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Antimicrobial activity of Indian medicinal plants, *Azadirachta indica*, *Carica papaya*, *Curcuma longa*, *Moringa oleifera* and *Tinospora cordifolia*: A review

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Abstract
Medicinal plants discovered by traditional societies are proving to be an important source of potentially therapeutic drugs and antimicrobial agents. Due to increasing drug resistance, there is need to search new infection-fighting strategies to control microbial infections. Plants represent the richest resource of drugs of traditional systems of medicine, modern medicines, nutraceuticals, food supplements, folk medicines, pharmaceutical intermediates and chemical entities for synthetic drugs. In the present paper, we present a picture of the potential of medicinal plants as source of natural phytochemicals that act as new antimicrobial agents. Plant extracts possess an antimicrobial activity due to presence of various phytochemicals like essential oils or isolated compounds such as alkaloids, trepenoids, lignans and flavonoids, tannins, glycosides, phenolics, sesquiterpene lactones, diterpenes, triterpenes or naphtoquinones, aliphatic compounds, steroids etc. Antimicrobial activity of plant extracts found in folk medicine further depends upon plant material used, techniques employed, growth medium and microorganisms tested. The antimicrobial activity of some known medicinal plants like *Azadirachta indica* (Neem), *Carica papaya* (Papita), *Curcuma longa* (Turmeric), *Moringa oleifera* (Drumstick tree) and *Tinospora cordifolia* (Giloy) found in India, has been reviewed in present paper that presents a picture of broad spectrum antimicrobial activity of various plant tissue extracts of these plants. The results of various studies support the folkloric use of these plants in the treatment of infections and various ailments by the people in Indian subcontinent. Thus, the study ascertains the value of plants used in ayurveda, which could be of considerable interest to the development of new antimicrobial drugs.

Keywords: Antimicrobial, medicinal plants, phytochemicals, *Azadirachta indica*, *Carica papaya*, *Curcuma longa*, *Moringa oleifera* and *Tinospora cordifolia*

Introduction
For a long period of time, plants have been a valuable source of natural products for maintaining human and animal health. Plants are an important source of potentially useful bioactive compounds for the development of new chemotherapeutic agents. The number of multi-drug resistant microbial strains and the appearance of strains with reduced susceptibility to antibiotics are continuously increasing. In addition to this, in developing countries, synthetic drugs are not only expensive and inadequate for the treatment of diseases but also often with side effects and adulterations. Therefore, there is need to search new infection-fighting strategies to control microbial infections. Various medicinal plant extracts have been subjected to chemical investigations extensively and a number of chemical constituents belonging to different groups such as alkaloids, trepenoids, lignans and flavonoids, tannins, phenolics, glycosides, aliphatic compounds, steroids, etc. have been reported which may account for the antimicrobial property of their extracts. Therefore medicinal plants should be investigated to better understand their properties, safety and efficiency. The use of plant extracts and phytochemicals, both with known antimicrobial properties, can be of great significance in therapeutic treatments. The aim of the present study was to present a picture of antimicrobial activity of some medicinal plant used in traditional medicinal system for treatment of manifestations caused by microorganisms. India is home to many medicinal plants. The antimicrobial activity of some known Indian medicinal plants like *Azadirachta indica* (Neem), *Carica papaya* (Papita), *Curcuma longa* (Turmeric), *Moringa oleifera* (Drumstick tree) and *Tinospora cordifolia* (Giloy), is presented under respective headings.

Antimicrobial activity of *Azadirachta indica*

Azadirachta indica (Neem) is one of the most useful traditional medicinal plant. Every part of the tree has been used as traditional medicine for household remedy against various ailments. The tree is still regarded as "Village dispensary" in India. The Neem tree occurs throughout India. Normally it thrives in areas with sub-arid to sub-humid conditions, with an annual rainfall between 400 and 1200 mm. It can tolerate high temperatures. Individual Neem tree may vary in chemical make-up because of genetic and environmental factors. The studies carried out by different scientists during different times have proved the natural variability in percentage content of the phytochemicals. Most of the parts of the plant such as fruits, seeds, leaves, bark and roots contain compounds with proven antiseptic, antiviral, antipyretic, anti-inflammatory, antiulcer and antifungal properties. Many compounds have been isolated from different parts of Neem. Sulphur-containing compounds such as cyclic trisulphide and tetrasulphide isolated from the steam distillate of fresh and matured Neem leaves have antifungal activity against *Trichophyton mentagrophytes*. *A. indica* extract has shown antimicrobial activity against *S. epidermidis, S. aureus,* and moderate antibacterial activity against *E. coli, P. aeruginosa* and *E. aerogenes*. Prashant *et al*. (2007) [66] demonstrated that Neem stick extract produced maximum zone of inhibition against *S. mutans* at 50% concentration. Bohora *et al*. (2010) [14] concluded that Neem leaf extract has a significant antimicrobial effect against *E. faecalis, C. albicans* and mixed culture (Bohora *et al*., 2010) [14]. It has been shown that leaf extract of Neem is very effective against *S. mutans* and *S. aureus* with MIC value of 125 µg. The maximum antimicrobial activity was observed on *S. mutans* at 3 mg concentration with zone of inhibition of (24.67 ± 2.517) mm. The Neem oil, also known as oil of Margosa, is believed to have medicinal properties, such as antibacterial (Singh and Sastri, 1981) [82] and antifungal (Kher and Chaurasia, 1977) [35]. Singh *et al*. (2016) [81], observed activity of Neem extract against *Klebsiella* species and *S. aureus*. Neem extract showed anti *Staphylococcal* activity (Bezalwar *et al*., 2014) [11]. Neem extracts possess antibacterial activity against different organisms including *S. aureus, E. coli*, etc. (Pandey *et al*., 2014) [62]. Werner Fabry *et al.* (1998) [93] in their study tested the extracts of *Azadirachta indica* (stem bark and leaves) against 105 strains of bacteria from seven genera (*Staphylococcus, Enterococcus, Pseudomonas, Escherichia, Klebsiella, Salmonella* and *Mycobacterium*). The minimum inhibitory concentration reached by 50% (MIC50%) and 90% (MIC90%) of the strains for the extracts of *A. indica* (stem bark) ranged from 0.25 to 2 mg/mL and from 0.5 to 2 mg/mL, respectively. Moreover extracts of flowers of *A. indica* also showed antibacterial activity against *B. cereus, S. aureus, L. monocytogenes, E. coli* and *S. infantis* (Alzoreky and Nakahara, 2003) [3].

Further studies found that methanolic and acetone extracts were more effective against the bacteria compared to that of aqueous extract (Rajasekaran 2008) [68]. Gram positive bacterial strains were found more sensitive than the Gram-negative ones (Sinaga *et al*., 2016) [80]. Paray *et al*. (2018) [63] demonstrated the antibacterial activity of crude aqueous extracts of *Azadirachta indica* against *Escherichia coli*, *Proteus* spp., *Enterococcus faecium, Enterococcus faecalis*, *Staphylococcus aureus* and *Streptococcus agalactiae.* The extracts of Neem when used as medicinal plant, could be useful for the growth inhibition of the carcinogenic bacterium, *S. sobrinus* (Bhuiyan *et al*., 1997) [12]. Maragathavalli *et al*. (2012) [43] demonstrated antibacterial activity of Neem leaf extracts. Owolabi *et al*. (2017) [60], conducted an experiment on test organisms *E. coli, S. typhimurium, B. subtilis* and *S. aureus. A. Indica* leaf water extract and stem bark ethanol extract showed a clear zone of inhibition ranging from 10 ± 0 mm to 15.5 ± 0.71 mm and 10 ± 0 mm to 15.5 ± 2.12 mm respectively against all four test isolates, while others extracts had clear zones of inhibition against at least three test isolates with inhibition zones ranging from 10.5 ± 0.71 mm to 15 ± 1.41 mm.

Neem contains different active phytoconstituents such as alkaloids, glycosides, trepenoids, steroids and tannins (Prabhat *et al.*, 2010) [65]. Constituents of alkaloids, terpenoids tannins and flavonoids of *A. indica* (Makkar *et al*., 2007) [41] are responsible to overcome microbial infection specially having antioxidant and antimicrobial biological activities (Scalbert and Scalbert and Williamson, 2000) [75]. These antibiotic principles are actually the defensive mechanism of plants. These chemicals might show the antibacterial activity by their ability to make a complex with the bacterial cell walls. Inhibitory activity towards DNA topoisomerase II enzyme by azadiractin, a bioactive metabolite of Neem (Scalbert, 1991) [74] might also involve in the antibacterial potential. *Azadirachta indica* leaves possessed good anti bacterial activity (Saradha and Subbarao, 2011) [73]. Some bioactive compounds from Neem leaves include nimbidin and mahmoodin having antibacterial activity; and cyclic trisulphide and cyclic tetrasulphide, having antifungal activity (Biswas *et al*., 2002) [13].

Antimicrobial activity of *Carica papaya*

Carica papaya (Papaya/Papita) belongs to family Caricaceae, and is commonly known as papaya in English, Papita in Hindi and Erandakarkati in Sanskrit. The plant is native to tropical America and was introduced to India in 16th century. The plant is recognised by its weak and usually unbranched soft stem yielding copious white latex and crowded by a terminal cluster of large and long stalked leaves. Traditionally leaves have been used for treatment of a wide range of ailments, including malaria, dengue and jaundice, etc. It is believed to have immunomodulatory and antiviral activity. Papaya seeds have antibacterial properties and are effective against *E. coli, Salmonella* and *Staphylococcus infections*. Fruit and seed extracts have antibacterial activity against *S. aureus, B. cereus, E. coli*, and *P. aeuroginosa* (Tang *et al.*, 1972 [86]; Emeruwa, 1982) [20]. The seed of papaya has antimicrobial activity against *T. vaginalis*. The seeds, irrespective of its fruit maturity stages have bacteriostatic activity on gram positive and negative organisms which could be useful in treating chronic skin ulcer.

Singh *et al*. (2016) [81], observed activity of *C. papaya* water extract against gram positive *S. aureus*. Aqueous, n-hexane and ethanol extract of *C. papaya* leaves were investigated by Chandra *et al*. (2011) [18] for antibacterial activity against *S. aureus, B. subtilis, E. coli*, and *P. auruginasa*. It was observed that the three extracts were able to inhibit all the bacteria tested. Among the three extracts (30 mg per disc), n-hexane and ethanol had highest inhibition against *S. aureus* (17.33 and 15.67 mm), while aqueous extract had inhibition of 9 mm (30 mg per disc) also in case of *B. subtilis, E. coli* and *P. auruginasa.* Mangalanayaki and Nirosha, 2013 [42] examined the antibacterial activity of the leaves of the *Carica papaya* using solvents ethanol and ethyl acetate against *S. aureus, S.*

pneumonia, B. cereus, S. typhi, E. coli and *P. aeruginosa* by well diffusion method. The extract demonstrated higher activities against all the Gram negative bacteria than Gram positive bacteria tested, with the highest activity (16 mm zone of inhibition) demonstrated against *Salmonella typhi*. The ethanolic extract of leaves and roots moderately killed all the bacterial pathogens than aqueous extract of leaves and root. Ogunjobi and Ogunjobi (2011) [58] reported activity against eight bacterial strains *Staphylococcus aureus, Salmonella typhi, Shigella dysenteria, Pseudomonas aeruginosa, Serratia marcescens, Pseudomonas fluorescens, Proteus vulgaris* and *Bacillus subtillis.* Romasi *et al.* (2011) [70] studied the ethanol, ethyl acetate, and hexane extract of papaya leaf against *Bacillus stearothermophilus*, *Listeria monocytogenes*, *Pseudomonas* spp., and *Escherichia coli* by agar diffusion method. Ethanolic extract of *Carica papaya* leaf, in a study was found active against *Bacillus subtilis* with zone of inhibition of 11.5 ± 0.71 mm (Owolabi *et al*. (2017) [60]. Paray *et al*. (2018) [63] observed the antibacterial activity of crude aqueous extract of leaves of *Carica papaya* against *E. coli*, *Proteus* spp., *E. faecium*, *E. faecalis*, *S. aureus* and *S. agalactiae.* The results of the study conducted by Hema *et al*. (2013) [31] showed that the propanolic extracts of *Carica papaya* were more effective than the ethanol extracts demonstrated the highest activity. Among the Gram-positive and Gram-negative bacteria tested against the leaf extract of *C. papaya*, the Gram-negative bacteria were more susceptible especially *Proteus vulgaris* to the extracts. This result, however, is at disparity with an earlier report indicating that plant extracts are more active against Gram-positive bacteria than Gram-negative bacteria while that of the leaf extract of *C. papaya* was next to the most sensitivity with the Gram-negative bacteria especially *Proteus mirabilis* (Jigna and Sumitra, 2006) [33]. The fact that the extracts were active against both Gram negative and Gram positive bacteria tested may indicate a broad spectrum of activity and the phytochemical analysis revealed the presence of many phyto constituents. Romasi *et al.* (2011) [70] reported that the extracts of Papaya leaves could inhibit the growth of *Rhizopus stolonifer*. In a study, Papaya leaf extracts were tested against *B. stearothermophilus*, *L. monocytogenes*, *Pseudomonas* spp. and *E. coli* by agar diffusion method. This research indicated that Papaya leaves have potential natural antibacterial compounds. Sherwani *et al.* (2013) [79] and, Omojasola and Awe (2004) [59] also examined the leaf extract of *C. papaya* against plant and human pathogenic bacteria. Nirosha and Mangalanayaki (2013) [57] observed and reported that extract of *C. papya* demonstrated higher activities against all the Gram negative bacteria than Gram positive bacteria tested, with the highest activity (16 mm zone of inhibition) demonstrated against *S. typhi*. Increase in temperature enhanced the activity of the extracts, while alkaline pH decreased the activity. The MIC of the extracts ranged between 50-200 mg/mL.

Preliminary phytochemical analyses showed that the extracts contain alkaloids, tannins, saponins and phenols (Nirosha and Mangalanayaki, 2013) [57]. Papaya leaf extracts have phenolic compounds, such as protocatechuic acid, p-coumaric acid, 5, 7- dimethoxycoumarin, caffeic acid, kaempferol, quercetin, chlorogenic acid (Romasi *et al.*, 2011) [69]. Young leaves are rich in flavonoids (kaempferol and myricetin), alkaloids (carpaine, pseudocarpaine, dehydrocarpaine I and II), phenolic compounds (ferulic acid, caffeic acid, chlorogenic acid), the cynogenetic compounds (benzylglucosinolate) found in leaves. Both leaf and fruit of the *Carica papaya* possess carotenoids namely β- carotene, lycopene, anthraquinones glycoside, as compared to matured leaves and hence possess medicinal properties like anti-inflammatory hypoglycaemic, anti-fertility, abortifacient, hepatoprotective, wound healing, recently its antihypertensive and antitumor activities have also been established (Anjum *et al*., 2013) [5].

Antimicrobial activity of *Curcuma longa*

Curcuma longa (Turmeric) belongs to Zingiberaceae family. Curcumin or diferuloylmethane with chemical formula of (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) and other curcuminoids constitute the main phytochemicals of *Curcuma longa* rhizome (Ammon *et al*., 1991) [4]. Turmeric along with its polyphenolic compound curcumin have been subjected to various antimicrobial investigations. *Curcuma longa* rhizome has been traditionally used as antimicrobial agent (Rudrappa *et al*., 2008) [71]. Several studies have reported the broad-spectrum antimicrobial activity for curcumin including antibacterial, antiviral, antifungal, and antimalarial activities.

The antibacterial study on aqueous extract of *C. longa* rhizome demonstrated the minimum inhibitory concentration (MIC) value of 4 to 16 g/L and minimum bactericidal concentration (MBC) value of 16 to 32 g/L against *S. aureus*, *S. epidermis*, *K. pneumonia*, and *E. coli* (Niamsa *et al*., 2009) [55]. The methanol extract of turmeric showed MIC values of 16 µg/mL and 128 µg/mL against *Bacillus subtilis* and *S. aureus*, respectively (Ungphaiboon *et al*., 2005) [89]. The study of hexane and ethanol turmeric extract and curcuminoids against 24 pathogenic bacteria isolated from the chicken and shrimp showed the highest antimicrobial activity for ethanol extract with the MIC value of 3.91 to 125 ppt (Lawhavinit *et al*., 2010) [39]. The hexane and methanol extracts of *C. longa* demonstrated antibacterial effect against *Vibrio, Bacillus, Aeromonas, Streptococcus, Staphylococus and Edwardsiella* species (Lawhavinit *et al*., 2010) [39]. Indeed, it was shown that the addition of 0.3% (w/v) of aqueous curcumin extract to the cheese caused the reduction in bacterial counts of *S. typhimurium*, *P. aeruginosa* and *E. coli*. Moreover, it has decreased the *S. aureus*, *B. cereus*, and *L. monocytogenes* contamination after 14 days of cold storage (Hosny *et al*., 2011) [32]. Curcumin also exhibited inhibitory activity on methicillin-resistant *S. aureus* strains (MRSA) with MIC value of 125–250 µg/mL (Mun *et al*., 2013) [51]. Curcumin showed significant antibacterial activity with MIC values between 5 and 50 µg/mL against 65 clinical isolates of *Helicobacter pylori*. Kumar *et al*. (2016) [37], demonstrated activity of methanolic extract of Neem and Turmeric and found 11±1 mm zone of inhibition against *E.coli* for extracts of both, using leaves of Neem and rhizome of Turmeric for extract prepration.

The methanol extract of turmeric demonstrated antifungal activity against *Candida albicans* and *Cryptococcus neoformans* with MIC values of 256 and 128 µg/mL, respectively (Ungphaiboon *et al*., 2005) [89]. The study of hexane extract of *C. longa* at 1000 mg/L demonstrated antifungal effect against *Phytophthora infestans*, *Rhizoctonia solani*, and *Erysiphe graminis*. It was also shown that 1000 mg/L of ethyl acetate extract of *C. longa* exhibited inhibitory effect against *R. solani*, *Puccinia recondita*, *P. infestans*, and *Botrytis cinerea.* Curcumin at 500 mg/L also showed antifungal activity against *R. solani*, *P. recondita*, and *P. infestans* (Kim *et al*., 2003) [36]. Curcumin and turmeric oil

exert antifungal effect against two phytophagous fungi, namely, *Fusarium solani* and *Helminthosporium oryzae*. Turmeric oil exhibited the most effective antifungal activity against *F. solani* and *H. oryzae* (Chowdhury *et al*., 2008) [19]. The crude methanol extract of *C. longa* has inhibitory effect against some clinical isolates of dermatophytes. Turmeric oil showed activity against pathogenic molds such as *Sporothrix schenckii*, *Exophiala jeanselmei*, *Fonsecaea pedrosoi*, and *Scedosporium apiospermum* with MIC values of 114.9, 459.6, 459.6, and 114.9 µg/mL, respectively (Apisariyakul *et al*., 1995) [8]. However, curcumin showed more significant effect against *Paracoccidioides brasiliensis* than fluconazole, although it did not affect the growth of *Aspergillus* species (Martins *et al*., 2009) [44]. The possible mechanism underlying the mentioned antifungal effect was found to be downregulation of desaturase (ERG3) leading to significant reduction in ergosterol of fungal cell. Reduction in production of ergosterol results in accumulations of biosynthetic precursors of ergosterol which leads to cell death via generation of ROS (Sharma *et al*., 2010) [77]. Reduction in proteinase secretion and alteration of membrane-associated properties of ATPase activity are other possible critical factors for antifungal activity of curcumin (Neelofar *et al*., 2011) [54]. In another study, anti-*Candida* activity of curcumin was demonstrated against 38 different strains of *Candida* including some fluconazole resistant strains. Curcumin also showed inhibitory effect on *Cryptococcus neoformans* and *C. dubliniensis* with MIC value of 32 mg/L (Martins *et al*., 2009) [44].

Antimicrobial activity of *Moringa oleifera.*

Moringa oleifera is a medicinally important plant, belonging to family Moringaceae. The plant is native to the Indian subcontinent and is well recognized in India, Pakistan, Bangladesh and Afghanistan as a folkloric medicine (Mughal *et al*., 1999) [50]. The tree is known by many regional names such as Benzolive, Drumstick tree, Horseradish tree, Kelor, Mlonge, Marango, Mulangay, Sajna and Saijihan (Fahey, 2005) [21]. *M. oleifera* is a small or medium sized tree up to 10 m tall, with thick, soft, corky, deeply fissured bark, growing mainly in semiarid, tropical and subtropical areas. It can grow well in the humid tropics or hot dry lands and can survive in less fertile soils and is also little affected by drought (Anwar *et al*., 2007) [7]. Different parts of the tree have been used in the traditional system of medicine. *Moringa* contains a range of fairly unique phytochemicals containing the simple sugar, rhamnose, and it is rich in a fairly unique group of compounds called glucosinolates and isothiocyanates. Six such phytochemicals have been reported to have hypotensive, anticancer, and antibacterial activity, which include benzyl isothiocyanate, niazimicin, pterygospermin, and 4-{a-L-rhamnopyranosyloxy} benzyl glucosinolate (Fuglie, 2000; Fuglie *et al*., 2001) [24, 25].

Plants represent the cheapest and safer alternative sources of antimicrobials. *Moringa oleifera* has wide range of antimicrobial properties which have been investigated by a number of studies, using different part and different way of extraction (Adriana *et al*., 2007) [2]. Extracts of various *Moringa* tissues have been used as anti-cancer (Guevarra *et al.*, 1999), anti-trypanosomal (Mekonnen *et al*., 1999) [48], antimicrobial (Caceres *et al*., 1991) [16] and anti-inflammatory and hepatoprotective (Kurma and Mishra, 1998) [38] agents. *Moringa* leaf is a natural antihelmintic, antibiotic, detoxifer, outstanding immune builder used in some countries for the treatment of malnutrition and malaria (Thilza *et al*., 2010) [87].

Bukar *et al*. (2010) [15] studied antimicrobial profile of *Moringa oleifera* extracts against some food-borne microorganisms and concluded that *M. oleifera* leaf ethanol extract exhibited broad spectrum activity against the test organisms with *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Enterobacter aerogenes* being susceptible. The MIC values ranged between 2.0 and >4.0 mg/mL for all the organisms. Gomashe *et al*. (2014) [29] revealed that aqueous and ethanol extract of *Moringa oleifera* was inhibitory to *Escherichia coli* (12 mm inhibition zone each), *Proteus vulgaris* (10 mm each) and *Salmonella typhi* (12 mm and 10 mm respectively). All the organisms were sensitive to ethanol extract except *Bacillus subtilis* and *Escherichia coli*. Acetone and chloroform extract of *Moringa oleifera* did not show any antibacterial activity. Antibacterial activities would most probably be due to the differences in the phytochemical constituents. Nikkon *et al*. (2003) [56] reported *in-vitro* antimicrobial activity of the compound isolated from chloroform extract of *Moringa oleifera* against *Shigella boydii*, *Shigella dysenteriae* and *Staphylococcus aureus*.

Abalaka *et al*. (2012) [1] conducted antibacterial evaluation of *Moringa oleifera* leaf extracts on selected bacterial pathogens and result showed that aqueous crude extracts of the leaf of *Moringa oleifera* were active against *E. coli, S. typhi and P. aeruginosa* was resistant to the activity of the aqueous extract. MIC of the aqueous leaf extract on *E. coli* and *S. typhi* were 0.417 mg/mL. Aqueous extract of the leaf of *M. oleifera* revealed that the minimum bactericidal concentration (MBC) on *E. coli* and *S. typhi* were 1.667 mg/mL. *Moringa oleifera* leaves water extract exhibit variable activity against bacteria. *Staphylococcus albus, Escherichia coli and Shigella spp* show highest zone of inhibition (3, 2, and 1.5 mm respectively). *Providencia* spp, *K. pneumoniae* and *S. auras* show same zone of inhibition (1 mm). Water extracts exhibit variable activity against bacteria; some bacteria like *Staphylococcus albus* and *Escherichia coli* showed high zone of inhibition and some tested bacteria showed resistance to the *Moringa* leave water extract. Various researchers reported antimicrobial activity of *Moringa oleifera* leave water extract against variety of pathogens with some variations that may be due to a variety of bacterial gene that lead bacteria to be resistant to antimicrobial agent. Priya *et al*. (2011) [67] evaluated the antibacterial activity in the aqueous leaf extracts of *Moringa oleifera* against pathogenic bacteria like *Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus and Shigella* species. Paray *et al*. (2018) [63] reported the antibacterial activity of crude aqueous extract of leaves of *Moringa oleifera* against *Escherichia coli*, *Proteus* spp., *Enterococcus faecium, Enterococcus faecalis, Staphylococcus aureus* and *Streptococcus agalactia.* Thilza *et al*. (2010) [87] evaluated the *in vitro* antimicrobial activity of *Moringa oleifera* leave extracts against *E. coli, S. aureus, S. albus, P. aeruginosa* and they found that *E. coli* among tested bacteria showed inhibition zone. Anthonia, (2011) [6] in South-Western Nigeria found that aqueous leaf extract had inhabitation zone different pathogen include *Escherichia coli, Klebsiella pneumoniae, Providencia stuartii, Yesinia enterocolitica*. Locally isolated organism like *Salmonella, Staphylococcus aureus, Enterococcus faecalis* showed inhibition zone less than one mm while *Pseudomonas aerogenosa* resist to *Moringa oleifera* leaf aqueous extract. Vinoth *et al*. (2012) [90] screened *Moringa oleifera* leaf water extract for antibacterial activity, *S. aureus* only tested bacteria showed sensitivity

while for *P. aerogenosa*, *E. coli* and *S. typhi* no activity was detected. The seeds of *Moringa oleifera* are used to exert its protective effect as an antimicrobial agent (Faizi *et al*., 1994) [22]. Further, scientists investigated antimicrobial properties of *Moringa oleifera* and reported its cyanobacteriacidal activity, (Lurling and Beekman, 2010) [40], antipyretic, anti-inflammatory, antiulcer (Pal *et al*., 1995) [61], antibacterial and antifungal activities (Nikkon *et al*., 2003) [56].

Moringa oleifera leave extraction using methanol showed remarkable result against *Enterococcus faecalis, Yersinia enterocolitica, Providencia spp.* with zone of inhibition measuring 3.5 mm, 2.5 mm, 2.25 mm, respectively. Gram positive cocci *S. auras* and *S. albus*, showed almost same result with zone of inhibition of 1.25 mm and 1 mm, respectively. Methanol extraction only gave result against *Pseudomonas aeruginosa* (1 mm). These results corroborate as by Patil and Jane (2013) [64]. Susceptible bacteria to ethanol extraction showed almost same result. *Salmonella spp., Yersinia enterocolitica, Escherichia coli, Enterococcus faecalis, Providencia spp* with zone of inhibition 1.5 mm, 1.5 mm, 1.25 mm, 1.25 mm and 1 mm, respectively were seen susceptible. Only four bacteria showed result with petroleum ether extract which include, *Providencia spp, Yersinia enterocolitica, Enterococcus faecalis, Escherichia coli* (2.5 mm, 1.25 mm, 1.125 mm, 1 mm, respectively). Studies showed that methanol extraction was the only effective type to *Candida albicans* with 4 mm zone of inhibition. Ethanol extraction was the only extract that showed activity against *A. flavus* (4 mm) while *A. niger* resisted to all *Moringa oleifera* leaf extracts. In their investigation, different zones of inhibition were found in extracts from leaf against all the tested bacteria.

Petroleum ether leaf extracts had the lowest activity against tested bacteria. *Providencia spp, Yesinia enterocolitica, Enterococcus faecalis,* and *Escherichia coli* were found susceptible to it. The inactivity of petroleum ether extract may be due to the reason that active compounds which possess the antimicrobial properties are polar in nature and not possibly extracted by petroleum ether. (Saadabi *et al.*, 2011) [72]. Priya *et al.* (2011) [67] also reported that petroleum ether leave extracts showed moderate inhibition against *Bacillus subtilis, E. coli, K. pneumoniae, S. aureus and S. dysentriae. Salmonella spp.* and *Y. enterocolitica* showed highest zone of inhibition with ethanol extract, *Escherichia coli, Enterococcus faecalis* and *Providencia spp.* showed considerable activity, rest of tested bacteria showed no result. (Mashiar *et al*., 2009) [45] pointed out that, ethanol extracts of fresh leaves were noticed to be more susceptible to *S. shinga, P. aeruginosa, S. sonnei, Pseudomonas spp.* Vinoth *et al.* (2012) [90] investigated the antibacterial activity in the ethanolic leaf extracts of *Moringa oleifera* against pathogenic bacteria. *Salmonella typhi* showed maximum zone of inhibition while less inhibition zone was seen for *E. coli*.

Jonathan *et al*. (2012) [34] assessed the antifungal activity of methanol and ethanol extract of *Moringa oleifera* leaves, and reported that, *Aspergillus flavus* had highest inhibition zone (30 mm), *Candida albicans* (5 mm) while *Aspergillus niger* had no zone of inhibition to methanol extract. Ethanol extract showed variable result with (25, 10 and 15 mm) to *Candida albicans, Aspergillus niger* and *Aspergillus flavus* respectively.

Abalaka *et al*. (2012) [1] conducted a study showing the antimicrobial potential of *M. oleifera* leaves chloroform and aqueous extracts comparable with that of the antibiotic ampiclox against the gram negative and gram positive bacteria tested. They advocated that *M. oleifera* could be a promising natural antimicrobial agent.

Ashok *et al*. (2003) [9] reported aqueous extracts of *Moringa oleifera* as inhibitory against *S. aureus* (10 mm), *E. coli* (12 mm), *P. vulgaris* (10 mm) and *S. typhi* (12 mm). All the selected bacterial pathogens were found resistant to acetone and chloroform extract of *M. oleifera.* Ethanol extract was effective against *E. coli* (12 mm) while both ethanol and methanol extracts were inhibitory against *P. vulgaris* and *S. typhi* (zone of inhibition of 10 mm for both). Petroleum extract was not effective against all the test pathogens except *P. aeruginosa* (12 mm). This *in vitro* study demonstrated that plants like *Moringa oleifera*, represent an economic and safe alternative to combat microbial contamination by making use of their antimicrobial activity.

Antimicrobial activity of *Tinospora cordifolia*

Tinospora cordifolia (Giloy) is one of the noncontroversial and extensively used herbs in Ayurvedic medicine. *Tinospora cardifolia* is a large deciduous climbing shrub found throughout India. It is known by multiple names like Guduchi, Giloy or Amrita, etc. *T. cordifolia* is a member of Menispermaceae family. It is a succulent, woody climbing shrub, found in India, Burma and Sri Lanka. The stem is deeply cleft spirally and longitudinally and grey or creamy white in colour. The wood is soft, white and porous. The freshly cut surface assumes a yellow tint upon exposure to air.

It is well known that *Tinospora cordifolia* has antimicrobial property (Reddy *et al*., 2015) [69]. Narayanan *et al.* (2011) [53] assayed anti-bacterial activity of *Tinospora cordifolia* extracts against *E. coli, K. pneumoniae, P. vulgaris, S. aureus, S. typhi, S. flexneri, S. paratyphi, S. typhimurium, P. aeruginosa*, and *S. marcesenses* (Gram-positive bacteria). Aqueous, ethanol and acetone extracts of leaves and stem of *Tinospora cordifolia* were observed to have inhibitory activity against *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* (Shanthi and Nelson, 2013) [77]. The active compound [(5R,10R)-4R, 8R-Dihydroxy-2S, 3R:15, 16-diepoxycleroda-13(16), 17, 12S, 18, 1S-dilactone] was isolated from ethanol extract of *Tinospora cordifolia* stem, which showed activity against bacterial and fungal species. Results of the study conducted by Francesca *et al*. (2014) [23] indicate that constituents from *Tinospora cordifolia* exhibited a higher inhibitory activity against reference microbial strains and clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenemase producing *Klebsiella pneumoniae* (Francesca *et al*., 2014) [23].

Nagaprashanthi *et al*. (2012) [52] observed antibacterial activity of hydro alcoholic stem extract of *Tinospora cordifolia* against bacterial species including *Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia, Pseudomonas spp.* as well as antifungal activity against *Aspergillus niger, Aspergillus fumigates, Mucor species and Pencillium.* Mishra *et al.* (2014) [49] observed antibacterial activity of *T. cordifolia* against *E. coli, S. aureus***,** *P. vulgaris, P. aeruginosa, B. subtilis***,** *S. epidermidis and M. luteus.*

In a study, maximum inhibitory effect of the aqueous extract was observed only on *Staphylococcus epidermidis, Staphylococcus aureus,* and moderate antibacterial against *Escherichia coli, Pseudomonas aeruginosa, Enterobacter aerogenes,* but mild inhibitory effect on *Salmonella typhi, Salmonella typhimurium, Proteus vulgaris*. Methanol and ethanol extract showed strong antibacterial effect against

Staphylococcus epidermidis and *Staphylococcus aureus* and moderate antibacterial against *Proteus vulgaris, Escherichia coli, Enterobacter aerogenes, Salmonella typhi* and *Salmonella typhimurium,* but mild effect on *Pseudomonas aeruginosa.* Acetone extract showed maximum inhibitory effect on *Staphylococcus aureus, Proteus vulgaris, Staphylococcus epidermidis, Pseudomonas aeruginosa, Salmonella typhi, Salmonella typhimurium,* but moderate inhibitory effect on *Escherichia coli, Enterobacter aerogenes.* Several researchers have reported medicinal properties of plants derived compounds. *Tinospora cordifolia* was observed to have antibacterial activity against *Escherichia coli*, *Proteus* spp., *Enterococcus faecium*, *Enterococcus faecalis*, *Staphylococcus aureus* and *Streptococcus agalactiae* (Paray *et al*., 2018) [63] Sharma and Prajapati (2016) [78], observed the antibacterial activity of *Tinospora cordifolia* (Giloye) against *E. coli, P. aeruginosa, S. aureus* and *S. typhi* with different zone of inhibitions at different concentrations. Samples showed significant antibacterial activity and possess great potential against microorganisms. Phytochemical analysis for various functional groups revealed the presence of glycosides, alkaloids, tannins, phenols, starch and sterols in it, which might be accountable for their antimicrobial potential. Various phytochemicals found in *T. cordifolia* stem extracts are as listed in Table 1. This plant has been subjected to chemical investigations extensively and a number of chemical constituents belonging to different groups such as alkaloids, trepenoids, lignans and flavonoids, tannins, cardiac glycosides, phenolics, aliphatic compounds and steroids have been reported (Bansal *et al*., 2012) [10] which may account for the antimicrobial property of its extracts.

Table 1: Phytochemical profile of *Tinospora cordifolia*

Chemical class	Phytoconstituents	References
Alkaloids	Berberine, Tembeterine, Palmitine	Singh *et al*., 2003 [83] Sinha *et al*., 2004 [84]
Glycosides	18-norclerodane glucoside, furanoid diterpene glucoside, cordiofolioside A, cordiofolioside B, palmatosides C, palmatosides P1, cordiofolioside C, cordiofolioside D, cordiofolioside E	Gagan *et al*., 1994 [27] Wazir *et al*., 1995 [92] Gagan *et al*., 1996 [26] Ghosal *et al*.,1997 [28] Maurya *et al*.,1997 [47] Singh *et al*., 2003 [83]
Sesquiterpenoids	Tinocordifolin	Maurya *et al*.,1998 [46]
Steroids	β sitosterol, -sitosterol, giloinsterone, ecdysterone, makisterone A, 20 -hydroxy ecdysone.	Singh *et al*., 2003 [83]
Diterpenoid lactones	Clerodane derivatives, tinosporon, tinosporides, jaiterine, columbin	Maurya *et al*., 1997 [47] Swaminathan *et al*., 1989 [85] Singh *et al*., 2003 [83]
Aliphatic compounds	Octacosanol, heptacosanol, nonacosan-15-one	Singh *et al*., 2003 [83] Thippeswamy *et al*., 2008 [88]

It has been reported that many of these phytochemicals present in stem extracts of this plant have antimicrobial activity, like Berberine (Cernakova *et al.,* 2002) [17], Palmitine (Yuan *et al*., 2010) [94], Isocolumbin, Jatorrhizin (Yuan *et al*., 2010) [94]. Palmitine and Barberine (Vollekova *et al*., 2003) [91] have been reported to have an antifungal activity too.

Conclusion

The review ascertains the value of plants used in Ayurveda and traditional folklore medicine as an important source of potentially useful bioactive compounds which could be of considerable interest to the development of new antimicrobial and chemotherapeutic agents. Various plant tissue extracts of *Azadirachta indica*, *Carica papaya*, *Curcuma longa*, *Moringa oleifera* and *Tinospora cordifolia* are potential sources of natural phytochemicals. These could be a possible source to obtain new and effective antimicrobial agents of plant origin that can be efficiently used to treat infections caused by multi-drug resistant strains of pathogens. However, it is necessary to further investigate the active bio components, their toxicity, side effects and pharmaco-kinetic properties. These plant based infection-fighting agents coupled with new strategies can pave way for economic and safe alternative to combat microbial contamination and infections.

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