

Anti-infectious activity in plants of the genus *Tabebuia*

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Abstract

Infectious diseases are a worldwide public health problem. There is growing research in the field of new plant-based drugs for treating such diseases. Our objective was to perform a systematic literature review to evaluate the anti-infectious activity (antibacterial, antifungal, antiviral and antiparasitic) attributed to plants of the *Tabebuia* (Bignoniaceae) genus. We conducted a search for the period of 2000-2013 in ScienceDirect, Scopus, PubMed, Embase, Napralert and SciELO databases using the following MeSH terms: *Tabebuia*, biological activity, bioactive compounds, chemical compounds, diseases, traditional medicine, tropical infections, infections and treatment. We found ethnobotanical and experimental (*in vitro*) evidence supporting the use of *Tabebuia* species for treating infectious diseases. In addition, the compounds responsible for their antimicrobial activity have been isolated, and their structures have been elucidated, emphasizing among them naphthoquinones such as lapachol. Natural products isolated from *Tabebuia* plants may be an alternative for developing new anti-infectious agents.

Keywords: Anti-infective agents, Bignoniaceae, *Tabebuia*, Naphthoquinones, Lapachol.

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Introduction

Plants produce large amounts of compounds known as phytochemicals, and each plant synthesizes a vast variety of these phytochemicals. Phytochemicals not only maintain the plant's physiological activities, but they also protect it against foreign agents such as bacteria, fungi, insects and animals that feed on them (Dixon 2001, Schultz 2002). Since ancient times, phytochemicals have been used as treatments to cure various diseases.

Presently, multiple pharmaceutical agents contain natural compounds, including drugs that contain variations of these natural molecules (Kinghorn 2001). Many plants have been used as



the base or as precursors for developing several synthetic or semi-synthetic drugs (Wessjohann 2000, Newman et al. 2003). In fact, studies by Newman clearly demonstrate that 61% of all new small-molecule drugs introduced during 1981-2002 have been produced using natural products (7% natural products, 27% natural-product derivatives, 5% synthetic derivatives from natural products and 23% synthetic compounds designed from a natural product). Natural products are an innovative source of therapeutic agents for treating infectious diseases, and other ailments (Altmann 2001).

The decreased susceptibility of infectious agents to antimicrobials has warranted the need to increase the therapeutic arsenal of anti-infectious agents, emphasizing antibacterial, antiparasitic and antifungal agents (Gould 2008, Pitman et al. 2011, Wise 2011). The scientific community and pharmaceutical companies have given medicinal plants special attention in the last years because of their promising potential to be used to develop innovative anti-infectious agents of natural origin (Osborn 1996, Tagboto & Townson 2001, Ginsburg & Deharo 2011).

The *Tabebuia* genus includes approximately 100 species and is the largest genus in the Bignoniaceae family. This plant family is distributed from the southwestern United States to the northern regions of Argentina and Chile (Dvorkin-Camiel & Whelan 2008), where almost one-half of its genus and species are located (Olmstead et al. 2009).

Species of the *Tabebuia* genus have been used empirically as anti-inflammatory, anti-cancer and anti-microbial agents in rural areas of Colombia, Bolivia, Brazil and other Latin-American countries (Bueno et al. 2001, Agra et al. 2007, Negrelle & Fornazzari 2007, Gomez-Estrada et al. 2011, Hajdu & Hohmann 2012); the *Tabebuia* genus is commonly recognized as a therapeutic alternative by rural or remote populations. The results of ethnobotanical and ethnopharmacological studies indicating the potential use of these plants to treat a large variety of diseases has encouraged the search of new phytotherapeutic drugs using plant biodiversity (Ospina et al. 2011).

The extensive use of *Tabebuia* species for the treatment of infectious diseases in traditional medicine in Latin America, and the lack of reviews in the field motivated this systematic review of literature summarizing the relevant information published in the last 13 years. To our knowledge, this is the first literature review concerning the anti-infectious activities of plants of the genus *Tabebuia*. Several *Tabebuia* species have been used in traditional medicine to treat infectious diseases; Lapachol, for example, (which was first isolated from *Tabebuia avellanedae*) has antibacterial, antiviral, antiparasitic and antifungal activities (like other naphthoquinones). However, it is necessary to clearly identify compounds other than lapachol that have anti-infectious activity and the mechanisms of action responsible for these activities.

Materials and Methods

We performed a systematic review in the databases of Index Medicus/MEDLINE (www.pubmed.com), Scopus (www.scopus.com), ScienceDirect (www.sciencedirect.com), Embase (www.embase.com), Napralert (www.napralert.com) and SciELO (www.scielo.org) using the following combination of MeSH (Medical Subject Headings) terms: “*Tabebuia*” OR “biological activity” OR “bioactive compounds” OR “chemical compounds” OR “diseases” OR “traditional medicine” OR “tropical infections” OR “infections” AND “treatment”. To uncover the prominence of *Tabebuia* plants in the development of new anti-infectious agents, we included all articles published in English, Spanish or Portuguese during the years 2000-2013. Completed the search, we identified 264 articles and selected 36 based on their titles, abstracts and review of the full text. The selected articles were grouped according to the associated biological (i.e., antibacterial, antifungal, antiviral and antiparasitic) activity; we also considered all complementary general references related to the review. Because the objective of this review was to show a general context of the ethnopharmacology of the genus *Tabebuia* and the compounds related with the anti-infectious activity, we excluded investigations related to phytochemical, chemical and genetic studies.

Discussion

Antibacterial activity: The most extensive studies conducted have been on the antibacterial activity of extracts obtained from *Tabebuia* plants; this includes ethnobotanical and ethnopharmacological studies (Negrelle & Fornazzari 2007, Gomez-Estrada et al. 2011). The ethyl acetate extract obtained from the inner bark of *Tabebuia ocracea* and *Tabebuia rosea* inhibits *Staphylococcus aureus* growth at concentrations ranging between 1.25 and 10 mg/well. This characteristic may be attributed to the presence of quinone-type compounds that have displayed activity against *Staphylococcus aureus* strains (Riffel et al. 2002). However, no inhibitory activity was found against *Escherichia coli* and *Pseudomonas aeruginosa* by *Tabebuia ocracea* and *Tabebuia rosea* in the ethyl acetate extract (Franco Ospina et al. 2013).

The hexane extract of the *Tabebuia avellanedae* (synonym *Tabebuia impetiginosa*) heartwood and

its fractions exhibited antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA). This inhibitory effect is mainly attributed to the naphthoquinones α -lapachone (**1**) and α -xiloidone (**2**) (Figure 1) at minimum inhibitory concentrations (MICs) of 62.5 mg/L and 125 mg/L, respectively (Machado et al. 2003). The biological activity of *Tabebuia avellanedae* naphthoquinones and those stereoselectively synthesized were recently evaluated. It was found that the (-)-5-hydroxy-2-(1'-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione (**3**) and its positional isomer (-)-8-hydroxy-2-(1'-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione (**4**) had a strong activity against *Staphylococcus aureus* and *Bacillus subtilis*, with MICs varying between 0.78 and 6.25 μ g/mL (0.78 and 6.25 mg/L) (Yamashita et al. 2009); these naphthoquinones are found in the inner bark of *Tabebuia avellanedae* (Wagner et al. 1989). Other naphthoquinone derivatives obtained from the *Tabebuia avellanedae*-isolated lapachol (**5**),

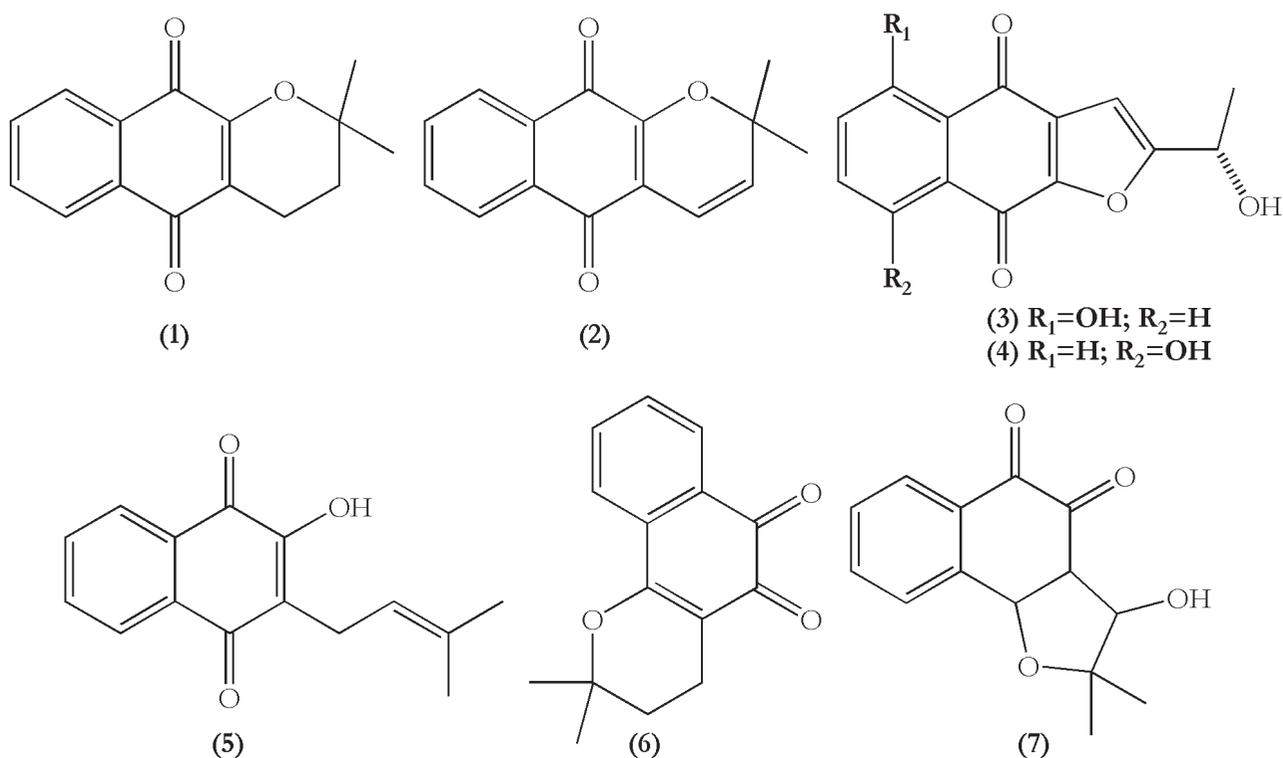


Fig. 1. Chemical structure of naphthoquinone and naphthoquinone derivatives isolated from *Tabebuia avellanedae*. α -lapachone (**1**), α -xiloidone (**2**), (-)-5-hydroxy-2-(1'-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione (**3**), (-)-8-hydroxy-2-(1'-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione (**4**), lapachol (**5**), β -lapachone (**6**) (\pm) 3-hydroxy- β -N-lapachone (**7**).

such as β -lapachone (**6**) and (\pm) 3-hydroxy- β -N-lapachone (**7**), displayed a considerable inhibitory activity against *Staphylococcus aureus* growth, with MICs of 8 $\mu\text{g}/\text{mL}$ (8 mg/L) for both compounds; however, no bactericidal activity was observed (Minimum Bactericidal Concentration, $\text{MBC} \geq 512 \mu\text{g}/\text{mL}$ (512 mg/L) (Pereira et al. 2006). Lapachol, which is a biologically active naphthoquinone showed activity against several agents such as bacteria, fungus, viruses and parasites and has therefore been used as a target for the synthesis of naphthoquinone derivatives with potent antimicrobial activity (Hussain et al. 2007).

The ethanol extracted from the leaf of *Tabebuia rosea* has also been evaluated; at concentrations between 50 and 300 mg/mL (50,000 and 30,000 mg/L) it can inhibit the growth of *Klebsiella pneumoniae* (Sathiya & Muthuchelian 2008). This antibacterial activity can be associated with the presence of various active principles or phytoconstituents such as phenolic compounds, quinoids and flavonoids present in the leaf ethanol extract of *Tabebuia rosea* (Joselin et al. 2013).

When comparing the activity of furanonaphthoquinones, isolated from the inner bark of *Tabebuia impetiginosa*, against *Helicobacter pylori* with that of drugs used to treat infections caused by this bacteria such as amoxicillin, metronidazole and tetracycline, (Figure 2), three new compounds

were identified: 2-(hydroxymethyl)anthraquinone (**8**) (MIC 2 $\mu\text{g}/\text{mL}$; 2 mg/L), anthraquinone-2-carboxylic acid (**9**) (MIC 8 $\mu\text{g}/\text{mL}$; 8 mg/L) and lapachol (**5**) (MIC 4 $\mu\text{g}/\text{mL}$; 4 mg/L). These compounds displayed antibacterial activity against *Helicobacter pylori*, exhibiting higher effectiveness than metronidazole (MIC 32 $\mu\text{g}/\text{mL}$; 32 mg/L) but lower effectiveness than amoxicillin (MIC 0.063 $\mu\text{g}/\text{mL}$; 0.063 mg/L) and tetracycline (MIC 0.5 $\mu\text{g}/\text{mL}$; 0.5 mg/L) (Park et al. 2006). This activity has been previously reported by Nagata et al (1998). Not only do *Tabebuia avellanedae* inner-bark compounds exert a direct effect on *Helicobacter pylori* but their ethanol extracts also have a direct protective effect on the gastric mucosa by inducing mucus production (Twardowschy et al. 2008).

The leaf methanolic extract from *Tabebuia chrysantha* inhibited the growth of *Staphylococcus aureus* at a concentration of 125 mg/mL (125,000 mg/L). This extract was more active than the chloroform and ether extracts used at the same concentration (Pérez et al. 2007). These results suggest that the polar compounds found in the methanolic extract could be responsible for this activity; however, the antibacterial activity found was small. In addition, the authors found that none of the extracts obtained from *Tabebuia chrysantha* inhibited the growth of *Escherichia coli*, *Proteus vulgaris* and *Pseudomonas aeruginosa*.

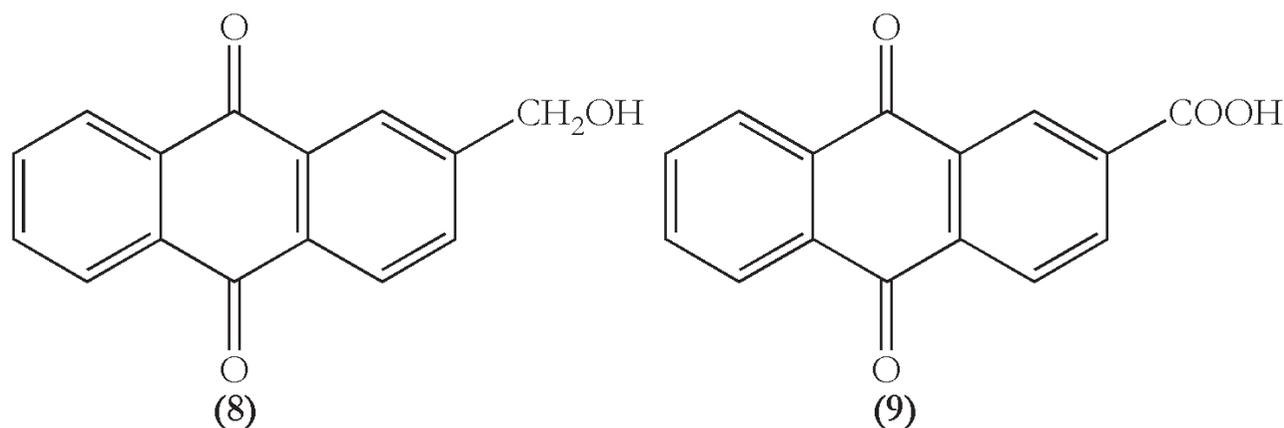


Fig. 2. Chemical structure of anthraquinones isolated from *Tabebuia impetiginosa* inner bark. 2-(hydroxymethyl)anthraquinone (**8**), anthraquinone-2-carboxylic acid (**9**).

In a more recent study, the antibacterial activity of 21 herbal extracts and four essential oils against *Helicobacter pylori* and *Campylobacter jejuni* was evaluated. *Tabebuia impetiginosa* hydro-alcoholic extract inhibited 36% of *Helicobacter pylori* growth but had no effect on *Campylobacter jejuni* (Cwikla et al. 2010), or on the adhesion of *Campylobacter jejuni* to human colon epithelial cells, demonstrated by IC₅₀ values less than 3 mg/mL (3,000 mg/L) (Bensch et al. 2011). The effect of *Tabebuia impetiginosa* inner-bark compounds on a group of human intestinal bacteria was also evaluated; anthraquinone-2-carboxylic acid efficiently inhibited *Clostridium paraputrificum* growth at a dose of 1 µg/disc, while lapachol only moderately inhibited bacterial growth. Both compounds slightly inhibit the growth of *Clostridium perfringens* and *Escherichia coli* at a dose of 100 µg/disc (Park et al. 2005). These results suggest that *Tabebuia impetiginosa* compounds may be valuable in the development of new effective agents against the growth of damaging intestinal bacteria such as *Clostridium spp.*

For the period evaluated in this review, we found only one report related to the antimycobacterial activity of a medicinal drink prepared with the hydro-alcoholic extract from the bark of *Tabebuia avellanedae*, which inhibited the growth of *Mycobacterium tuberculosis* H37Rv (Oliveira et al. 2007).

Natural products have also been used to inhibit the development of periodontal disease, as an adjunct to conventional oral-hygiene methods. For this reason, the antibacterial activity of a hydro-alcoholic extract formulation consisting of various plant species, including *Tabebuia impetiginosa*, was tested; this formulation inhibits the growth of *Staphylococcus aureus* and *Bacillus subtilis*, with a MIC of 312.5 µL/mL (Cordeiro et al. 2006).

Antifungal activity: Powerful antifungal drugs currently exist; however, the development of fungal resistance to these drugs, drug toxicity and limitations in the bioavailability have created a need for the development of new drugs to control evolving fungal infections. Natural products might be of great utility in this field.

Fourteen plants commonly used in Paraguayan traditional medicine, including *Tabebuia avellanedae*, have been evaluated; dichloromethane extract from the bark of *Tabebuia avellanedae* was found to exert a broad antifungal action particularly against *Aspergillus fumigatus*, *Candida albicans*, *Cryptococcus neoformans*, *Microsporium gypseum*, *Penicillium purpurogenum*, *Saccharomyces cerevisiae* and *Trichophyton mentagrophytes*. These aqueous and methanolic extracts displayed great inhibitory activity against *Cryptococcus neoformans*, *Microsporium gypseum*, *Penicillium purpurogenum* and *Trichophyton mentagrophytes* (Portillo et al. 2001).

A study of 11 plant species traditionally used in the Cerrado region of Brazil revealed that only four extracts, including the ethanol extract from *Tabebuia caraiba*, inhibited the growth of *Candida albicans* at a dose of 20 mg/mL (20,000 mg/L). *Tabebuia caraiba* hexane and dichloromethane extracts inhibited the growth of *Trichophyton rubrum*. This inhibition was also determined from clinical isolates of the fungus, with MIC mean geometric values within the range of 170.39 to 23.23 µg/mL (170.39 to 23.23 mg/L) (Melo e Silva et al. 2009).

In a research center in Campinas, Brazil, six plants were selected for evaluation of their potential activity against ten *Candida* species. The results revealed that the methanol extract from *Tabebuia avellanedae* exerts an inhibitory activity against *Candida albicans*, *Candida dubliniensis*, *Candida parapsilosis*, *Candida tropicalis*, *Candida guilliermondii*, *Candida utilis*, *Candida krusei*, *Candida lusitanae*, *Candida glabrata* and *Candida rugosa*, with MIC values in the range of 0.06 to 0.0001 mg/mL (60 to 0.1 mg/L). The dichloromethane extract has inhibitory activity only against *Candida krusei*, with an MIC value of 0.06 mg/mL (60 mg/L) (Hofling et al. 2010).

Furthermore, naphthoquinones (-)-5-hydroxy-2-(1'-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione and their positional isomer (-)-8-hydroxy-2-(1'-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione (stereoselectively synthesized) exhibited a moderate antifungal activity against *Candida albicans*, *Cryptococcus albidus* and *Aspergillus fumigatus*, with MIC values of 25, 1.56 and 12.5 µg/mL (25, 1.56 and 12.5 mg/L), respectively (Yamashita et al. 2009).

Antiviral activity: We found only two studies evaluating the antiviral activity of extracts from Bignoniaceae species despite the urgency to develop new antiviral agents to combat the resistance and toxicity issues encountered when using existing antiviral drugs.

The results revealed no activity of *Tabebuia aurea* stem ethanol extracts and *Tabebuia cassinooides* stem and leaf ethanol extracts against encephalomyocarditis virus (EMCV), human herpes virus 1 (HHV-1) and vaccinia virus (Western Reserve strain, [VACV-WR]). This lack of activity was most likely caused by the high cytotoxicity of naphthoquinones present in the extracts (Brandão et al. 2010a). A second study evaluated the antiviral activity of *Tabebuia impetiginosa*, *Tabebuia serratifolia* and *Tabebuia stenocalyx* stem ethanol extracts and *Tabebuia stenocalyx* leaf ethanol extract against EMCV, HHV-1 and VACV-WR viruses. The results demonstrated that only the *Tabebuia impetiginosa* extract exerted activity against HHV-1, with a one-half maximal effective concentration (EC₅₀) of 166.6 µg/mL (Brandão et al. 2010b).

Antiparasitic activity: Despite the high prevalence of parasitic diseases in tropical and subtropical regions, their pharmacological treatment is difficult, especially the cases of neglected tropical diseases (NTDs) such as Leishmaniasis, Chagas disease and Malaria. The ineffectiveness of pharmacological treatments

in the chronic phase of the majority of these pathologies, the drug's toxic effects, the presence of secondary effects and the parasitic resistance to these agents have stimulated interest in identifying new antiparasitic agents.

Lapachol, although structurally related to Atovaquone, exhibits low activity against *Plasmodium berghei* in mice and against *Plasmodium falciparum* *in vitro*. This fact has led to the synthesis of phenazines from lapachol, β-lapachone and their derivatives, thereby allowing the synthesis of compounds, such as 3-sulfonic acid-beta-lapachone-derived phenazine. The latter compound achieves 98% inhibition of the *Plasmodium berghei*-induced parasitemia in mice (De Andrade-Neto et al. 2004). *Tabebuia billbergii* inner bark and wood extracts have been categorized based on their bioactivity; this has allowed the isolation and identification of several compounds. Naphthofurandiones, for example, display significant antimalarial activity *in vitro* against *Plasmodium berghei* (Gómez-Estrada et al. 2012); in particular, 2-acetyl—naphtho-[2,3b]-furan-4,9-dione (**10**) (Figure 3), which had an IC₅₀ of 0.002 µM, surpassing chloroquine (IC₅₀ : 0.110 µM).

Several studies have revealed the trypanocidal activity of *Tabebuia* plant naphthoquinones, their heterocyclic derivatives (De Moura et al. 2001) and their β-lapachone naphthoimidazole derivative (Menna-Barreto et al. 2005). These two studies have tested the activity of 38 compounds against *Trypanosoma cruzi* and suggest that chemically

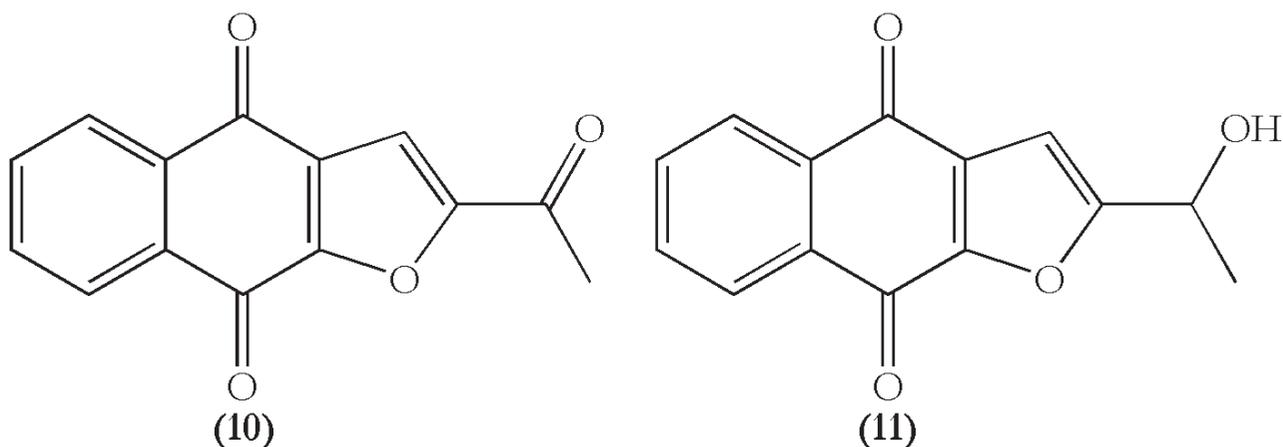


Fig. 3. Chemical structure of naphthofurandiones with antiparasitic activity. 2-acetyl-4H,9H-naphtho[2,3-b]furan-4,9-dione (**10**), 2-(1-hydroxyethyl)-4H,9H-naphtho[2,3-b]furan-4,9-dione (**11**).

modifying the naphthoquinones, especially their imidazole ring, could produce compounds with high trypanocidal activity.

Hexane, chloroform and hydro-alcohol extracts obtained from the bark of *Tabebuia serratifolia*, a plant used in traditional Peruvian medicine for treating cutaneous leishmaniasis, were recently tested for their trypanocidal and anti-leishmanial activity (Gonzalez-Coloma et al. 2012).

The chloroform extract was the most effective against *Trypanosoma cruzi* and *Leishmania infantum* parasites, with inhibition percentages greater than 96% and extract concentrations between 400 and 800 µg/mL (400 and 800 mg/L). A mixture of saturated alkanes, such as tricosane,

tetracosane and pentacosane, among others, together with rotenone and naphthoquinones 2-acetyl-4*H*,9*H*-naphtho[2,3-*b*]furan-4,9-dione (**10**) and 2-(1-hydroxyethyl)-4*H*,9*H*-naphtho[2,3-*b*]furan-4,9-dione (**11**) (Figure 3), were isolated and identified from the hydro-alcoholic extract. Naphthoquinone (**11**) was the most active of these agents against *Leishmania infantum* and *Trypanosoma cruzi*, with a growth-inhibition (GI₅₀) concentration of 0.01 µg/mL (0.01 mg/L). This value was lower than the Nifurtimox GI₅₀ and similar to that of Amphotericin B. These naphthoquinones were previously isolated from *Tabebuia cassinoides* and *Tabebuia ochracea* (Zani et al. 1991). We present a summary of the results on anti-infectious activity the genus *Tabebuia* in **Table 1**.

Table 1. *Tabebuia* genus plants with anti-infectious activity.

Plant	Part Used	Extract	Activity	Reference
<i>Tabebuia ochracea</i>	Inner bark	Ethyl acetate	Antibacterial, Antioxidant and Anti-inflammatory	Franco Ospina et al. (2013)
<i>Tabebuia rosea</i>	Inner bark	Ethyl acetate	Antibacterial, Antioxidant and Anti-inflammatory	Franco Ospina et al. (2013)
	Leaf	Ethanol	Antibacterial	Sathiyá & Muthuchelian (2008)
<i>Tabebuia avellanedae</i>	Heartwood and Inner bark	Hexane	Antibacterial, Antiproliferative, Antitumor, Antifungal and Antimicrobial	Machado et al. (2003) Yamashita et al. (2009)
	Bark	Dichloromethane, Aqueous and Methanol	Antifungal	Portillo et al. (2001) Hofling et al. (2010)
<i>Tabebuia impetiginosa</i>	Inner bark	Methanol	Antimicrobial	Park et al. (2006)
	Bark	Hydroalcohol	Antibacterial and anti-mycobacterial	Cwikla et al. (2010) Oliveira et al. (2007) Cordeiro et al. (2006)
	Stem	Ethanol	Antiviral	Brandão et al. (2010b)
<i>Tabebuia caraiba</i>	Stem bark, stem wood	Ethanol, hexane, dichloromethane	Antifungal	Melo e Silva et al. (2009)
<i>Tabebuia billbergii</i>	Inner bark; wood	Dichloromethane	Antimalarial	Gómez-Estrada et al. (2012)
<i>Tabebuia serratifolia</i>	Bark	Hydroalcoholic	Antiparasitic	González-Coloma et al. (2012)

Conclusion

The resistance of several microorganisms to antimicrobial treatment has increased in the last years; natural products may potentially be a source to produce new drugs to treat infectious diseases. Various *Tabebuia* species have been used in traditional medicine to treat bacterial, fungal, viral and parasitic diseases, and other ailments. *Tabebuia avellaneda*, also known as *Tabebuia impetiginosa*, is the species that has been most extensively studied. In these studies, various compounds exhibiting biological activities have been isolated, naphthoquinones such as lapachol and β -lapachone being the most significant. Compounds isolated from different *Tabebuia* species have been characterized and utilized to synthesize derivatives. These derivatives can potentially be used as a source for new antimicrobial agents; however, it is essential we evaluate their mechanisms of action. Because the experimental methods employed in the evaluated literature differ significantly, it is impossible to conduct a side-by-side comparison of the results reported for each group of microorganisms. By understanding the traditional use of these plants, and conducting phytochemical research and investigations of their biological activities (*in vivo* and *in vitro*), we will attain the knowledge necessary for future discovery of new compounds for the control of infectious diseases.

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Conflict of interest

The author(s) declare that they have no conflicts of interest.

References

- Agra MF, Baracho GS, Nurit K, Basilio IJLD, Coelho VPM (2007) Medicinal and poisonous diversity of the flora of “Cariri Paraibano”, Brazil. *Journal of Ethnopharmacology* 111(2):383-395
doi: 10.1016/j.jep.2006.12.007
- Altmann KH (2001) Microtubule-stabilizing agents: a growing class of important anticancer drugs. *Current Opinion in Chemical Biology* 5(4):424-431
doi: 10.1016/S1367-5931(00)00225-8
- Bensch K, Tiralongo J, Schmidt K, Matthias A, Bone KM, Lehmann R, Tiralongo E (2011) Investigations into the antiadhesive activity of herbal extracts against *Campylobacter jejuni*. *Phytotherapy Research* 25(8):1125-1132
doi: 10.1002/ptr.3384
- Brandão GC, Kroon EG, Dos Santos JR, Stehmann JR, Lombardi JA, Braga de Oliveira A (2010a) Antiviral activity of Bignoniaceae species occurring in the State of Minas Gerais (Brazil): part 1. *Letters in Applied Microbiology* 51(4):469-476
doi: 10.1111/j.1472-765X.2010.02924.x
- Brandão GC, Kroon EG, dos Santos JR, Stehmann JR, Lombardi JA, de Oliveira AB (2010b) Antiviral activities of plants occurring in the state of Minas Gerais, Brazil. Part 2. Screening Bignoniaceae species. *Brazilian Journal of Pharmacognosy* 20(5):742-750
doi: 10.1590/S0102-695X2010005000035
- Bueno JG, Isaza G, Gutierrez F, Carmona WD, Pérez JE (2001) Estudio etnofarmacológico de plantas usadas empíricamente por posibles efectos inmunoestimulantes. *Revista Médica de Risaralda* 7:8-12
- Cordeiro CHG, Do Sacramento LVS, Corrêa MA, Pizzolitto AC, Bauab TM (2006) Herbal extracts in an experimental mouthwash: Pharmacognostics analysis and antibacterial activity. *Revista Brasileira de Ciências Farmacêuticas* 42(3):395-404
- Cwikla C, Schmidt K, Matthias A, Bone KM, Lehmann R, Tiralongo E (2010) Investigations into the antibacterial activities of phytotherapeutics against *Helicobacter pylori* and *Campylobacter jejuni*. *Phytotherapy Research* 24(5):649-656
- De Andrade-Neto VF, Goulart MO, da Silva Filho JF, da Silva MJ, Pinto Mdo C, Pinto AV, Zalis MG, Carvalho LH, Krettli AU (2004) Antimalarial activity of phenazines from lapachol, beta-lapachone and its derivatives against *Plasmodium falciparum* *in vitro* and *Plasmodium berghei* *in vivo*. *Bioorganic & Medicinal Chemistry Letters* 14(5):1145-1149
doi: 10.1016/j.bmcl.2003.12.069
- De Moura KCG, Emery FS, Neves-Pinto C, Pinto MDCFR, Dantas AP, Salomão K, De Castro

- SL, Pinto AV (2001) Trypanocidal Activity of Isolated Naphthoquinones from *Tabebuia* and Some Heterocyclic Derivatives: A Review from an Interdisciplinary Study. *Journal of the Brazilian Chemical Society* 12(3):325-338
- Dixon RA (2001) Natural products and plant disease resistance. *Nature* 411(6839):843-847
- Dvorkin-Camiel L, Whelan JS (2008) Tropical american plants in the treatment of infectious diseases. *Journal of Dietary Supplements* 5(4):349-372 doi: 10.1080/19390210802519648
- Franco Ospina LA, Castro Guerrero JP, Ocampo Buendía YC, Pájaro Bolívar IB, Díaz Castillo F (2013) Antiinflammatory, antioxidant and antibacterial activity of two species of *Tabebuia* genus. *Revista Cubana de Plantas Medicinales* 18(1):34-46
- Ginsburg H, Deharo E (2011) A call for using natural compounds in the development of new antimalarial treatments - an introduction. *Malaria Journal* 10 Suppl 1:S1 doi: 10.1186/1475-2875-10-S1-S1
- Gomez-Estrada H, Diaz-Castillo F, Franco-Ospina L, Mercado-Camargo J, Guzman-Ledezma J, Medina JD, Gaitan-Ibarra R (2011) Folk medicine in the northern coast of Colombia: an overview. *Journal of Ethnobiology and Ethnomedicine* 7:27 doi: 10.1186/1746-4269-7-27
- Gómez-Estrada H, Gaitán-Ibarra R, Díaz-Castillo F, Pérez HA, Medina JD (2012) *In vitro* antimalarial activity of fractions and constituents isolated from *Tabebuia billbergii*. *Revista Cubana de Plantas Medicinales* 17(2):172-180
- Gonzalez-Coloma A, Reina M, Saenz C, Lacrete R, Ruiz-Mesia L, Aran VJ, Sanz J, Martinez-Diaz RA (2012) Antileishmanial, antitrypanosomal, and cytotoxic screening of ethnopharmacologically selected Peruvian plants. *Parasitology Research* 110(4):1381-1392 doi: 10.1007/s00436-011-2638-3
- Gould IM (2008) The epidemiology of antibiotic resistance. *International Journal of Antimicrobial Agents* 32 Suppl 1:S2-9 doi: 10.1016/j.ijantimicag.2008.06.016
- Hajdu Z, Hohmann J (2012) An ethnopharmacological survey of the traditional medicine utilized in the community of Porvenir, Bajo Paraguá Indian Reservation, Bolivia. *Journal of Ethnopharmacology* 139(3):838-857 doi: 10.1016/j.jep.2011.12.029
- Hoffing JF, Anibal PC, Obando-Pereda GA, Peixoto IA, Furletti VF, Foglio MA, Goncalves RB (2010) Antimicrobial potential of some plant extracts against *Candida* species. *Brazilian Journal of Biology* 70(4):1065-1068 doi: 10.1590/S1519-69842010000500022
- Hussain H, Krohn K, Ahmad VU, Miana GA, Green IR (2007) Lapachol: an overview. *ARKIVOC* (II):145-171
- Joselin J, Brintha TSS, Florence AR, Jeeva S (2013) Phytochemical evaluation of Bignoniaceae flowers. *Journal of Chemical and Pharmaceutical Research* 5(4):106-111
- Kinghorn AD (2001) Pharmacognosy in the 21st century*. *Journal of Pharmacy and Pharmacology* 53(2):135-148 doi: 10.1211/0022357011775334
- Machado TB, Pinto AV, Pinto MC, Leal IC, Silva MG, Amaral AC, Kuster RM, Netto-dosSantos KR (2003) In vitro activity of Brazilian medicinal plants, naturally occurring naphthoquinones and their analogues, against methicillin-resistant *Staphylococcus aureus*. *International Journal of Antimicrobial Agents* 21(3):279-284 doi: 10.1016/S0924-8579(02)00349-7
- Melo e Silva F, de Paula JE, Espindola LS (2009) Evaluation of the antifungal potential of Brazilian Cerrado medicinal plants. *Mycoses* 52(6):511-517 doi: 10.1111/j.1439-0507.2008.01647.x
- Menna-Barreto RF, Henriques-Pons A, Pinto AV, Morgado-Diaz JA, Soares MJ, De Castro SL (2005) Effect of a beta-lapachone-derived naphthoimidazole on *Trypanosoma cruzi*: identification of target organelles. *Journal of Antimicrobial Chemotherapy* 56(6):1034-1041 doi: 10.1093/jac/dki403
- Nagata K, Hirai KI, Koyama J, Wada Y, Tamura T (1998) Antimicrobial activity of novel furanonaphthoquinone analogs. *Antimicrobial Agents and Chemotherapy* 42(3):700-702
- Negrelle RRB, Fornazzari KRC (2007) Ethnobotanical study in two rural communities (Limeira and Riberião Grande) in Guaratuba (Paraná, Brazil). *Revista Brasileira de Plantas Medicinaiis* 9(2):36-54
- Newman DJ, Cragg GM, Snader KM (2003) Natural products as sources of new drugs over the period 1981-2002. *Journal of Natural Products* 66(7):1022-1037 doi: 10.1021/np030096l
- Oliveira DG, Prince KA, Higuchi CT, Santos ACB, Lopes LMX, Simões MJS, Leite CQF (2007) Antimycobacterial activity of some Brazilian indigenous medicinal drinks. *Revista de Ciências Farmaceuticas Básica e Aplicada* 28(2):165-169
- Olmstead RG, Zjhra ML, Lohmann LG, Grose SO, Eckert AJ (2009) A molecular phylogeny and classification of Bignoniaceae. *American Journal of Botany* 96(9):1731-1743
- Osborn AE (1996) Preformed Antimicrobial Compounds and Plant Defense against Fungal Attack. *The Plant Cell* 8(10):1821-1831 doi: 10.1105/tpc.8.10.1821

- Ospina LF, Aragón DM, Vergel NE, Isaza G, Pérez JE (2011) Anti-inflammatory and antioxidant activities of *Phenax rugosus* (poir.) wedd and *Tabebuia chrysantha* G. Nicholson. *Vitae* 18(1):49-55
- Park BS, Kim JR, Lee SE, Kim KS, Takeoka GR, Ahn YJ, Kim JH (2005) Selective growth-inhibiting effects of compounds identified in *Tabebuia impetiginosa* inner bark on human intestinal bacteria. *Journal of Agricultural and Food Chemistry* 53(4):1152-1157
doi: 10.1021/jf0486038
- Park BS, Lee HK, Lee SE, Piao XL, Takeoka GR, Wong RY, Ahn YJ, Kim JH (2006) Antibacterial activity of *Tabebuia impetiginosa* Martius ex DC (Taheebo) against *Helicobacter pylori*. *Journal of Ethnopharmacology* 105(1-2):255-262
- Pereira EM, Machado Tde B, Leal IC, Jesus DM, Damaso CR, Pinto AV, Giambiagi-deMarval M, Kuster RM, Santos KR (2006) *Tabebuia avellanedae* naphthoquinones: activity against methicillin-resistant *Staphylococcal* strains, cytotoxic activity and *in vivo* dermal irritability analysis. *Annals of Clinical Microbiology and Antimicrobials* 5:5
doi: 10.1186/1476-0711-5-5
- Pérez JE, Isaza G, Acosta SM (2007) Actividad antibacteriana de extractos de *Phenax rugosus* y *Tabebuia chrysantha*. *Biosalud* 6:59-68
- Pitman SK, Drew RH, Perfect JR (2011) Addressing current medical needs in invasive fungal infection prevention and treatment with new antifungal agents, strategies and formulations. *Expert Opinion on Emerging Drugs* 16(3):559-586
doi: 10.1517/14728214.2011.607811
- Portillo A, Vila R, Freixa B, Adzet T, Canigueral S (2001) Antifungal activity of Paraguayan plants used in traditional medicine. *Journal of Ethnopharmacology* 76(1):93-98
- Riffel A, Medina LF, Stefani V, Santos RC, Bizani D, Brandelli A (2002) *In vitro* antimicrobial activity of a new series of 1,4-naphthoquinones. *Brazilian Journal of Medical and Biological Research* 35(7):811-818
- Sathiya M, Muthuchelian K (2008) Studies on Phytochemical Profile and Antibacterial Activity of Ethanolic Leaf Extract of *Tabebuia rosea* (Bertol.) DC. *Ethnobotanical Leaflets* 12:1153-1157
- Schultz JC (2002) Biochemical ecology: How plants fight dirty. *Nature* 416(6878):267-267
- Tagboto S, Townson S (2001) Antiparasitic properties of medicinal plants and other naturally occurring products. *Advances in Parasitology* 50:199-295
- Twardowschy A, Freitas CS, Baggio CH, Mayer B, dos Santos AC, Pizzolatti MG, Zacarias AA, dos Santos EP, Otuki MF, Marques MC (2008) Antiulcerogenic activity of bark extract of *Tabebuia avellanedae*, Lorentz ex Griseb. *Journal of Ethnopharmacology* 118(3):455-459
doi: 10.1016/j.jep.2008.05.013
- Wagner H, Kreher B, Lotter H, Hamburger MO, Cordell GA (1989) Structure Determination of New Isomeric Naphtho[2,3-b]furan-4,9-diones from *Tabebuia avellanedae* by the selective-INEPT technique. *Helvetica Chimica Acta* 72(4):659-667
doi: 10.1002/hlca.19890720406
- Wessjohann LA (2000) Synthesis of natural-product-based compound libraries. *Current Opinion in Chemical Biology* 4(3):303-309
doi: 10.1016/S1367-5931(00)00093-4
- Wise R (2011) The urgent need for new antibacterial agents. *The Journal of antimicrobial chemotherapy* 66(9):1939-1940
doi: 10.1093/jac/dkr261
- Yamashita M, Kaneko M, Tokuda H, Nishimura K, Kumeda Y, Iida A (2009) Synthesis and evaluation of bioactive naphthoquinones from the Brazilian medicinal plant, *Tabebuia avellanedae*. *Bioorganic & Medicinal Chemistry* 17(17):6286-6291
doi: 10.1016/j.bmc.2009.07.039
- Zani CL, De Oliveira AB, De Oliviera GG (1991) Furanonaphthoquinones from *Tabebuia ochracea*. *Phytochemistry* 30(7):2379-2381
doi: 10.1016/0031-9422(91)83653-3

Actividad anti-infecciosa en plantas del género *Tabebuia*

Resumen. Dada la importancia de las enfermedades infecciosas como problema de salud pública a nivel mundial y la búsqueda de nuevos medicamentos basados en plantas para tratar dichas enfermedades; se realizó una revisión sistemática de literatura con el fin de evaluar la actividad anti-infecciosa (antibacteriana, antifúngica, antiviral y antiparasitaria) reportada en plantas pertenecientes al género *Tabebuia* (Bignoniaceae). Las bases de datos fueron: ScienceDirect, Scopus, Pubmed, Embase y Napralert, SciELO, durante 2000 – 2013. Se utilizaron términos en MeSH como: *Tabebuia*, biological activity, bioactive compounds, chemical compounds, diseases, traditional medicine, tropical infections, infections and treatment. Existe evidencia tanto etnobotánica como experimental (*in vitro*) que soporta el uso de especies del género *Tabebuia* en el tratamiento de enfermedades infecciosas. Adicionalmente, se encontró reportado y se esclareció estructuralmente los compuestos responsables de la actividad antimicrobiana, donde se destacan naftoquinonas como el lapachol. Se concluye a partir de la revisión que los productos naturales aislados de las plantas del género *Tabebuia* podrían considerarse alternativas para el desarrollo de nuevos agentes anti-infecciosos.

Palabras clave: Actividad anti-infecciosa, Bignoniaceae, *Tabebuia*, Naftoquinonas, Lapachol.

Atividade anti-infecciosa em plantas do gênero *Tabebuia*

Resumo. Dada a importância das doenças infecciosas como problema de saúde pública a nível mundial e a procura crescente de novos medicamentos baseados em plantas para tratar tais doenças, realiza-se uma pesquisa sistematizada da literatura com o fim de avaliar a atividade anti-infecciosa (antibacteriana, antifúngica, antiviral e antiparasitária) reportada em plantas pertencentes ao gênero *Tabebuia* (Bignoniaceae). Foi realizada uma pesquisa nas bases de dados ScienceDirect, Scopus, Pubmed, Embase y Napralert, assim como em SciELO, durante o período 2000 – 2013, empregando os termos MeSH: *Tabebuia*, biological activity, bioactive compounds, chemical compounds, diseases, traditional medicine, tropical infections, infections and treatment. Existe evidencia tanto etnobotánica como experimental (*in vitro*) que suporta o uso das espécies do gênero *Tabebuia* no tratamento das doenças infecciosas e adicionalmente, há sido isolado e identificado estruturalmente os compostos responsáveis da sua atividade antimicrobiana, donde se destacam as naftoquinonas como o lapachol. Os produtos naturais isolados de plantas do gênero *Tabebuia* poderiam considerar-se como uma alternativa para o desenvolvimento de novos agentes anti-infecciosos.

Palavras-chave: Agentes anti-infecciosos, Bignoniaceae, *Tabebuia*, Naphthoquinones, Lapachol.