Herbal antibacterials: a review

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INTRODUCTION

India is well known for Ayurveda, which is one of important traditional medicine practiced. Herbs are widely exploited in the traditional medicine and their curative potentials are well documented [3]. Medicinal plants are relied upon by 80% of the world’s population, and in India the use of plants as therapeutic agents remains an important component of the traditional medicinal system. Medicinal plants are a source of great economic value all over the world. Nature has bestowed on us a very rich botanical wealth and a large number of diverse types of plants grow in different parts of the country. Emergence of pathogenic microorganisms that are resistant/multi-resistant to major class of antibiotics has increased in recent years due to indiscriminate use of synthetic antimicrobial drugs [4]. In addition, high cost and adverse side effects are commonly associated with popular synthetic antibiotics, such as hypersensitivity, allergic reactions, and immunosupression and are major burning global challenges..

Abstract

Plants are rich source of antibacterial agents because they produce wide array of bioactive molecules, most of which probably evolved as chemical defense against predation or infection. A major part of the total population in developing countries still uses traditional folk medicine obtained from plant resources. With an estimation of WHO that as many as 80% of world population living in rural areas rely on herbal traditional medicine as their primary healthcare. The study on properties and uses of medicinal plants are getting growing interests. In recent years this interest to evaluate plants possessing antibacterial activity for various diseases is growing. Different solvent extracts (aqueous, alcohol and ethanol) of leaves, flowers and seed of various plants were selected based on an ethnobotanical survey from India were subjected to in vitro antibacterial activity assay against Gram-positive and Gram-negative bacteria employing different diffusion method. Based on local use of common diseases and ethnobotanical knowledge, an attempt has been made to assess the antibacterial properties of selected medicinal plants viz. Argemone mexicana (Shalkanta), Aster lanceolatus (White panicle), Capparis thonningii and Capparis tomentosa (Woolly caper bush), Cardiospermum halicacabum (Balloonvine), Cassia alata (Herpetia alata), Centaurea sceleropis, Cinnamomum zeylanicum (Cinnamon), Curcuma longa (Turmeric), Cymbopogon nerevarus, Ficus religiosa (Peepal), Indigofera aspalathoides (Ajara), Marrubium vulgare (Horehound), Medicago Spp (Medick, Burclover), Morus alba (Mulberry), Ocimum sanctum (Tulsi), Origanum marjorana (Marjoram), Osulcs corniculata (Amli), Piper nigrum (Kala mirch), Plectranthus amboinicus (Indian borage, Patharchur), Plumeria acutifolia, Salvadora persica (Piludi), Sarcivia repens and Syzygium aromaticum (Clove) for potential antibacterial activity against some important bacterial strains, namely Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, Streptococcus pyogenes, Pseudomonas spp, Proteus spp, Salmonella Typhi, Escherichia coli, Shigella dysentriae, Klebsiella pneumoniae. The plant extracts were more active against Gram-positive bacteria than against Gram-negative bacteria.
issues in treating infectious diseases [5]. This situation forced scientists to search for new antimicrobial substances. In the present scenario, there is an urgent and continuous need of exploration and development of cheaper, effective new plant based drugs with better bioactive potential and least side effects. Hence, recent attention has been paid to biologically active extracts and compounds from plant species used in herbal medicines [6].

Antimicrobials of plant origin have enormous therapeutic potential and have been used since time immemorial. They have been proved effective in the treatment of infectious diseases simultaneously mitigating many of the side effects which are often associated with synthetic antibiotics [7]. Many infectious diseases have been known to be treated with herbal remedies based on ethnobotanical knowledge. Natural products, either as pure compounds or as standardized plant extracts, provide unlimited opportunities for new drug leads because of the unmatched availability of chemical diversity. Therefore, researchers are increasingly turning their attention to folk medicine, looking for new leads to develop better drugs against microbial infections. Thus, it is anticipated that phytochemicals with adequate antibacterial efficacy will be used for the treatment of bacterial infections.

**Argemone mexicana (Shialkanta)**

The sensitivity of two Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and two Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) pathogenic multi-drug resistant bacteria was tested against the crude extracts (cold aqueous, hot aqueous, and methanol extracts) of leaves and seeds of *Argemone mexicana* L. (Papaveraceae) by agar well diffusion method. The methanol extracts of *A. mexicana* (leaves and seeds) showed maximum antibacterial activity against *P. aeruginosa*, followed by *E. coli*, *B. sublitis*, and *S. aureus*. On the contrary, aqueous extracts (cold and hot) of *A. mexicana* seeds showed maximum activity against *B. sublitis*, followed by *P. aeruginosa*, *E. coli*, and *S. aureus*. Again, cold aqueous extract of *A. mexicana* leaves showed highest efficacy against *P. aeruginosa* followed by *B. sublitis*, *E. coli*, and *S. aureus* where as in case of hot aqueous extract of *A. mexicana* leaves, maximum sensitivity was shown against *E. coli*, followed by *B. sublitis*, *P. aeruginosa* and *S. aureus* [8].

**Aster lanceolatus** (White panicle)

The activity of the ethanolic extract of the flowers has been demonstrated against *Streptococcus pyogenes* in diffusion in gel and the activity of the ethanol extract of the stems and leaves against *Salmonella typhimurium* and *Streptococcus pyogenes* in minimal inhibitory concentration [9].

**Capparis thonningii** and **Capparis tomentosa** (Woolly caper bush)

The leaf methanol extract of *C. thonningii* and ethanol extract of *C. tomentosa* aerial parts were investigated in vitro antimicrobial activity using the agar disc diffusion technique. The extract of *C. tomentosa* displayed overwhelming concentration dependent antimicrobial properties, inhibiting the growth of *Staphylococcus aureus* and *Bacillus cereus*, far above that of ampicillin used in the study at a concentration of 1.0 g/ml. The methanol extract of *C. thonningii* also displayed a concentration related antibacterial activity, inhibiting the growth of *S. aureus* comparable to ampicillin at 1.0 g/ml.
The extract was least active against *Escherichia coli* with a mild activity at 1.0 g/ml [10].

**Cardiospermum halicacabum (Balloonvine)**

The antibacterial properties of leaf and its callus extracts were screened against ten human pathogenic bacteria by cup diffusion method. Powdered leaf and leaf derived callus material was subjected to extraction of aqueous and with different organic solvents viz., petroleum ether, chloroform, methanol and ethanol using soxhlet apparatus. Among all the solvents tested, significant inhibitory activity was observed in ethanol extract of both leaf and leaf derived callus followed by methanol. It also observed that the activity was more pronounced on Gram-positive bacteria than Gram-negative bacteria. Pathogenic bacteria only *Bacillus subtilis* and *Bacillus cereus* belongs to Gram-positive bacteria showed susceptible for leaf aqueous extract when compared to *Staphylococcus aureus*. In Gram-positive bacteria *Bacillus subtilis* showed maximum inhibition. Whereas Gram-negative bacteria showed least susceptible for leaf aqueous extract [11].

**Cassia alata (Herpetic alata)**

Crude ethanol and water extract of leaves from *Cassia alata* were tested *in vitro* against bacteria (*Staphylococcus aureus* and *Escherichia coli*) and *in vivo* to evaluate the effect of both extracts in liver cells of mice. Antibacterial activity of *Cassia alata* extracts on *Staphylococcus aureus* was detected. The water extract exhibited higher antibacterial activity than the ethanol extract from leaves (inhibition zone of 11-14 mm and 9-11 mm respectively). *Escherichia coli* showed resistant to both extract. Results were compared to commercial antibiotics, chloramphenicol, penicillin and aerofloxaxine, which had 19 mm, 29 mm and 22 mm respectively [12].

**Centaurea sclerolepis**

The antibacterial and general toxicity with brine shrimp lethality bioassay of the arctiin from the seeds of *C. sclerolepis* has been studied. According to the obtained MIC values, it is clear that arctiin’s antibacterial activity against bacteria is lower than the positive control chloramphenicol. Whereas arctiin has activity between the ranges of 62.5-250 μg/ml against both Gram-positive (*S. aureus, M. luteus, B. cereus*) and Gram-negative (*E. coli, P.aeroginosa*) bacteria, the positive control chloramphenicol was more effective within the ranges of 31.25-125 μg/ml [13].

**Cinnamomum zeylanicum (Cinnamon)**

The antimicrobial activity of cinnamon essential oil against *Paenibacillus larvae* was analyzed by means of a combination of *in vitro* techniques, such as the tube dilution method and bioautography, a method
employed to localize antibacterial activity on a chromatogram. Cinnamaldehyde and eugenol proved to have antibacterial effects against *P. larvae*. MIC and MBC for *C. zeylanicum* essential oil were between 25-100 μg/ml and 125-250 μg/ml, respectively, for all strains. Essential oil showed inhibitory capacity against strains of *P. larvae* [14].

*Curcuma longa (Turmeric)*

*Curcuma longa* rhizome extracts were evaluated for antibacterial activity against pathogenic strains of Gram-positive (*Staphylococcus aureus, Staphylococcus epidermidis*) and Gram-negative (*Escherichia coli, Pseudomonas aeruginosa, Salmonella typhimurium*) bacteria. The use of essential oil from turmeric as a potential antiseptic in prevention and treatment of antibacterial infections has been suggested [15].

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*Cymbopogon nervatus*

Antibacterial activity of essential oil of dried inflorescence of *Cymbopogon nervatus* was investigated. The essential oil remarkably inhibited the growth of tested bacteria except for *Salmonella typhi*. The maximum activity was against *Shigella dysenteriae* and *Klebsiella pneumonia* [16].

*Ficus religiosa (Peepal)*

The antimicrobial activity of ethanolic extracts of *F. religiosa* (leaves) was examined using the agar well diffusion method. The test was performed against four bacteria: *Bacillus subtilis* (ATCC 6633), *Staphylococcus aureus* (ATCC 6538), *Escherichia coli* (ATCC 11229) and *Pseudomonas aeruginosa* (ATCC 9027). The results showed that 25mg/ml of the extract was active against all bacterial strains. The antibacterial activity of different extracts from the bark of *F. religiosa* was tested against diarrhoeal enterotoxigenic *Escherichia coli* using disc diffusion method. The antibacterial activities of extract were compared with standard antibiotics. The sensitivity of the organisms
measured in terms of zone of inhibition ranged from 8.00 to 14.00 mm at 4mg/ml of different extract. The results revealed that methanol extract exhibits good activity compared to chloroform and aqueous extract. Petroleum ether and hexane extract did not show any activity [17].

**Indigofera aspalathoides (Ajara)**

The alcohol extract and fractions were tested for evaluation of the MIC to *Mycobacterium tuberculosis* H37Rv strain with microplate technique using alamar blue. The antimycobacterial activity of alcohol extract and fractions were compared with rifampicin. The benzene, ethyl acetate fractions and extract showed inhibition 61%, 27% and 48% respectively at 100 μg/ml of MIC. The n-butanol and diethyl ether fractions were found to be less active 6 and 9 μg/ml [18].

**Marrubium vulgare (Horehound)**

The antibacterial activity of the methanolic extract of *Marrubium vulgare* whole plant was tested by disc diffusion method. Zones of Inhibition produced by methanolic extract in a dose of 50, 100, 200, 400 and 600 mg/ml against selected strains was measured and compared with those of standard discs of antibiotic ciprofloxacin (10 μg/ml). The study revealed that methanolic extract of the crude drug was very much effective against *B. subtilis, S. epidermidis* and *S. aureus* (Gram-positive bacteria) and moderately effective against *P. vulgaris* and *E. coli* while ineffective in case of *P. aeruginosa* (Gram-negative bacteria). Thus on the basis of the results it is inferred that the methanolic extract of *M. vulgare* whole plant had *in vitro* antibacterial [19].

**Medicago Spp. (Medick, Burclover)**

The antimicrobial activity of saponins from *Medicago sativa, M. arborea* and *M. arabica* against a selection of medically important yeasts, Gram-positive and Gram-negative bacteria was investigated. The antimicrobial activity was especially high against Gram-positive bacteria (*Bacillus cereus, B. subtilis, Staphylococcus aureus* and *Enterococcus faecalis*) with *M. arabica* being the species showing a broader spectrum of action [20].

**Morus alba (Mulberry)**

Antibacterial activity of Kuwanon G (active antibacterial constituent) was investigated by the MIC test and the viable cell count method. MIC of Kuwanon G against *Streptococcus mutans* causing dental caries was determined to be 8 μg/ml. The bactericidal test
showed that Kuwanon G completely inactivated S. mutans at the concentration 20 µg/ml in 1 min. Kuwanon G also significantly inhibited the growth of other cariogenic bacteria such as Streptococcus sobrinus and Streptococcus sanguis and Porphyromonas gingivalis causing periodontitis. Transmission electron microscopy (TEM) of Kuwanon G treated cells demonstrated remarkable morphological damage of the cell wall and condensation of the cytoplasm [21].

Ocimum sanctum (Tulsi)

The antibacterial activity of ethanol extracts was determined by agar well diffusion method. The plant extracts were more active against Gram-positive bacteria than against Gram-negative bacteria among all the pathogens, all Gram-positive bacteria were inhibited by all four plant extract. All Gram-negative bacteria i.e. Pseudomonas spp, Proteus spp, Escherichia coli, Shigella dysenteriae, Klebsiella pneumonia and Salmonella typhi were showed zone of inhibition against extract of Ocimum sanctum [22].

Origanum marjorana (Marjoram)

In vitro microbicidal activity of the methanol extract of Origanum marjorana L. was tested against six bacteria (Bacillus subtilis, B. megaterium, Escherichia coli, Proteus vulgaris, Pseudomonas aeruginosa and Staphylococcus aureus). The methanol extract of O. marjorana can be used as an effective herbal protectant against different pathogenic bacteria [23].

Oxalis corniculata (Amli)

The inhibitory activity was highly significant in the aqueous extracts of Oxalis corniculata. Most of the plant extracts showed significant antibacterial activity than bacitracin. MIC of aqueous extract of twelve plants varied between 4-50 µl. Results indicate the potential of these plants for further work on isolation and characterization of the active principle responsible for antibacterial activity and its exploitation as whereas Oxalis Acacia nilotica varied between 9-35.5 mm. Whereas corniculata was effective against all the tested bacteria in case of Lawsonia inermis it varied between 9 to except Shigella sonnei and Proteus mirabilis [24].

Piper nigrum (Kala mirch)
Effectiveness of organic extracts of *Piper nigrum* fruit against pathogenic strains of *Escherichia coli* (MTCC 723), *Staphylococcus aureus* (MTSS 96), *Streptococcus pyogenes* (MTSCC 442), *Proteus mirabilis* (MTCC 1429) by tube dilution method. The study revealed that 70% alcoholic hot extract had higher antibacterial activity as compared to chloroform hot and petroleum ether cold extracts [25].

*Plectranthus amboinicus* (Indian borage, Patharchur)

The aqueous extract was found to be antibacterial and it was studied against various Gram-positive and Gram-negative bacterial strains by using MIC, agar well diffusion method to find zone of inhibition. The MIC results of aqueous extract of *Plectranthus amboinicus* indicated that *Proteus vulgaris*, *Bacillus subtilis* and *Staphylococcus aureus* were least susceptible among the organisms tested and *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* are not shown any inhibition to aqueous extract of *Plectranthus amboinicus* [26].

*Plumeria acutifolia* (Kachuchi)

The *in vitro* antimicrobial activity of *P. acutifolia* stem bark ethanol extract against the microorganisms employed was assessed qualitatively and quantitatively by the presence or absence of inhibition zones, zone diameters, MIC and MBC or MFC values. The data indicated that Gram-positive *E. faecalis* was the most sensitive strain tested to the ethanol extract of *P. acutifolia* stem bark with the greatest inhibition zone of 21 mm. The *B. subtilis* and *S. aureus* were also found to be more sensitive with inhibition zones of 26 and 26 mm, respectively. The ethanol extract of *P. acutifolia* stem bark also showed excellent activity against tested Gram-negative bacteria. *E. coli* was the most sensitive organism among Gram-negative bacteria with the inhibition zone of 33 mm more than that of standard gentamycin positive control. *K. pneumoniae*, *P. aeruginosa* and *S. typhimurium* also exhibited significant sensitivities to the tested ethanol crude extract with the inhibition zones of 18, 16 and 20 mm respectively. The extract did not show any toxic symptoms against the tested mice [27].

*Salvadora persica* (Piludi)
The aqueous extract of *S. persica* was active against all oral pathogens and *Streptococcus* species were the most sensitive; the highest inhibitory activity was seen against *S. faecalis* (zone of inhibition: 22.3 mm) using the extract concentration of 200 mg/ml, while the weakest activity was demonstrated against *P. aeruginosa*. On the other hand, the methanol extract of *S. persica* stems showed less inhibitory activity against the tested bacteria than did the aqueous extract. *L. acidophilus* and *P. aeruginosa* resisted all methanol extract concentrations, while *S. faecalis* was the most susceptible bacteria (zone of inhibition: 17.7 mm) to the highest extract concentration. The aqueous extract exhibited better antifungal results than the methanol extract and the strongest activity was observed. According to both antimicrobial assays the aqueous extract inhibited all isolated microorganisms, especially the *Streptococcus* species, and was more efficient than the methanol extract, which was resisted by *L. acidophilus* and *P. aeruginosa*. The strongest antibacterial activity was observed using the aqueous extract against *S. faecalis* (zone of inhibition: 22.3 mm; MIC: 0.781 mg/ml) [28].

**Salvia repens**

The antibacterial activity of the aerial parts of *Salvia repens* has shown that the acetone extract inhibited the growth of *Bacillus cereus*, *Streptococcus pyogenes* and *Escherichia coli* bacteria tested at MIC of 0.5 mg/ml. The methanol extracts effectively inhibited the growth of both *Staphylococcus epidermidis* and *Micrococcus kistinae* at minimum concentration of 0.5 mg/ml. At 0.1 mg/ml the methanol extract inhibited the following *B. cereus*, *S. pyogenes* and *E. coli* bacteria whose inhibition concentration was below 0.5 mg/l. The activity of the water extracts of the plants against Gram-negative and Gram-positive bacteria has shown inhibition at 1.0 and 2.5 mg/l, respectively [29].

**Syzygium aromaticum** (Clove)

The antibacterial property of *S. aromaticum* was studied. Compare to ethanolic extract, methanolic extract was showing best result against Gram-positive culture *Staphylococcus aureus* (MTCC 2940) and two Gram-negative cultures *Pseudomonas aeruginosa* (MTCC 2453) and *E. coli* (MTCC 739). The MIC value was determined by using broth dilution methods. Methanolic extract of clove was subjected to get the MIC against test organisms and it was found to be 2.31 mg/ml for *E. coli*, 0.385 mg/ml for *Staphylococcus aureus* and 0.01 mg/ml for *Pseudomonas aeruginosa*. The addition of metal ions (Zn**, Cu**, Pb**, Ca**, Mg**, Fe**) along with methanolic extract of clove samples gave positive results against test organisms. The metal ions increased antibacterial properties of clove samples but after optimization at various concentrations it could not increase the antibacterial activity of samples compare to 10%, 20% and 30% [30].

**DISCUSSION**

Plant essential oils and extracts have been used for many thousands of years, in food preservation, pharmaceuticals, alternative medicine and natural therapies. It is necessary to investigate those plants scientifically which have been used in traditional medicine to improve the quality of healthcare. Plant extracts are potential sources of novel antimicrobial compounds especially against bacterial pathogens. *In vitro* studies showed that the plant extracts inhibited bacterial growth but their effectiveness varied [31]. The antimicrobial activity of many plant extracts has been reviewed.

In general, the cell walls of Gram-negative organisms are more complex than Gram-positive organisms because of high lipid content and act as a diffusional barrier and make less susceptible to the antibacterial
agents than the Gram-positive organisms [32]. In spite of this permeability difference, however, aqueous extract, ethanol extract, methanol extract have still exerted some degree of inhibition against Gram-negative organisms as well.

The present antibacterial review of the plant extracts demonstrates that folk medicine can be as effective as modern medicine to combat pathogenic microorganisms. The millenarian use of these plants in folk medicine suggests that they represent an economic and safe alternative to treat infectious diseases.

CONCLUSION

Many medicinal plants have been found effective in the cure of bacterial diseases. Due to increasing antibiotic resistance in microorganisms and side effects of synthetic antibiotics medicinal plants are now gaining popularity in the treatment of bacterial infections. The use of traditional medicines and medicinal plants in most developing countries as therapeutic agents for the maintenance of good health has been widely observed. Furthermore, an increasing reliance on the use of medicinal plants in the industrialized societies has been traced to the extraction and development of drugs and chemotherapeutics from these plants as well as from traditionally used herbal remedies. Medicinal plants are considered as clinically effective and safer alternatives to the synthetic antibiotics. According to World Health Organization, medicinal plants would be the best source to obtain a variety of drugs. Extensive research in the area of isolation and characterization of the active principles of these plants are required so that better, safer and cost effective drugs for treating bacterial infections can be developed.

REFERENCES


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