# Bioactivity of tropical phanerogamae against bacterial pathogens: a mini review

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Diseases of bacterial etiology are acknowledged as a serious public health issue, with high treatment costs. In addition, there is an increasing incidence of bacterial resistant to marketed antibiotics. This scenario stands out in many countries, with negative impact on human health. One of the methods to obtain new substances against drug-resistant bacteria is to prospect for bioactive compounds in plants. The following study proposes to conduct a literature review on the antibacterial activity of tropical phanerogamae and macroalgae.

**Keywords** antibacterial compounds; human pathogens; medicinal plants.

## 1 Introduction

The rise of antibiotic-resistant bacterial pathogens is a public health problem that has been reported in different countries [1,2]. This statement serves as a prerogative to carry out researches aimed to prospect new antibacterial drugs. Recent studies indicate the recognition of antibacterial activity of plants frequently used in folk medicine in several countries [3,4,5,6,7,8,9,10,11], and identify different phytochemical compounds as possible antimicrobial agents: flavonoids, steroids, tannins, and glycine-rich peptide [12,13]. Furthermore, it is worth mentioning the inhibitory effect of some plant extracts against strains of methicillin-resistant *Staphylococcus aureus* [14]. Thus, the chemical compounds screening of photosynthetic organisms with antimicrobial effect against human pathogens proves to be of major importance. This study aims to conduct a brief literature review on the subject of bioactive plants against Gram-positive and Gram-negative bacterial pathogens.

## 2. Antibacterial activity in Phanerogamae

The antibacterial properties of tropical angiosperms have been explored in the folk medicine of many developing countries for centuries. The use of plants for medical purposes heightens the scientific community interest regarding possibilities of new antibacterial drugs discovery. Thus, some species of higher plants with bioactivity against bacteria of clinical interest will be briefly discussed below.

The *Psidium guajava* specie, widely known as "goiabeira", has its antimicrobial properties acknowledged. Vieira et al. [15] conducted an investigation on the microbicidal effect of goiabeira extracts, concluding that their sprout extracts constitute a treatment option for diarrhea caused by *E. coli* or by *S. aureus*-produced toxins, due to their curative action, availability in tropical countries and low cost. Rahim et al. [16] observed antibacterial activity of its leaf and bark against multiple antibiotic-resistant *V. cholerae* and suggested that the nature of its bioactive component was nonproteic. The authors also emphasize that *P. guajava* is extensively distributed in Bangladesh, offering a great potential for positive effects in using herbal medicine to control cholera outbursts. In Brazil, Gonçalves et al. [17] mention the bioactivity of *P. guajava* leaf extracts against *Staphylococcus aureus* and *Salmonella* sp. The authors consider the goiabeira an important potential source of new antimicrobial compounds. Ghan and Demello [18] had previously commented on the antibacterial activity of aqueous extracts from the guaja tree leaves against *S. aureus*, had then declared that the extracts could be an important source of food preservative. The bioactivity of the guava tree leaves extracts against pathogens associated with food-consumption related diseases was pointed out by Mahfuzul Hoque et al. [19], who detected growth inhibition of *Listeria monocytogenes* JCM 7676, *S. aureus* JCM 2151, *S. aureus* JCM 2179, *V. parahaemolyticus* IFO 12711, *Alcaligenes faecalis* IFO 12669, *Aeromonas hydrophila* NFRI 8282, and *A. hydrophila* NFRI 8283. The presence of bioactive chemicals compounds against micro-organisms in the *P. guajava* seed is a characteristic that must be highlighted. Pelegrini et al. [20] isolated and identified the Pg-AMP1 peptide from the guava seed and reported its bioactivity against Gram-negative bacteria associated with urinary and gastro-intestinal hospital infections - *Klebsiella* sp. and *Proteus* sp. In addition, Tavares et al. [13] tested the antimicrobial effect of the recombinant peptide Pg-AMP1 and observed a wide range of bioactivity against *E. coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Staphylococcus epidermides*. The authors suggest that the Pg-AMP1 is a promising biotechnological tool to be used for controlling human infectious diseases.

Studies and researches on the antimicrobial potential of the angiosperm family Annonaceae were conducted in Brazil. Takahashi et al. [21] confirmed bioactivity against micro-organisms in extracts from the *Xylopia frutescens*, *X. amazonica*, and *Annona ambotay* species. According to the authors, the diterpenoid trachylobanic acid derived from the

 

*Xylopia* genus showed bioactivity against *Bacillus subtilis* and *Staphylococcus aureus*. Other bioactive chemical compounds were previously described in the Announaceae family: acetogenins with a wide spectrum of action, including antibiotic effects. Annonaceous acetogenins are series of C-35/C-37 natural products derived from C-32/C-34 fatty acids and combined with a 2-propanol unit [22]. Antibacterial activity from extracts of the *Annona muricata* bark (a fruit known as graviola) was investigated by Vieira et al. [5], revealing favorable esults regarding its inhibitory effects against *S. aureus* ATCC 25923, *Vibrio cholerae* 569B and *Escherichia coli* collected from river water samples.

Lima et al. [23] performed a research on the antibacterial activity of some Brazilian medicinal plants, and reported promising effects against *S. aureus* from the extracts of *Jatropha elliptica* (rhizome), *Schinus terebinthifolius* (stem barks), *Erythrina mulungu* (stem barks), *Caesalpinia pyramidalis* (stems and leaves), *Serjania lethalis* (stems and leaves), and *Lafoensia pacari* (stem bark and leaves).

From the screening test of plants used in the Brazilian folk medicine for infectious diseases, Holetz et al. [24] confirmed the antibacterial effect of the following angiosperms: *Piper regnellii* (manifesting bioactivity against *S. aureus, Bacillus subtilis, Pseudomonas aeruginosa*, and *Escherichia coli*), *Punica granatum* (*S. aureus*), *Eugenia uniflora* (*S. aureus* and *E. coli*), *Psidium guajava*, *Tanacetum vulgare*, *Arctium lappa*, *Mikania glomerata*, *Sambucus canadensis*, *Plantago major* and *Erythrina speciosa*. Besides, the same authors detected anticandidal activity in P. *guajava, E. uniflora, P. granatum, A. lappa, T. vulgare, M. glomerata, L. alba, P. regnellii*, and *P. major*.

Sousa et al. [25] conducted researches on the bioactivity of two traditional plants (*Chenopodium ambrosioides* and *Kielmeyera neglecta*) used in the Brazilian folk medicine for infectious diseases and reported the bioactivity of *K. neglecta* extracts against multidrug-resistant *Enterococcus faecalis* ATCC 51299 and *S. aureus* ATCC 43300.

The latent possibilities of the Brazilian flora regarding antibiotics prospection was highlighted by Veras et al. [26]. The authors observed that the essential oil of *Lipia sidoides* (bioactivity against *Pseudomonas aerugionosa*) and thymol - its major component – interfere on the activity of aminoglycosides. Thus, it may be used as adjuvant in antibiotic therapy against bacterial pathogens of the respiratory tract. On the synergy of phanerogamae extract and antibiotics, Oliveira et al. [27] pointed out the synergistic antibiotic activity of the *Stryphnodendron rotundifolium* (bioactivity against standard and clinical isolates of *E. coli* and *S. aureu*s) , once its extracts showed a potentiating effect and were able to reduce the MIC (minimum inhibitory concentration) of the gentamicin, kanamycin, amikacin and neomycin antibiotics. In addition, Cunha et al. [28] combined subinhibitory concentrations of *Costus cf. arabicus* L.extracts with aminoglycosides and observed a synergistically enhanced antibiotic activity against multidrig-resistant strains of *Escherichia coli* and *S. aureus*. The authors also noted that the extracts tested may be considered a potential source of antibacterial and modulatory agents.

Other studies on the bioactivity evaluation against micro-organisms focused on phanerogamae that occur in Brazil:

- Leal et al. [29] described the anti-staphylococcal activity of the dichloromethane extract of the *Zizyphus joazeiro*. From the most active fraction against Staphylococcus, the authors identified three lupane-type triterpenes (methylbetulinate, betulinic, and alphitolic acids) and two ceanothane type triterpenes (methylceanothate and the epigouanic acid).
- Cunha et al. [30] showed promising results evaluating the antimicrobial effect of compounds derived from the methylene chloride extract of *Miconia ligustroides*, such as ursolic acid (bioactivity against *Bacillus cereus* ATCC 14579), oleanolic acid (bioactivity against *Bacillus cereus* ATCC 14579) and *Streptococcus pneumoniae* (ATCC 6305).
- Campos et al. [31] reported antibacterial activity of *Piper solmsianum* C. DC. var. *solmsianum* (Piperaceae) against Gram-positive bacteria (*Bacillus cereus, Staphylococcus aureus, Staphylococcus saprophyticus* and *Streptococcus agalactiae*). The authors suggest that the antimicrobial activity may be related to the presence of conocarpan and eupomatenoid-5 (neolignans).
- Oliveira et al. [32] emphasize the bioactivity of the *Lippia alba* and *Lippia alba* f. essential oils against bacteria and fungi. According to the authors, the bioactivity was probably a consequence of the high content of oxygenated monoterpenes, specially by aldehydes and alcohols.
- The antimicrobial effect of the phanerogam *Croton urucurana* against *Salmonella* Typhimurium and *S. aureus* was investigated by Perez at al. [33], who identified the acetyl aleuritolic acid as its bioactive compound.

Extracts from Argentinian plants are being considered significant sources of new chemical structures that can contribute to mitigate and/or cure some illnesses [34]. The same authors obtained data that proved the *Tripodanthus acutifolius* antibacterial efficiency against *Acinetobacter freundii*, *Pseudomonas aeruginosa* and *S. aureus* ATCC 25923. The following compounds were cited as potential responsibles for the antibacterial capacity: rutin (3,3',4',5,7-pentahydroxyflavone 3-beta-rhamnosilglucoside), iso-quercitrin (3,3',4',5,7-pentahydroxyflavone 3-beta-glucoside) and a terpene. Zampini et al. [35] demonstrated the antimicrobial activity of Argentinian plants used in folk medicine to treat bacteria-related infectious diseases. The authors detected bioactivity in ethanolic extracts from aerial parts of *Baccharis*, *Fabiana* and *Parastrephia* against methicillin, oxacillin and gentamicin-resistant *Staphylococcus*. *Baccharis boliviensis* and *Fabiana bryoides* also displayed bioactivity against *Enterococcus faecalis* with different phenotype. Other plants with antibacterial effects were also mentioned: *Chuquiraga atacamensis* and *Parastrephia*.

In the 1990's, Anesini and Perez [36] perfomed the screening test of 132 extracts from argentine folk-medicinal plants for antimicrobial activity and proved antibacterial efficiency against penicillin G resistant strain of

 

*Staphylococcus aureus*, *Escherichia coli* and/or *Aspergillus niger* in the following plants: *Tabebuia impetiginosa* (bark), *Achyrocline* sp. (aerials parts), *Larrea divaricata* (leaves), *Rosa borboniana* (flowers), *Punica granatum* (fruit pericarp), *Psidium guineense* (fruit pericarp), *Lithrea ternifolia* (leaves) and *Allium sativum* (bulbs). On the bioactivity of Argentinian plants, Gonzaléz et al. [37] verified the antibacterial and antifungal effects of the essential oil and methanol extract of *Xenophyllum poposum*.

In India, studies on the antimicrobial potential of higher plants are widely reported. Aqil et al. [38] confirmed the inhibitory effect of the following plants: *Camellia sinensis* (leaves), *Delonix regia* (flowers), *Holarrhena antidysenterica* (bark), *Lawsonia inermis* (leaves), *Punica granatum* (rind), *Terminalia chebula* (fruits) and *Terminalia belerica* (fruits) against clinical isolates of beta-lactamase producing methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA). *Ocimum sanctum* extracts showed bioactivity against the three MRSA strains. The authors cited phenols and flavonoids as the main active compounds against micro-organisms. Ahmed and Aqil [39] reported promising results on the antibacterial activity against ESbetaL-producing multidrug-resistant enteric bacteria (*Escherichia coli* and *Shigella*) in the following plants: *Acorus calamus, Hemidesmus indicus, Holarrhena antidysenterica* and *Plumbago zeylanica*.

In Cameroon, Misra et al. [40] performed researches on the medicinal properties of the *Zanthoxylum leprieurii* (Syn. *Fagara leprieurii*) and *Z. zanthoxyloides* plants, used in stomach disorders treatment, gonorrhea, intestinal parasites, sterility, wound dressing, sickle cell anaemia and as pain reliever. The authors observed moderate anticancer and antimicrobial activities in both plants, and identified the main elements that constitute its essential oil: citronellol, geraniol (Z. *zanthoxyloides*) and E-β-ocimene (*Z. leprieurii*).

Other Phanerogamae with antimicrobial potential are those that occur in mangrove ecosystems. Antibacterial activity from different parts of the crabapple mangrove tree - *Sonneratia caseolaris* was reported by Yompakdee et al. [41]. This plant occurs in estuarine and tidal creek areas and mangrove forests, and it is medicinally used as an astringent and antiseptic. The aforementioned authors found that ethanol extracts of all parts (leaves, pneumatophore, flowers and fruit) showed bactericidal effect against Gram-negative bacteria (Extended-spectrum beta-lactamase-*Escherichia coli*, multidrug-resistant-*Pseudomonas aeruginosa* and *Acenetobacter baumannii*) and bacteriostatic effect against Gram-positive bacteria (Methicillin-resistant *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium*).

Studies on the use of plants to combat cholera, tuberculosis, respiratory infections, wound infection, and against cariogenic microorganisms are also noteworthy. On cholerae, Morinaga et al. [42] described the inhibition of the cholera toxin (CT)-induced cyclic AMP accumulation in Vero cells cholerae by a natural polyphenol - resveratrol (3, 4', 5-trihydroxystilbene), found in red grapes, berries and peanuts. Other natural compounds – plant polyphenols – were able to suppress CT binding and internalization in Vero cells [43]. Chatterjee et al. [44] researched the use of natural compounds as virulence factors inhibitors in *V. cholerae* and found that the methanol extract of *Capsicum annuum* (red chilli) was able to inhibit CT production in *V. cholerae* O1 El Tor variant strains without affecting their viability. The authors also stress that the capsaicin – an active component of red chilli – was also able to inhibit CT production in *V. cholerae* strains from various serogroups and repressed the transcription of ctxA, tcpA and toxT genes, but not of toxR and toxS genes. Similar results were found by Yamasaki et al. [45], who reported that the regular intake of spices like red chili might be a good method to fight against devastating cholera. Also on cholerae, Thakurta et al. [46] noted satisfactory antibacterial effects when testing ethanolic extracts from the *Azadirachta indica* leaf against multi-drug-resistant *Vibrio cholerae* O1, O139 and non-O1, non-O139. The authors also mentioned antisecretory activity, and inhibition via oral administration of *V. cholerae*-induced hemorrhage in mouse intestine at a > or = 300 mg/kg dose. The results obtained in this study supports, from a scientific standpoint, the uses and mechanisms employed by the indigenous people in India for the treatment of diarrhea and cholera.

Tuberculosis is another relevant target on current researches that focus on the identification of new antimicrobial agents. Madikizela et al. [47] investigated the *in vitro* effect of traditional plants in South Africa used in the treatment of tuberculosis and its related symptoms, and identified the following species as most promising: *Abrus precatorius*, *Terminalia phanerophlebia*, *Indigofera arrecta*, and *Pentanisia prunelloides* validated their traditional use in the treatment of respiratory diseases. On this matter, Saikia et al. [48] also highlights the antimycobacterial activity of *Vetiveria zizanioides* L. Nash root extracts and their fractions against *Mycobacterium tuberculosis* H(37)Rv and H(37)Ra strains. For the authors, the root extract and hexane fraction of this plant might be considered candidates for new antituberculosis agents.

The medicinal plants *Maerua edulis*, *Securidaca longepedunculata*, *Zanthoxylum capense*, and *Tabernaemontana elegans* were cited for their antimycobacterial activity, and it was suggested that they might be sources of potential anti-tuberculosis drugs [49].

Some phanerogamae used for the treatment of respiratory ailments in rural Maputaland - *Ozoroa obovata*, *Sclerocarya birrea*, *Parinari capensis* subsp. *incohata*, *Tetradenia riparia* – are known for their bioactivity against some of the following micro-organisms: *Cryptococcus neoformans* (ATCC 14116), *Klebsiella pneumoniae* (ATCC 13883), *Moraxella catarrhalis* (ATCC 23246), *Mycobacterium smegmatis* (ATCC 14468) and *Staphylococcus aureus* (ATCC 6538) [50].

Wound infections caused by bacteria are also considered of interest to researches focused on finding and identifying new antimicrobial drugs. For Temrangsee et al. [51], some Thai medicinal plants are potential sources of antibacterial agents and may be used in alternative treatments for chronic wound infection. The authors points out theantibacterial activity of *Caesalpinia sappan* Linn. against *Staphylococcus aureus* and MRSA (methicillin-resistant *Staphylococcus aureus*).

Phanerogamae have been studies as an alternative source in cariogenic microorganisms treatment [52]. *Aristolochia cymbifera* (rhizomes), *Cocos nucifera* (husk fiber), *Ziziphus joazeiro* (inner bark), *Caesalpinia pyramidalis* (leaves) were cited for their inhibitory effects on oral bacteria (planktonic or in artificial biofilms) growth: *Prevotella intermedia, Porphyromonas gingivalis, Fusobacterium nucleatum, Streptococcus mutans* and *Lactobacillus casei* [53]. Sampaio et al. [54] observed that the fruit extracts from *Caesalpinia ferrea* - Brazilian ironwood - have *in vitro* bacterial activity against oral pathogens (*Candida albicans, Streptococcus mutans, Streptococcus salivarius, Streptococcus oralis* and *Lactobacillus casei*) in planktonic and biofilm models. Another plant with bioactivity against cariogenic bacterial species *Candida albicans* and *Stretptococcus mutans* is the *Lippia sidoides* Cham [55]. In recent studies, Castilho et al. [56] demonstrated that plant extracts derived from native species from the Amazon forest - *Ipomoea alba*, *Symphonia globulifera*, *Moronobea coccinea*, *Connarus ruber* var. *ruber*, *Psidium densicomum* and *Stryphnodendron pulcherrimum* - showed *in vitro* bioactivity against *Enterococcus faecalis*. Besides, some extracts were able to prevent the development of bacterial biofilm, and the authors highlighted the fact that nature itself might constitute a source of new and relevant chemicals for the dentistry industry.

## 3. Conclusions

The data presented in the current study provides solid evidence that some medicinal plants - including tropical phanerogams - present antibacterial activity. Therefore, they are also sources of bioactive compounds against Gram-positive and/or Gram-negative bacterial pathogens. The inhibitory action of certain plants against etiological agents, resistant or sensitive to antimicrobials, associated with diseases such as tuberculosis, respiratory infections, cholera, wound infections, diarrhea caused by *E. coli* or *S. aureus*-produced toxins and cavities indicates that their use as an alternative therapy may be of scientific value.

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