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REVIEW ARTICLE

Himatanthus Willd. ex Schult. (Apocynaceae): Review

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ABSTRACT

The genus *Himatanthus* Wild. ex Schult. (Apocynaceae) includes about 13 species and five subspecies widely distributed in South America, especially Brazil. The phytochemical reports on this genus have revealed mainly triterpenes and iridoids. The plants are traditionally used as anthelmintic, antitumor, and antiinflammatory agents. The most used parts of the plant are its bark, leaves, and latex. This review emphasizes the phytochemical constituents and medicinal properties, which may help in future research. The research was conducted with data obtained from books about medicinal plants, theses, dissertations, and articles in refereed journals.

Key words: Biological effects, botanical, ethnopharmacology, folk medicine, *Himatanthus*, phytochemistry

INTRODUCTION

The Apocynaceae family includes approximately 550 genuses and 3700–5100 species distributed in all continents except Antarctica. It is a rich source of secondary metabolites, because of which many of the genuses belonging to it, such as *Rauwolfia*, *Catharanthus*, *Allamanda*, *Strophantus*, and *Himatanthus*, are used on a large scale for medicinal use by small communities and/or pharmaceutical industry.[1]

In this review, we will be focused on the folk medicine uses, biological effects, and phytochemistry of the genus *Himatanthus* Willd. Ex Schult., in order to provide a basis for several different research areas, such as the botanic, pharmaceutical, medical, and chemical fields.

MATERIALS AND METHODS

The method used for this study was based on bibliographical research into books about medicinal plants, theses, dissertations, and articles in refereed journals. Presentations at conferences and symposia were not considered.

We performed extensive research in the Periodicals Portal of Capes (Coordination for the Improvement of Higher Education Personnel), which has several databases such as Chemical Abstracts, PubMed, Web of Science and Science Direct (consultation period: February to May 2014). The key word used in the research was *Himatanthus*; information on the plant parts used, the uses in folk medicine, the biological activities, and the chemical constituents was collected.

Data were compiled and organized into a table [Table 1], and the *Himatanthus* species have been arranged in alphabetical order.

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RESULTS AND DISCUSSIONS

The genus *Himatanthus* Willd. Ex Schult., initially included in the genus *Plumeria*, has large bracts involving the floral buttons, determinants for the separation of genus. The presence of these bracts has inspired the naming of this genus, which means "flower robe."[59]

It encompasses 13 species: *H. articulatus* (Vahl) Woodson, *H. attenuatus* (Benth.) Woodson, *H. bracteatus* (A.DC.) Woodson, *H. drasticus* (Mart.) Plumel, *H. fallax* (Muell. Arg.) Plumel, *H. lancifolius* (Muell. Arg.) Woodson, *H. obovatus* (Muell. Arg.) Woodson, *H. phagedaenicus* (Mart.) Woodson, *H. semilunatus* Markgraf, *H. speciosus* (Muell. Arg.) Plumel, *H. stenophyllus* Plumel, *H. sucuuba* (Spruce) Woodson, and *H. tarapotensis* (Schumann ex Markgraf) Plumel.[22,60] There are also five varieties of these species: *H. bracteatus var. bracteatus*, *H. bracteatus var. revolutus*, *H. obovatus var. obovatus*, *H. obovatus var. puberulus*, and *H. obovatus var. velutinus*.[60] They all occur in Brazil and some other countries in South and Central America.[22,60]

From among the 13 species of *Himatanthus*, four did not have any research records concerning their chemical composition and medicinal properties: *H. attenuatus*, *H. semilunatus*, *H. speciosus*, and *H. tarapotensis*. The research results with the other species are summarized in Table 1.

The *H. bracteatus*, *H. fallax*, and *H. stenophyllis* species have only reports of chemical composition studies, and the presence of the iridoid plumieride in the bark of these species is common.[10,21] This substance and the isoplumieride, generally, are present in the bark, latex, leaves, and/or roots of the species of *Himatanthus*.[2,10,21,23,36,38,41] This kind of spirolactone iridoid is not commonly found in nature. Some studies revealed that plumieride exhibits antimicrobial[61] and antioxidant effects,[62] arrests spermatogenesis in male rats without noticeable side effects, and presents cytotoxicity.[3]

The *H. articulatus*, *H. drasticus*, *H. lancifolius*, *H. obovatus*, *H. phagedaenicus*, and *H. sucuuba* species presented chemical and biological studies, and in general the barks are the most studied, followed by the leaves.

Although the presence of alkaloids in the barks of *H. articulates* is reported,[2] only from the barks of *H. lancifolius* were they isolated and identified,[24,25] and

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Table 1: List of *Himatanthus* species and plant parts used, folk medicine uses, biological properties, and chemical constituents

Species	Plant parts used	Folk medicine uses	Biological properties	Chemical constituents	References
H. articulatus	Latex	Antifungal, antibacterial, antiulcerogenic, antitumor, antiinflammatory, analgesic, antisyphilitic, antimalarial, tonic, aphrodisiac	Inhibits *Candida albicans*; antigenotoxic effect (protective against ADN damage induced by hydrogen peroxide)	α-amyrin cinnamate and β-amyrin acetate, lupeol, lupeol cinnamate, cycloartenol	[2-9]
	Bark	Vermifuge, laxative, antitussive, tonic, antisyphilitic, antiinflammatory, analgesic, antitumor, trypanocidal, leishmanicidal	Methanol extract inhibits *Bacillus subtilis*; Cytotoxic effect (antiproliferative activity against NCI-H460, HT-29, MCF-7, RXF-393, and OVCAR-3 cells); trypanocidal effect (*Trypanosoma cruzi*), leishmanicidal (*Leishimania donovani*)	Saponins, alkaloids, flavonoids, tannins. lupeol acetate, lupeol cinnamate, stigmasterol, sitosterol, plumericin, 1β-O-β-D-glucopyranosylplumeric acid, plumieride-1β-O-β-D-glucopyranosyl, isoplumericin, methyl-myo-inositol	
	Leaf	Vermifuge, laxative, antitussive, tonic, antisyphilitic, antiinflammatory, analgesic, antitumor, trypanocidal, leishmanicidal	Methanol extract inhibits *Staphylococcus aureus* and *B. subtilis*; trypanocidal effect (*T. cruzi*), leishimanicidal (*L. donovani*)	Ursolic acid	
H. bracteatus	Latex	-*	-	Plumieride, isoplumieride	[10]
	Bark	-	-	Plumieride, isoplumieride	
	Leaf	-	-	Plumieride, isoplumieride	
H. drasticus	Latex	Antitumor, gastric and intestinal disorders, worms, arthritis, fever, irregular menstruation, female infertility, rheumatism, bruises, herpes	Antiulcer (induced by ethanol and indomethacin); immunomodulator; antitumor activity of latex proteins (sarcoma 180 and Walker 256 carcinosarcoma); analgesic and antiinflammatory	Lupeol acetate; proteins	[1,11-20]
	Bark	Antitumor, gastric and intestinal disorders, worms, arthritis	Cytotoxic against *Artemia salina*; antinociceptive	Lupeol cinnamate, lupeol acetate, α-amyrin cinnamate, α-amyrin acetate, β-amyrin, plumieride, isoplumieride, protoplumericin A, cafeoilplumieride, acid derivative of 3-methoxy-3,4-dihydroplumieride	
	Leaf	Antiherpes; "impinges" warts (diseases of the skin); urethral irritation and uterine inflammation	Methanol extract with antitumor activity and low toxicity	Rutin, quercitrin; lupeol cinnamate, lupeol acetate, α-amyrin cinnamate, α-amyrin acetate, β-amyrin	
	Root	Purgative and vermifuge	-	-	
H. fallax	Bark	-	-	Isoplumericin, plumericin; lignan 7(*R*)-methoxy-8-*epi*-matairesinol, plumieride, matairesinol, pinoresinol	[21]
H. lancifolius	Latex	Skin diseases, asthma, syphilis, stimulating uterine contractions, assist conception, menstrual regulation, anthelmintic and febrifuge; constipation; if used in excess can cause menstrual cramps and gastrointestinal disorders; and children, diarrhea and dehydration	-	-	[22-35]
	Bark	Febrifuge, stimulating menstruation, abortive	Alkaloidal fraction has antioxidant, cytotoxic action (tumor cells); antimicrobial, antiulcer, antispasmodic, gastroprotective, antiinflammatory, immunomodulatory; inhibits acetylcholinesterase, inhibits *S. aureus* including MRSA strains, *Staphylococcus epidermidis, Enterococcus faecalis, Escherichia coli, Pantoea agglomerans; Acinetobacter baumannii, and S. aureus* canine	Uleine, yohimbine, epi-uleine, ajmaline, and demethoxyaspidospermine (indole alkaloids); sitosterol; glucosylplumieride	
	Leaf	Galactogogues	-	-	
	Root	Disorders of the uterus and ovaries	-	-	
H. obovatus	Latex	Treatment of gastric ulcers	-	-	[1,5,22, 36,37]

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Table 1: Contd...

Species	Plant parts used	Folk medicine uses	Biological properties	Chemical constituents	References
	Bark	-	Extract in ethyl acetate has no action against *Aspergillus fumigatus, Candida albicans, Cryptococcus neoformans*; inhibits *in vitro* replication of human peripheral blood lymphocytes stimulated by phytohemagglutinin	Lupeol acetate, α-amyrin cinnamate, α-amyrin acetate, β-amyrin; plumieride and isoplumieride	
	Leaf	Treatment of tumors; depurative for the treatment of high pressure, skin blemishes, pimples and rashes	Extract in ethyl acetate has no action against *Aspergillus fumigatus, Candida albicans, Cryptococcus neoformans*; inhibits *in vitro* replication of human peripheral blood lymphocytes stimulated by phytohemagglutinin	Isoquercitrin; lignans: pinoresinol, isolariciresinol, hydroxypinoresinol, lariciresinol and olivil; norisoprenoids: blumenol C, blumenol A; iridoid: plumieride; mixture of terpenes: lupeol acetate, α-amyrin and β-amyrin acetate, germanicol, stigmasterol, sitosterol, campesterol; glycitol inositol (after acetylation of the crude ethanolic extract)	
	Wood	-	Extract in ethyl acetate has no action against *A. fumigatus, C. albicans, C. neoformans*	-	
	Root	Stimulating menstruation, purgative and febrifuge	Leishimanicidal (*L. donovani*); extract in ethyl acetate has no action against *A. fumigatus, C. albicans, C. neoformans*	Plumericin, isoplumericin, fulvoplumierin	
H. phagedaenicus	Latex	Anthelmintic, herpetic diseases, ulcers, psoriasis, and warts	-	-	[31,38-40]
	Bark	Cathartic, depurative, anthelmintic	Spasmogenic action	Amyrin acetate and lupeol acetate; sitosterol; iridoids plumericin, allamandin, isoplumericin, plumieride; sucrose	
	Wood	-	Inhibition of diuresis in the rat induced water drinking, increased blood glucose levels in alloxan-diabetic rats, increased pain induced by acetic acid in mice; spasmogenic action	3-β-O-acethyl-12-eno, o 3-β-O-acethyl-olean-12-eno, 3-β–O-acethyl-lupeol, plumericin, allamandin, isoplumericin, glucosyl-octadecyl-plumieride coumarate	
	Root	-	-	Iridoid β-dihidroplumericinic acid	
H. stenophyllus	Latex	-	-	Plumieride, isoplumieride	[10]
	Bark	-	-	Plumieride, isoplumieride	
	Leaf	-	-	Plumieride, isoplumieride	
H. sucuuba	Latex	Anthelmintic, skin disorders, especially in relieving the itch; antitumor; antifungal, antianemic, treatment of gastritis and arthritis	Selective cytotoxic; antimicrobial; analgesic and antiinflammatory; potent leishmanicidal activity against intracellular amastigotes of *Leishmania amazonensis*; immunoregulatory	Cis-polyisoprene; Na, Al, K, Mn, Fe, Sr, Ti, V, Cr, Co, Ni, Cu, Zn, Ba, Zr, Th, Pb, Ca (354 μg/g), Mg (250 μg/g); xylose, arabinose, glucose, galactose; glutamic acid; myo-inositol; gallic acid; flavonoids myricetrin and quercitrin, catechol; fulvoplumierin, plumericin, isoplumericin, plumieride, isoplumieride, 15-desmethylisoplumieride acid, 15-demethylplumieride; α- and β-amyrin cinnamates, α- and β-amyrin acetates, lupeol cinnamate, and lupeol acetate	[8,41-58]
	Bark	Wound healing, antitumor, antiarthritic, anthelmintic, laxative, and hallucinogen; antiulcerogenic, aphrodisiac; analgesic, antitussive; treatment of boils, edemas	Antimicrobial, cytotoxic, analgesic, antiinflammatory; selective inhibitor of monoamine oxidase B enzyme; healing, antibacterial against *Clostridium histolyticum* and *Bacteroides fragilis*; low reproductive and teratogenic toxicity in rats; immunoregulatory; action on blood pressure and smooth muscle; capillary permeability; Antitumor in different cell lines	Plumeridoid C; allamandin, fulvoplumierin, isoplumericin and plumericin; plumieride, isoplumieride, 15-desmethylisoplumieride acid; confluentic acid and 2'-O-methylperlatolic acid; vanillic acid, p-coumaric acid, 4-hydroxy-3-methoxy-benzoic acid and p-hydroxybenzoic acid (phenolic compounds); α- and β-amyrin cinnamates, lupeol cinnamate, lupeol acetate, lupeol β-phenyl-propionate	
	Leaf	Constipation, antitumor, antifungal, antianemic, anthelmintic, and in the treatment of gastritis and arthritis	Cytotoxic; mild analgesic activity in the abdominal contractions test	Plumericin, isoplumericin, plumieride and isoplumieride; α- and β-amyrin cinnamates, α- and β-amyrin acetates, lupeol cinnamate and lupeol acetate	

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Table 1: Contd...

Species	Plant parts used	Folk medicine uses	Biological properties	Chemical constituents	References
	Root	-	Antimicrobial	Plumericin, isoplumericin; β-dihydroplumericin lupeol, β-amyrin cinnamate, lupeol cinnamate, and lupeol acetate; allamandin	
	Flower	-	-	β-amyrincinnamate,germanicol,myo-inositol	

*Information not found in the literature

these are indole and have antimicrobial, gastroprotective, antiinflammatory, and antioxidant properties and showing cytotoxic activity against tumor cells.[26-30] However, there are no data on the ethnopharmacological use of the plant as an antitumor agent.[23,30,31]

H. articulatus latex is popular as an antifungal and antitumor agent, these effects evidenced by biological studies.[4] Their barks showed cytotoxic and trypanocidal and leishmanicidal effects, also reported in folk medicine.[2,3,5,6] Leishmaniasis is a parasitic disease responsible for considerable mortality and morbidity, affecting many people every year.[4] *Leishmania donovani* is the causative agent of visceral leishmaniasis, which is fatal in the absence of treatment.[63] Its various side effects and resistance to available drugs, in addition to the increase in new cases, have led to an urgent need for new therapeutic agents. This activity was also determined in *H. articulatus* leaves, *H. obovatus* roots, and *H. sucuuba* latex,[4,36,42] which are certainly promising sources of treatment.

There are studies of *H. drasticus* latex evaluating its antiulcerogenic, antitumor, analgesic, and antiinflammatory activities, which somehow justify their popular uses in the treatment of cancer, gastric disorders, rheumatism, and bruises.[1,11-18]

H. sucuuba is the most studied species, with a record of chemical composition of the latex, bark, leaves, roots and leaves, and the presence of triterpene amyrin cinnamate.[41,43-46] Latex, bark, and leaves have antitumor action, justifying the popular use for the same purpose.[41,46-50] The latex and bark showed antiinflammatory and analgesic effects, which are reasons for some popular uses of the plant: In treatment of arthritis, boils, and edema.[41,44,46,48-50]

Biological studies on *H. obovatus* roots have no relation with the ethnopharmacological information about the plant.[36] However, the popular use of the leaves as antitumor agent[36] can be justified by the presence of iridoids and triterpene esters.

The triterpenoids are considered promising anticancer drugs due to their diverse pharmacological activities, including antiangiogenic, antiinflammatory, and antioxidant effects and the ability to increase cell differentiation.[64] These compounds, along with iridoids, are certainly responsible for most of the plant's medicinal properties reported in both folk medicine and biological studies.

CONCLUSION

Among the nine species studied, six species were evaluated chemically and biologically. The most studied species was *H. sucuuba*.

In general, the species are traditionally used as an anthelmintic, antitumor, and antiinflammatory agent. There were no evaluation studies of anthelmintic activity for any species of the genus; however, there are several studies evaluating antitumor and antiinflammatory activities.

Regarding the chemical composition, the genus is distinguished by the presence of triterpene esters and iridoids, predominantly in the bark and leaves. These compounds exhibit valuable pharmacological properties such as antimicrobial, antioxidant, antiinflammatory, and antitumor properties, which warrant further exploration.

The chemical and pharmacological data presented in this study should inspire further study of the species of *Himatanthus* for future use in therapies, including treatment of leishmaniasis.

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Conflicts of interest

There is no conflicts of interest with this article.

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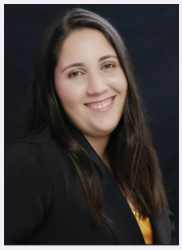
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