

Review on Medicinal Plant Activity against *Corynebacterium* spp.

Revisão sobre Atividade de Plantas Medicinais Contra *Coynebacterium* spp.

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Abstract

Cases of human infections related to species of the genus *Corynebacterium* spp. have increased gradually both in industrialized and developing countries. Species of the genus, often multidrug-resistant, has been cited as a pathogen of nosocomial infections associated with sepsis, endocarditis, infections of surgical wounds, prostheses, and infections related to the central venous catheter. Medicinal plants represent the oldest “weapons” used by humans for the treatment of all types of diseases, that is, the use of plants in the diseases prevention and/or healing is a habit that has always existed in human history. In this sense, this review aimed to research articles about the antibacterial action of medicinal plants against *Corynebacterium* species. The methodology used was bibliographic survey in the main scientific research databases. Seventy-one species of medicinal plants showed antibacterial activity against the genus *Corynebacterium* spp., in addition to the product havan samagri, which is composed of a mixture of 54 plant species; among them, eleven plants did not show any inhibitory activity for different species of that genus. Thus, there is a clear relevance in conducting new research in the area due to the possibility of validating popular information and the development of new antimicrobial drugs.

Keywords: Medicinal Plants. Antibacterial Activity. *Corynebacterium* spp.

Resumo

Casos de infecções humanas relacionadas às espécies do gênero *Corynebacterium* têm sido relatados, tanto em países industrializados quanto em desenvolvimento. Espécies do gênero, muitas vezes, multirresistentes aos antimicrobianos, são citadas como agentes de quadros como sepse, endocardite, infecções de feridas cirúrgicas, próteses e infecções relacionadas ao cateter venoso central. As plantas medicinais representam as mais antigas “armas” empregadas pelo homem no tratamento de enfermidades de todos os tipos, ou seja, a utilização de plantas na prevenção e/ou na cura de doenças é um hábito que sempre existiu na história da humanidade. Nesse sentido, esta revisão teve como objetivo pesquisar artigos sobre plantas medicinais com atividade antibacteriana contra corinebactérias. A metodologia utilizada foi o levantamento bibliográfico nos principais bancos de dados de pesquisas científicas. Setenta e uma espécies de plantas medicinais, além do produto havan samagri, que é composto por uma mistura de 54 espécies vegetais, demonstraram atividade antibacteriana contra o gênero *Corynebacterium*. Onze plantas estudadas não apresentaram nenhuma atividade inibitória para diferentes espécies de corinebactérias. Em função da possibilidade de validar as informações populares e o desenvolvimento de novas drogas antimicrobianas fica clara a relevância da realização de novas pesquisas na área.

Palavras-chave: Plantas Medicinais. Atividade Antibacteriana. *Corynebacterium* spp.

1 Introduction

The genus *Corynebacterium* is part of the family *Corynebacteriaceae* and is characterized by having complex cell walls, mycolic acids, string factor and cross-reactivity, which are highly relevant virulence factors. *Corynebacterium* spp comprises Gram-positive, pleomorphic, aerobic bacilli devoid of mobility and sporulation capacity. *Corynebacteria* may appear individually, in pairs or as palisades. Some species have metachromatic granules that are reserves of high energy phosphates (BIBERSTEIN, 1994).

This genus has more than 130 species, including species of medical veterinary and/or biotechnology relevance (LEHMANN; NEUMANN, 1896). *Corynebacterium* species have been cited with an increasing frequency as

pathogens of health care-associated infections (HCAIs) such as pneumonia, endocarditis, osteomyelitis and sepsis, including patients making use of indwelling medical devices (MARTINS *et al.*, 2009; BAIIO *et al.*, 2013; BURKOVSKI, 2014). *Corynebacterium diphtheriae* is the main species of the genus, however, other species are well known, such as *Corynebacterium ulcerans*, *Corynebacterium pseudotuberculosis*, *Corynebacterium pseudodiphtheriticum*, *Corynebacterium jeikeium*, *Corynebacterium amycolatum*, *Corynebacterium striatum*, among others (BAIO *et al.*, 2013; BURKOVSKI, 2014; SOUZA *et al.*, 2015; SIMPSON-LOURÊDO *et al.*, 2019).

The incidence of infections caused by multiresistant corynebacteria has been increasing and, mainly, making it

difficult to treat HCAs (MARTINS *et al.*, 2009; BAIO *et al.*, 2013; BURKOVSKI, 2014)

Medicinal plants represent the oldest “weapons” used by humans for the treatment of all types of diseases, that is, the use of plants in the prevention and/or healing of diseases is a habit that has always existed in human history (MACIEL *et al.*, 2002). Evidence of the use of medicinal and toxic plants is found in the oldest civilizations, serving as an important source of biologically active compounds (ANDRADE; CARDOSO; BASTOS, 2007).

In recent decades, there has been a growing interest in the use of medicinal plants and their extracts in therapy, constituting, in certain circumstances, an aid in primary health care and a therapeutic complement compatible with conventional medicine. For this, there must be a guarantee of safety in relation to toxic effects, in addition to knowledge about side effects, interactions, contraindications, mutagenicity, among others. The existence of pharmacological trials and clinical experimentation that demonstrate the efficacy of this type of medication is also extremely important (ARAÚJO *et al.*, 2007).

Popular knowledge on the use of medicinal plants as a therapeutic means is kept through oral tradition and, due to this factor, there is a lack of scientific knowledge on its pharmacological and toxicological properties and little information is proven about beneficial and harmful effects (OLIVEIRA; ARAÚJO, 2007).

It is estimated that 80% of the world population uses resources from popular medicines to meet the needs of private medical assistance, which may cost around 22 billion dollars (BANDARANAYAKE, 2006).

In the 19th century, the empiricism of alchemy was supplanted by experimental chemistry, which allowed the laboratory synthesis of new organic substances. This was one of the determining factors of the industrial and technological revolution that triggered the accelerated production of new medicines and, as more pure and concentrated derivatives of plants became available, doctors prioritized synthetic drugs and disregarded the important role of herbal medicine (SIMÕES; SCHENKEL; SIMON, 2001).

For some years, the government and professional interest in associating technological advances with popular knowledge and sustainable development have been fostered aiming an effective, comprehensive, humanized and independent health care policy (FRANÇA *et al.*, 2008).

Numerous scientific studies have been carried out to validate popular information regarding the use of medicinal plants. We can mention the current and intense interest that scientists, as well as the pharmaceutical industry, show by developing research in order to discover new active principles and to improve discoveries of new pharmacological activities of already known substances from plants. The segments mentioned above show concern regarding the development

of techniques for isolation and identification, production and cultivation of drugs (plant origin), biogenesis of active principles and other methods that lead to the improvement of their products (GURIB-FAKIM, 2006). The popular use of plants has been verified to obtain the most varied medicinal effects, including its application as antimicrobials (NOUMEDEM *et al.*, 2013).

The investigation of natural materials as sources of new antibacterial agents has potentially increased in recent years. Different extracts of medicinal plants are tested to provide scientific guarantees for this therapeutic practice, bringing advantages, such as low cost and easy access, reduction of adverse effects and prevention or reduction of risks of intoxication due to inappropriate use. (BANDARANAYAKE, 2006; VIANA *et al.*, 2020; OLIVEIRA *et al.*, 2020).

Thus, this review aimed to research articles about the antibacterial action of medicinal plants against *Corynebacterium* species.

2 Material and Methods

This work is a study of literature review with quantitative character, being carried out a survey of articles in databases of scientific research, national and international, such as Scielo, PubMed and Google Scholar. The keywords “antibacterial activity”, “medicinal plants”, “antimicrobial” and “*Corynebacterium* spp.” were used. These descriptors should be included in title or abstract of article. The period established for the research was from 1999 to 2016. The data obtained were organized in table with the following information: microorganism, plant species, popular name, family, part used, whether there is inhibition of microbial growth and the reference of the article.

3 Results and Discussion

The articles analyzed reported that, for the identification of the active principles of plants, sensitivity and bacterial resistance, antibacterial tests were performed *in vitro* using mainly the crude extract from different parts of plants, such as, leaf, bark, flower, twig and oil, and fractioning them using solvents (Tables 1, 2 and 3).

The evaluation of antibacterial activity was performed mainly by diffusion agar method, characterized by being a quick, simple test capable of evaluating the sensitivity of bacterial strains and by minimum inhibitory concentration assay, which consists in determining the lowest concentration of a certain principle capable of inhibiting microbial growth.

Seventy-one species of medicinal plants belonging to thirty-four distinct families showed antibacterial activity against *Corynebacterium* spp., in addition to the product havan sámagri, which is composed of a mixture of 54 plant species, as shown in Tables 1, 2 and 3.

Table 1 - Classification of plants and inhibitory activity against *Corynebacterium diphtheriae* and *Corynebacterium pseudodiphthericum*

Microorganism	Vegetable Species	Common Name	Family	Used Part	Inhibition	Citation
<i>C. diphtheriae</i>	<i>Anredera diffusa</i>	Madeira vine	Basellaceae	Flower	Yes	[1]
	<i>Asclepias curassavica</i>	Tropical milkweed	Asclepidaceae	Flower	No	[1]
	<i>Cassia tomentosa</i>	Glandular senna	Fabaceae	Flower	No	[1]
	<i>Cestrum auriculatum</i>	Cestrum	Solanaceae	Flower	No	[1]
	<i>Himatanthus sucuuba</i>	Bellaco caspi	Apocynaceae	Flower	No	[1]
	<i>Krameria triandra</i>	Rhatany	Krameriaceae	Flower	Yes	[1]
	<i>Peperomia galioides</i>	White cinnamon	Piperaceae	Flower	Yes	[1]
	<i>Sambucus peruviana</i>	Elderberry	Caprifoliaceae	Flower	Yes	[1]
	<i>Boswellia sacra</i>	Frankincense	Burseraceae	Oil and resin	Yes	[2]
	<i>Boswellia frereana</i>	Coptic frankincense	Burseraceae	Resin	Yes	[2]
	<i>Butea monosperma</i>	Flame-of-the-forest	Fabaceae	Leaf, bark and flowers	Yes	[3]
	<i>Polyalthia cerasoides</i>	Narela	Annonaceae	Bark	Yes	[4]; [5]
	<i>Saraca thaipingensis</i>	Yellow Saraca	Leguminosae	Flower, leaf and twig	Yes	[6]
	<i>Piper betle</i>	Betel pepper	Piperaceae	Leaf	Yes	[7];[8]
<i>Terminalia catappa</i>	Tropical almond	Combretaceae	Leaf and Fruit	Yes	[9];[10]	
<i>Adathoda vasica</i>	Malabar, nut	Acanthaceae	Leaf	Yes	[10]	
<i>C. pseudodiphthericum</i>	<i>Asclepias curassavica</i>	Milkweed	Asclepidaceae	Flower	No	[1]
	<i>Cassia tomentosa</i>	Glandular senna	Fabaceae	Flower	No	[1]
	<i>Cestrum auriculatum</i>	Cestrum	Solanaceae	Flower	No	[1]
	<i>Himatanthus sucuuba</i>	Bellaco caspi	Apocynaceae	Flower	No	[1]
	<i>Krameria triandra</i>	Rhatany	Krameriaceae	Flower	Yes	[1]
	<i>Peperomia galioides</i>	White cinnamon	Piperaceae	Flower	Yes	[1]
	<i>Sambucus peruviana</i>	Elderberry	Caprifoliaceae	Flower	No	[1]
	<i>Anredera diffusa</i>	Bertalha	Basellaceae	Flower	No	[1]
	<i>Terminalia catappa</i>	Tropical almond	Combretaceae	Leaf and Fruit	Yes	[9]

[1] = Camaioni Neto *et al.* (2002); [2] = Hasson *et al.* (2011); [3] = Pooja *et al.* 2016; [4] = Treeratanapiboon *et al.* (2011); [5] = Hemalatha *et al.* (2013); [6] = Prachayasittikul *et al.* (2012); [7] = Nandam, Prasad and Kandru (2013); [8] = Swapna, Ammani and Saripalli (2013); [9] Naz *et al.* (2007).

Source: Research data.

Table 2 - Classification of plants and inhibitory activity against *Corynebacterium xerosis*, *Corynebacterium pyogenes*, *Corynebacterium macginleyi* and *Corynebacterium rubrum*.

Microorganism	Vegetable Species	Common Name	Family	Used part	Inhibition	Citation
<i>C. xerosis</i>	<i>Liquidambar orientalis</i>	Oriental sweetgum	Hamamelidaceae	Bark	Yes	[11];[12]
<i>C. pyogenes</i>	<i>Khaya senegalensis</i>	African mahogany	Meliaceae	Leaf and bark	Yes	[13]
	<i>Cassia goratensis</i>	Winter cassia	Leguminosae	Leaf and bark	Yes	[13]
	<i>Boswellia dalzielli</i>	Frankincense tree	Burseraceae	Leaf and bark	Yes	[13]
	<i>Bauhinia thonningi</i>	Hano	Leguminosae	Leaf and bark	Yes	[13]
	<i>Butyrospermum parkii</i>	Shea	Sapotaceae	Leaf and bark	Yes	[13]
	<i>Guiera senegalensis</i>	Sabara	Combretaceae	Leaf and bark	Yes	[13]
	<i>Anogeissus schimperi</i>	Bakli	Combretaceae	Leaf and bark	Yes	[13]
	<i>Anacardium occidentale</i>	Cashew tree	Anacardiaceae	Leaf and bark	Yes	[13]
	<i>Terminalia catappa</i>	Tropical almond	Combretaceae	Leaf	Yes	[14]
	<i>C. macginleyi</i>	<i>Acacia leucophloea</i>	Acacia	Fabaceae	Bark	Yes
<i>Acalypha indica</i>		Indian copperleaf	Euphorbiaceae	Shoots	Yes	[15]
<i>Albizia lebeck</i>		Woman's tongue tree	Fabaceae	Bark	Yes	[15]
	<i>Ammania baccifera</i>	Blistering ammania	Lythraceae	Whole plant	Yes	[15]

<i>Microorganism</i>	<i>Vegetable Species</i>	Common Name	Family	Used part	Inhibition	Citation
	<i>Boerhaavia diffusa</i>	Punarnava	Nyctaginaceae	Whole plant	Yes	[15]
	<i>Bombax ceiba</i>	Red silk-cotton	Malvaceae	Bark	Yes	[15]
	<i>Butea monosperma</i>	Flame-of-the-forest	Fabaceae	Bark	Yes	[15]
	<i>Calotropis procera</i>	Rubber tree	Apocynaceae	Flower	Yes	[15]
	<i>Cardiospermum halicacabum</i>	Love in a puff	Sapindaceae	Whole plant	Yes	[15]
	<i>Cassia occidentalis</i>	Coffee senna	Leguminosae	Whole plant	Yes	[15]
	<i>Catharanthus roseus</i>	Madagascar periwinkle	Apocynaceae	Whole plant	Yes	[15]
	<i>Datura stramonium</i>	Devil's snare	Solanaceae	Whole plant	Yes	[15]
	<i>Cissus quadrangularis</i>	Devil's backbone	Vitaceae	Whole plant	Yes	[15]
	<i>Cleome viscosa</i>	Asian spiderflower	Cleomaceae	Whole plant	Yes	[15]
	<i>Clitoria ternatea</i>	Asian pigeonwings	Fabaceae	Whole plant	Yes	[15]
	<i>Embllica officinalis</i>	Myrobalan	Phyllanthaceae	Fruit	Yes	[15]
	<i>Ficus bengalensis</i>	Bargad	Moraceae	Bark	Yes	[15]
	<i>Ficus religiosa</i>	Fig tree	Moraceae	Bark	Yes	[15]
	<i>Hibiscus rosa sinensis</i>	Hibiscus	Malvaceae	Leaf	Yes	[15]
	<i>Hildegardia populifolia</i>	Poplar leaved ardor	Sterculiaceae	Stem bark	Yes	[15]
	<i>Hyptis suaveolens</i>	Pignut	Lamiaceae	Whole plant	Yes	[15]
	<i>Justicia adhatoda</i>	Malabar nut	Acanthaceae	Whole plant	Yes	[15]
	<i>Lantana camara</i>	Lantana	Verbenaceae	Whole plant	Yes	[15]
	<i>Lawsonia inermis</i>	Egyptian privet	Lythraceae	Leaf	Yes	[15]
	<i>Morus alba</i>	White mulberry	Moraceae	Bark	Yes	[15]
	<i>Solanum khasianum</i>	Nightshade	Solanaceae	Whole plant	Yes	[15]
	<i>Ocimum sanctum</i>	Basil	Lamiaceae	Leaf and seed	Yes	[15]
	<i>Phyllanthus amarus</i>	Seed-under-leaf	Phyllanthaceae	Whole plant	Yes	[15]
	<i>Physalis minima</i>	Wild cape gooseberry	Solanaceae	Whole plant	Yes	[15]
	<i>Piper betle</i>	Betel pepper	Piperaceae	Leaf	Yes	[15]
	<i>Plumbago zeylanica</i>	Ceylon leadwort	Plumbaginaceae	Whole plant	Yes	[15]
	<i>Pongamia pinnata</i>	Indian beech	Fabaceae	Bark and seed	Yes	[15]
	<i>Rosa indica</i>	Rose	Rosaceae	Flower	Yes	[15]
	<i>Sida acuta</i>	Common wireweed	Malvaceae	Whole plant	Yes	[15]
	<i>Tamarindus indicus</i>	Tamarind	Fabaceae	Bark	Yes	[15]
	<i>Terminalia catappa</i>	Tropical almond	Combretaceae	Bark	Yes	[15]
	<i>Terminalia arjuna</i>	Arjuna	Combretaceae	Bark	Yes	[15]
	<i>Terminalia chebula</i>	Chebulic myrobalan	Combretaceae	Bark and fruit	Yes	[15]
	<i>Tridax procumbens</i>	Tridax daisy	Asteraceae	Whole plant	Yes	[15]
	<i>Vernonia cinerea</i>	Ash colored Fleabane	Asteraceae	Whole plant	Yes	[15]
<i>C. rubrum</i>	<i>Terminalia catappa</i>	Tropical almond	Combretaceae	Leaf	Yes	[16]
	<i>Avicennia marina</i>	White mangrove	Avicenniaceae	Leaf, stem and root	Yes	[17]
	<i>Aegle marmelos</i>	Japanese bitter orange	Rutaceae	Leaf, fruit and seed	No	[18]
	<i>Annona squamosa</i>	Custard-apple	Annonaceae	Leaf and seed	Yes	[18]
	<i>Citrus limon</i>	Lemon	Rutaceae	Leaf and seed	Yes	[18]
	<i>Azadiracta indicates</i>	Neem	Meliaceae	Fruit	No	[18]
	<i>Piper betle</i>	Betel pepper	Piperaceae	Leaf	Yes	[18]
	<i>Mangifera indica</i>	Mango tree	Anacardiaceae	Fruit	Yes	[19]

[11] = Gurdal and Kultur (2013); [12] = Sagdiç *et al.* (2005); [13] = Kudi *et al.* (1999); [14] = Obafemi *et al.* (2006); [15] = Koday *et al.* (2010); [16] = Chanda *et al.* (2013); [17] = Moteriya, Dalsaniya and Chanda (2015); [18] = Padalia, Trivedi and Chanda (2016); [19] = Rakholiya *et al.* (2013).

Source: Research data.

Table 3 - Classification of plants and inhibitory activity against *Corynebacterium urealyticum*, *Corynebacterium ulcerans* and *Corynebacterium* spp.

Microorganism	Vegetable species	Common name	Family	Used part	Inhibition	Citation
<i>C. urealyticum</i>	*havan sámagri	-	-	-	Yes	[20]
<i>C. ulcerans</i>	<i>Stryphnodendron coriaceum</i>	barbatimão	Leguminosae-Mimosoideae	Leaf	Yes	[21]
<i>Corynebacterium</i> spp.	<i>Syzygium cumini</i>	Malabar plum	Myrtaceae	Leaf	Yes	[22]
	<i>Ageratum conyzoides</i>	Billygoat-weed	Asteraceae	Leaf	Yes	[23]

* material used for oblation in India, a mixture of 54 plant species. [20] = Nautiyal, Chauhan and Nene (2007); [21] = Santos *et al.* (2020); [22] = Loguercio *et al.* (2005); [23] = Singh *et al.* (2016)

Source: Research data.

The species *Boswellia sacra*, *Boswellia frereana*, *Butea monosperma*, *Anredera diffusa*, *Krameria triandra*, *Peperomia galioides*, *Piper betle*, *Terminalia catappa*, *Adathoda vasica*, *Sambucus peruviana*, *Saraca thaipingensis* and *Polyalthia cerasoides* show antibacterial activity against *C. diphtheriae*. *T. catappa*, *K. triandra* and *P. galioides* also inhibited *C. pseudodiphtheriticum*. *A. diffusa* and *S. peruviana* did not show antibacterial activity against *C. pseudodiphtheriticum*, although it did show for *C. diphtheriae*. *Asclepias curassavica*, *Cassia tomentosa*, *Cestrum auriculatum* and *Himatanthus sucuuba* didn't inhibit *C. diphtheriae* and *C. pseudodiphtheriticum* (Table 1).

The extract of the species *Liquidambar orientalis* at a concentration of 10% completely inhibits the growth of *C. xerosis*. *Khaya senegalensis*, *Cassia goratensis*, *Boswellia dalzielii*, *Bauhinia thonningi*, *Butyrospermum parkii*, *Guiera senegalensis*, *Anogeissus schimperi*, *Anacardium occidentale* and *T. catappa* show activity against *Corynebacterium pyogenes*. *T. catappa*, *Avicennia marina*, *Annona squamosa*, *Citrus limon*, *P. betle*, *Mangifera indica* also exhibited inhibitory activity against *Corynebacterium rubrum*. However, *Aegle marmelos* and *Azadiracta indica* did not demonstrate such activity (Table 2). *Corynebacterium urealyticum* was inhibited by havan sámagri (Table 3), produced in order to demonstrate that the treatment with medicinal smoke is effective (NAUTIYAL; CHAUHAN; NENE, 2007).

As show in Table 2, the species *Albizia lebbeck*, *Acacia leucophloea*, *Acalypha indica*, *Ammania baccifera*, *B. monosperma*, *Boerhaavia difusa*, *Bombax ceiba*, *Calotropis procera*, *Cardiospermum halicacabum*, *Cassia occidentales*, *Catharanthus roseus*, *Datura stramonium*, *Cissus quadrangulares*, *Cleome viscosa*, *Clitoria ternatea*, *Embllica officinalis*, *Ficus bengalensis*, *Ficus religiosa*, *Hibiscus rosasinensis*, *Hildegardia populifolia*, *Hyptis suaveolens*, *Justicia adhatoda*, *Lantana câmara*, *Lawsonia inermis*, *Morus alba*, *Solanum khasianum*, *Ocimum sanctum*, *Phyllanthus amarus*, *Physalis minima*, *P. betle*, *Plumbago zeylanica*, *Pongamia pinnata*, *R. indica*, *Sida acuta*, *T. catappa*, *Terminalia chebula*, *Rosa indica*, *Tamarindus indicus*, *Terminalia arjuna*, *Tridax procumbens* and *Vernonia cinerea* was effective to inhibit *Corynebacterium macginley*.

Finally, the plant species *Syzygium cumini* and *Ageratum conyzoides* show antibacterial activity against the genus *Corynebacterium* spp (Table 3).

The plant species most tested against corynebacteria strains was *T. catappa*, which was effective in inhibiting *C. diphtheriae*, *C. pseudodiphtheriticum*, *C. pyogenes*, *C. rubrum* and *C. macginleyi* (Tables 1 and 2). The most studied strains in relation to the antibacterial activity of plants were *C. macginleyi* and *C. diphtheriae* (Tables 1 and 2).

4 Conclusion

The relevance of conducting studies on medicinal plants is because of the possibility of validating popular information, discovering new active principles, and researching new pharmacological activities of already known substances. Few studies correlating plants and corynebacteria have been found, emphasizing the need for more research on this topic since multidrug-resistant *Corynebacterium* spp have been reported with increased frequency as pathogens of invasive infections and/or nosocomial outbreaks.

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