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, trepennoids, 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, trepennoids, 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, 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 Azadirachta indica, demonstrated the antibacterial activity of crude aqueous extracts (2000) [20] and moderate antibacterial activity against at least three test isolates identified to have medicinal properties, such as S. aureus, 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 four all 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, terpenoids, steroids and tannins (Prabhat et al., 2010) [65]. Constituents of alkaloids, terpenoids tannins and flavonoids of A. indica (Makkar et al., 2007) [61] 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 nimbinid and mahmoodin having antibacterial activity; and cyclic trisulphide and cyclic tetrasulphide, having antifungal activity (Biswa 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. aeruginosa (Tang et al., 1972 [80], 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. aeruginosa. 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. aeruginosa. 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.

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 four all 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.

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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 dysenteriae, Pseudomonas aeruginosa, Serratia marcescens, Pseudomonas fluorescens, Proteus vulgaris and Bacillus subtilis. 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. Ethanol 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) [34] 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) [39] and, Omojosa and Awe (2004) [59] also examined the leaf extract of C. papaya against plant and human pathogenic bacteria. Nirosha and Mangalanayaki (2013) [53] observed and reported that extract of C. papaya 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- dimethoxycomarain, caffeic acid, kaempferol, quercetin, chlorogenic acid (Romasi et al., 2011) [69]. Young leaves are rich in flavonoids (kaempferol and myricetin), alkaloids (carpine, pseudocarpane, dehydrocarpane I and II), phenolic compounds (ferulic acid, caffeic acid, chlorogenic acid), the cyanogenic 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 curcuminoinds 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 (Unghaiboob et al., 2005) [89]. The study of hexane and ethanol turmeric extract and curcuminoinds 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 pP (Lahwahvinit et al., 2010) [39]. The hexane and methanol extracts of C. longa demonstrated antibacterial effect against Vibrio, Bacillus, Aeromonas, Streptococcus, Staphylococcus and Edwardsiella species (Lahwahvinit 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 preparation.

The methanol extract of turmeric demonstrated antifungal activity against Candida albicans and Cryptococcus neoformans with MIC values of 256 and 128 μg/mL, respectively (Unghaiboob et al., 2005) [89]. The study of hexane extract of C. longa at 1000 mg/L demonstrated antifungal effect against Phythophthora 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 mL/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 jeaneselmi, Fonsecaea pedrosoi, and Scedosporium apiospermum with MIC values of 114.9, 459.6, 459.6, and 114.9 µg/mL, respectively (Apsariaykul 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) [81]. 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) [80]. The tree is known by many regional names such as Benzolive, Drumstick tree, Horseradish tree, Kelor, Mlonge, Marango, Mulangay, Sajna and Saijihan (Fahey, 2005) [25]. 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 affected by drought (Anwar et al., 2007) [1]. 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 benzy l isothiocyanate, niazimicin, pterygospermin, and 4-[α-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, detoxifier, outstanding immune builder used in some 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 was 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. aur us 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, E. 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 cyanobactericidial activity, (Lurling and Beekman, 2010) [40], antipyretic, anti-inflammatory, anti-ulcer (Pal et al., 1995) [61], antibacterial and antifungal activities (Nikkon et al., 2003) [56].

*Moringa oleifera* leaf 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. aureus* 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.*, *Yersinia enterocolitica*, *Enterococcus faecalis*, *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) [12], Priya et al. (2011) [63] also reported that petroleum ether leaf 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. (Masjat 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 cordifolia* is a large deciduous climbing shrub found throughout India. It is known by multiple names like Gaduchi, 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. marcescens* (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-diepoxychloro-dihydroxy-13(16), 17, 12S, 18, 15-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 pneumoniae*, *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 microorganism. 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, terpenoids, 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

<table>
<thead>
<tr>
<th>Chemical class</th>
<th>Phytoconstituents</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids</td>
<td>Berberine, Tembeterine, Palmitine</td>
<td>Singh et al., 2003 [83]</td>
</tr>
<tr>
<td>Glycosides</td>
<td>18-norclerodane glucoside, furanoid diterpene glucoside, cordifolioside A, cordifolioside B, palmatosides C, palmatosides P1, cordifolioside C, cordifolioside D, cordifolioside E</td>
<td>Gagan et al., 1994 [41], Wazit et al., 1995 [42], Gagan et al., 1996 [26], Ghosal et al., 1997 [28], Maurya et al., 1997 [47], Singh et al., 2003 [83]</td>
</tr>
<tr>
<td>Sesquiterpenoids</td>
<td>Cinocordifolin</td>
<td>Maurya et al., 1998 [46]</td>
</tr>
<tr>
<td>Steroids</td>
<td>β sitosterol, -sitosterol, giloinstereone, ecdysonone, makisterone A, 20 -hydroxy ecdysonae.</td>
<td>Singh et al., 2003 [83]</td>
</tr>
<tr>
<td>Diterpenoid lactones</td>
<td>Clerodane derivatives, tinosporon, tinosporides, jaiteren, columbin</td>
<td>Maurya et al., 1997 [47], Swaminathan et al., 1989 [85], Singh et al., 2003 [83]</td>
</tr>
<tr>
<td>Aliphatic compounds</td>
<td>Octacosanol, heptacosanol, nonacosan-15-one</td>
<td>Singh et al., 2003 [83], Thippeswamy et al., 2008 [88]</td>
</tr>
</tbody>
</table>

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) [84], Isocolumbin, Jatorrhizin (Yuan et al., 2010) [85], Palmitine and Barberine (Volleko et al., 2003) [86] 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 chemotherapy 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.

References
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