowledge, this is the first pilot study

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have been framed to focused on antimicrobial activity of *T. chebula* against various pathogens. Hence it may form a footstep for the researchers to carry out their progression towards the invention of new natural drugs for the therapeutic uses.

2.CHEMOTHERAPEUTIC EFFECTIVENESS OF *T. chebula*

2.1. Antibacterial activity

The fruits from *T. chebula* appear to have evolved as complex antibiotic compounds that have shown activity against bacteria [15, 16, 17]. The antibacterial activity of *T. chebula* fruits extracts on the agar plates varied in different organic (methanol, ethanol and acetone) and aqueous (hot and cold) extracts. Positive controls produced significantly sized inhibition zones against the tested bacteria (ranging between 16.3 mm and 56.3 mm) and the yeast (with zone of inhibition 21.6 mm) and the negative control produced no observable inhibitory effect against any of the test organism [18]. There are several reports about the antibacterial activity of *T. chebula* fruit extracts against uropathogenic *Escherichia coli*, *Helicobacter pylori* and *S. aureus*, *Salmonella typhi*, *S. epidermidis*, *Bacillus subtilis*, *Proteus vulgaris* and *Pseudomonas aeruginosa* [18- 22].

Two antibacterial compounds, gallic acid and ethyl ester against Methicillin - resistant *Staphylococcus*, have been isolated from ethyl alcohol extract of fruits of *T. chebula* [23]. *T. chebula* is well effective against *Helicobacter pylori*, a bacterium responsible for gastritis, ulcer and stomach cancers. The ether, alcoholic and aqueous extracts of *T. chebula* were tested against *Helicobacter pylori*, but aqueous extract of the plant, at a concentration of 1-2.5 mg/ml, inhibited urease activity of *H. pylori* [24]. Several biologically active components were isolated from butanol fraction of fruit extract of *T. chebula* and tested against six intestinal bacteria. Ethanedioic acid showed strong and moderate inhibitory activity against *Clostridium perfringens* and *Escherichia coli.* Ellagic acid exerted a potent inhibitory effect against *C. perfringens* and *E. coli*, but little or no inhibition was observed for behenic acid, β-caryophyllene, eugenol, isoquercitrin, oleic acid, α-phellandrene, β-sitosterol, stearic acid, α-terpinene, terpinen-4-ol, terpinolene, or triacontanoic acid [25]. The ethanolic extract of *T. chebula* fruit was found effective against both Gram - positive and Gram - negative bacteria such as *Salmonella typhi* SSFP 4S, *Staphylococcus epidermidis* MTCC 3615, *Staphylococcus aureus* ATCC 25923, *Bacillus subtilis* MTCC 441 and *Pseudomonas aeruginosa* ATCC 27853 suggesting its broad spectrum antimicrobial activity [26].

Kau (1980) reported that tannic acid is having bacteriostatic or bactericidal to some Gram positive and Gram negative pathogens. There have been reports of antimicrobial properties in gallic acid [27] and in some gallate esters. Moreover, *T. chebula* has been also reported for its antimicrobial properties [28, 29, 30]. Tannic acid represents the major constituent of the fruit of *T. chebula* [31]. Quercitin is an important compound found in *T. chebula*. Thus, it helps in reducing the production of uric acid by inhibiting xanthine oxidase (XO). Decrease in uric acid production indicated the liver to be in good rather than in damaged condition [32].

Many physiological activities such as stimulation of phagocytic cells, host mediated tumor activity and a wide range of anti infective actions have been assigned to tannins. Their mode of antimicrobial action may be related to their ability to inactivate microbial enzymes and transport proteins [33]. [34] proposed the combination of antibiotics and flavonoids as a potential new strategy for development of new therapies in the future for infections caused by ESBL producing bacteria. Ciprofloxacin, which was used as a positive experimental control against all bacterial strains assayed, produced a good zone of inhibition, while no inhibitory effect could be observed for DMSO used as negative control [35].

2.2. Antifungal activity

Aqueous extract of *T. chebula* have been reported to show antifungal activity against a number of dermatophytes (e.g. *Epidermophyton*, *Floccosum*, *Microsporum gypseum* and *Tricophyton rubrum*) and yeasts (*e.g. Candida albicans*) [36, 37, 38]**.** Aqueous, alcoholic and ethyl acetate extracts of leaves of *T. chebula* were also tested against five pathogenic fungi (*Aspergillus flavus*, *A. niger*, *Alternaria brassicicola*, *A. alternata* and *Helminthosporium tetramera*) using paper disc method and were found effective compared to that of the reference standard Carbendazim [39]**.**

2.3. Anti amoebic and immunomodulatory activities

The anti amoebic effect of a crude drug formulation of *T. chebula* was investigated in experimental caecal amoebiasis in rats with a curative rate of 89% at 500 mg/kg body weight due varying degrees of inhibition of enzyme

activities such as DNase, RNase, aldolase, alkaline phosphatase, acid phosphatase, α-amylase and protease in axenically cultured amoebae [40]. In another study, *T. chebula* was evaluated in experimental amoebic liver abscess in golden hamsters and in immunomodulation studies. The formulation had a maximum cure rate of 73% at 800 mg/kg body weight in hepatic amoebiasis. In immuno modulation studies, humoral immunity was enhanced where T - cell counts remained unaffected in the animals but cell - mediated immune response was stimulated [41].

2.4. Antiplasmodial activity

The water extract of *T. chebula* showed anti plasmodial activity *in vitro* by its ability to inhibit the uptake of [3H] hypoxanthine into the *Plasmodium falciparum* K1 multidrug-resistant strain and *in vivo* [42]. Acetone seed extract of *T. chebula* was also found to have well anti plasmodial activity in a study [43].

2.5. Molluscicidal activity

The molluscicidal activity of ethanolic extract of *T. chebula* fruit powder was studied against the vector snail *Lymnaea acuminata* and was found time and concentration dependent. Column, thin layer and high performance liquid chromatography analyses demonstrated that the active molluscicidal component in *T. chebula* was tannic acid. Hence, *T. chebula* could be a potent source of molluscicides against the snail *L. acuminate* [44].

2.6 Antihelminthic activity

The ovicidal and larvicidal activities of ethyl acetate, acetone, and methanol extracts of dried leaves and seeds of *T. chebula* were tested *in vitro* on *Haemonchus contortus* based on egg hatch and larval development assays at 50, 25, 12.5, 6.25 and 3.13 mg/ml. The extracts of leaves and seeds of *T. chebula* showed complete inhibition at 50 mg/ml [45].

2.7. Antiviral activity

The fruit extracts of *T. chebula* showed inhibitory effects on human immunodeficiency virus-1 reverse transcriptase [46]. Hot water extract of *T. chebula* showed anti-herpes simplex virus (HSV) activity *in vivo* and anti-cytomegalovirus (CMV) activity both *in vitro* and *in vivo* [47]. Ledretan-96 and each of its 23 individual components were tested on an epithelial tissue culture cell line for their protective activity against cytotoxic effects caused by influenza A virus. Of the 23 components tested, only one component showed a significant protective effect when applied to the epithelial cells individually [48]. [49], has proved that *T. chebula* fruits contain four human HIV-type 1 integrase inhibitors such as gallic acid and three galloyl glucoses, and suggested that galloyl moiety had a major role for inhibition of the 3 - processing of HIV-1 integrase by these compounds. *T. chebula* can also be used in sexually transmitted diseases and AIDS [50]. Recently, acetone extract of *T. chebula* has emerged as a new alternative to treat pandemic swine influenza A infection due to its low cost, easy preparation and potential effect [51]. Herpes simplex virus 1 (HSV-1) is the cause of lifelong latent infection of sensory neurons. Two hydrolyzable tannins, chebulagic acid and punicalagin, isolated from the dried fruits of *T. chebula* inhibited HSV-1 entry at non-cytotoxic doses in A549 human lung cells by preventing binding, penetration, and cell-to-cell spread as well as secondary infection [52].

3. CONCLUSION

T. chebula is one of the most commonly used plants all over the world, having a wide spectrum of pharmacological and medicinal activities. This 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, very little work has been done on the credible medicinal applications of this plant against the diseases, particularly on multi drug resistant bacterial uropathogens. Hence, extensive investigation is needed to exploit their therapeutic ability to combat diseases including drug resistant infections.

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