SVOA Microbiology

ISSN: 2634-534X

ScienceVolks Open Access

Research Article

Phytochemistry and Bioactivities of *Duguetia furfuracea* (A.St.-Hil.) Saff.

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DOI: https://doi.org/10.58624/SVOAMB.2024.05.043

***Received:** June 10, 2024* ***Published:** July 15, 2024*

Abstract

Duguetia furfuracea, belonging to the Annonaceae family, is a perennial plant found in the Central-West, Southeast, and Northeast regions of Brazil, known for its various uses in traditional medicine. Used as a hypocholesterolemic, anorexigenic, and for treating various conditions including cancer and infections, its medicinal properties have garnered scientific interest. Studies have identified several bioactive compounds in different parts of the plant. The leaves contain phenolic acids, flavonoids, and alkaloids such as duguetine and dicentrinone, which exhibit antioxidant, anti-inflammatory, and antimicrobial properties. Phytochemical analysis revealed the presence of rare sesquiterpenes such as α-santalene and (-)-ishwarane, strengthening the chemotaxonomic relationship between Annonaceae and Aristolochiaceae. The species has shown larvicidal activity against *Aedes aegypti*, pediculicidal activity against Pediculus capitis, and antiplasmodial activity against *Trypanosoma cruzi*. Additionally, it possesses anti-inflammatory, antinociceptive, and cytotoxic activities, being effective against *Candida* spp. strains and cancer cells. However, its toxicity was observed in studies with *Drosophila melanogaster* and cellular models, indicating the need for further studies to ensure its safe use. The plant shows potential for therapeutic applications due to its chemical diversity, but it is essential to deepen investigations into its mechanisms of action and develop extraction and isolation methods to maximize its medicinal potential safely and effectively. Continued research is crucial to integrate *D. furfuracea* into modern phytotherapy and the development of new drugs. The presence of these bioactive compounds highlights the importance of exploring the full pharmacological potential of D. furfuracea for future therapeutic advancements, emphasizing its promising role in natural medicine. the pharmacological properties of *D. furfuracea* underscore its potential for innovative drug development and traditional medicinal enhancement.

***Keywords:** Annonaceae, Araticum, Chapada do Araripe*

Introduction

Medicinal plants are important sources of natural remedies for treating ailments and diseases. The use of medicinal plants has been practiced for thousands of years and is still widespread worldwide. Scientific studies have shown that some medicinal plants have anti-inflammatory, antioxidant, antimicrobial, and antiviral properties, making these plants a useful tool in disease prevention and treatment. Therefore, these biological species are a safe, natural, and effective form of treatment and prevention of diseases [1-2].

Among the prominent botanical taxa is the Annonaceae family. This taxon is represented by tree and shrub species globally distributed in tropical and subtropical regions. It is noted for its colorful flowers and edible fruits, as well as its significant biodiversity, with about 108 genera and approximately 2,400 species [3-4]. Some species of this family are widely used in agriculture, medicine, the food industry, and cosmetics. Thus, the Annonaceae family has been the target of numerous studies, as its species provide important economic resources for tropical regions [5].

One of the most important genera of this family is *Duguetia* A.St.-Hil., with a total of 95 described species. One of its representatives is *Duguetia furfuracea* (A.St.-Hil.) Saff., a perennial and shrub species found in the Central-West, Southeast, and Northeast regions of Brazil. It is popularly known as "Araticum-Miudo," "Araticum-seco," and "Ata-brava," and is used in Brazilian folk medicine as a hypocholesterolemic and anorexigenic. Additionally, it is indicated for treating vaginal discharge, cancer, anemia, hypertension, as a diuretic, for kidney infections, bone fractures, and rheumatism [6]. Recent studies have shown that *D. furfuracea* possesses various biological and pharmacological properties directly linked to its chemical heterogeneity [7].

The plant has a stem covered with pilosity on young branches, containing lepidote trichomes. The leaves are elliptical or narrowly obovate, with hairs on both surfaces. Its base is acute, obtuse, or attenuated, with an acuminate, acute, or obtuse apex. The inflorescence, which has few flowers, is broadly ovoid or globose, with a cream or greenish color. The sepals are ovate-triangular, and the outer petals are elliptical, as are the inner ones, and the stamens are pink. The fruit is brown, green, or greenish, with an ellipsoid or globose shape (Figure 01) [8].

Figure 1: *Duguetia furfuracea (A.St.-Hil.) Saff.. A: Leaves; B: Habit; C: Fruit. D: Flower.*

Despite the numerous pharmacological and phytochemical properties reported for *D. furfuracea*, no systematic study has been conducted to compile the existing research data on the plant to date. For this reason, this review article aims to provide a comprehensive overview of the chemical constituents of the botanical species and their biological activities, as well as to discuss important issues related to the species' pharmacological properties.

Methodology

This research constitutes a critical analysis of the literature, being elucidative and exploratory, which enables the gathering of various data to obtain general conclusions about a specific domain of knowledge through a synthesis of published works within the examined perspective.

The investigation followed these steps: I. Identifying the topic and selecting the premise or question for constructing the systematic review; II. Establishing criteria for the inclusion and exclusion of studies/sampling or research in the literature; III. Defining the information to be extracted from the selected studies/classification of studies; IV. Evaluating the studies included in the systematic review; V. Interpreting the results; and VI. Presenting the review/summary of knowledge.

This study approach was based on previous studies conducted by Mendes, Silveira, and Galvão (2019). The guiding question of this review was: What is the scientific evidences regarding the phytochemistry and biological and pharmacological activities of *Duguetia furfuracea*?

To address this question, a search was conducted in the Medical Literature Analysis and Retrieval System Online (MEDLINE), National Library of Medicine (PUBMED), SCOPUS, Web of Science, Scientific Electronic Library Online (SCIELO), and Science Direct databases. The advanced search method was used, targeting titles, abstracts, and keywords. In each database, the subject descriptors were defined and cross-referenced, using: *Duguetia furfuracea*, *Annona furfuracea* A.St.-Hil., *Aberemoa furfuracea* (A.St.-Hil.) Baill. var. *furfuracea*, *Duguetia coriacea* Sond., *Aberemoa furfuracea* (A.St.-Hil.) Baill., *Duguetia furfuracea* (A.St.-Hil.) Saff., with the boolean operators AND and OR, paired by different researchers.

The articles underwent a filtering process based on inclusion criteria: full-text articles available electronically, primary studies published in Portuguese, English, or Spanish without time limitation, addressing the investigated topic. Duplicated or repeated studies were excluded.

Results

Table 1:

Part used	Method	Constituents	Reference
Leaves	NMR	(-)-ishwarane, α-santalene, bicyclogermacren, (+)-spathulenol, β-caryophyllene oxide, (-)-α-santalen-11-one	[11]
	HPLC	Caffeic acid, rutin, quercitrin, isoquercitrin	[13]
	HPLC-DAD	gallic acid, catechin, chlorogenic acid, caffeic acid, ellagic acid, rutin, isoquercitrin, quercitrin, quercetin, kaempferol	[10]
	LC-PDA	Duguetine, dicentrinone, N-methylglaucine	[9]
Aerial parts	NMR	*N*-nitrosoanonaine, *N*-Nitrosoxylopine	[17]
		(+)-Isocorydine, —Norisocorydine, Xylopine, Obovanine-anonaine mixture, (-)-Asimilobine, Isochondodendrine	[15]
Underground parts	NMR	(-)-Duguetine β-N-oxide, (-)-N-Methyltetrahydropalmatine, (+)-N-Methylglaucine	[6]
	GC–MS	α-asarona	[21]
	CG/EM	(E)-asarone, bicyclogermacrene, 2,4,5-trimethoxystyrene, α-gurjunene, cyperene, (E)-caryophyllene	[19]
	GC-MS	α-asarone, 2,4,5-trimethoxystyrene	[22]

Roots	RMN- MS	α-asarone, asaraldeyde, staudine, β-sitosterol 3-O-β -D-glucopyranoside, stigmasterol 3-O-β-D-glucopyranoside	[18]
Underground parts and Leaves	GC-MS	(E)-asarone, 2,4,5-trimethoxystyrene, bicycloger-macrene, spathulenol,	[16]

NMR: (Nuclear Magnetic Resonance), HPLC: (High-Performance Liquid Chromatography) HPLC-DAD: (Diode Array Detector), LC-PDA: (Liquid Chromatography with Diode Array Detector), GC-MS: (Gas Chromatography-Mass Spectrometry), CG/EM: (Gas Chromatography with Electron Emission Detection), RMN-MS: (NMR-Mass Spectrometry).

Table 2

Biological Activity	Organisms	Quantitative data	Compounds	Reference
larvicidal	*Aedes aegypti*	(valores de LC50 de 56,6 µg/ml, respectivamente)	Extracts ethanolic	[20]
Pediculicidal	*Pediculus capitis*	1.00, 0.50, 0.25 mg/ cm3	essential oil from underground stem bark	[21]
Antiplasmodial e Antiprotozoal	*Trypanosoma cruzi*	128,0 mM (IC50 de 57,2 mM).	Extracts alcaloides e não alcaloides	[15]
Antigenotóxicas e Anticitotóxicas	*Salmonella typhimurium, Mus Musculus*	2 mg foi usada no SOS-Inductest e a dose de 200 mg/kg foi usada no teste de micronúcleos	Aqueous extract of Duguetia furfurace	[14]
Antioxidante Anti-inflamatória Anti-reumática	*Mus musculus*	(624.37 mg/g, 580.21 mg/g and 254.44 mg/g,)	methanolic extract obtained from D. furfuracea leaves	[9]
Antitumoral Trypanocidal leishmanicidal	Glyoblastoma, colon câncer, melanoma, *Trypanosoma cruzi, Leishmania braziliensis*	(IC50 9.32 mM)	The alkaloid extract and five alkaloids isolated	[23]
anti-infammatory and antinociceptive	*Mus musculus*	10 and 30 mg/kg)	phenylpropanoids from *D. fufuracea* essential oil	[22]
Cytotoxic	*Mus musculus* *Escherichia coli*	1, 2, 5 e 10 mg/0.1 mL (solução estoque 100 mg/ mL)	*Duguetia furfuracea* lyophilized leaf ex-tract	[12]
Antioxidant, Anti-fungal	*C. albicans* *C. krusei* *C. tropicalis*	IC50 de 33,15 µg/ mL	hydroethanolic ex-tract (HEDF), frac-tions of *Duguetia furfuracea*	[10]
anti-inflammatory and antinociceptive	*Mus musculus*	1, 3 e 10 mg/kg	Essential oil of D. furfuracea	[19]
Toxicity	*Drosophila melanogaster*	(1–50 mg/mL) for 7 day	Duguetia furfuracea Hydroalcoholic Ex-tract	[13]
Larvicidal	*C. quinquefasciatus*	(LC50 de 15,23 µg/ mL e 21,97 µg/mL)	essencial oils	[16]

Using the methodological procedures listed above, it was possible to obtain an overview of the biological and pharmacological activities of *D. furfuracea*. Furthermore, the main information about its popular use as a herbal medicine was highlighted, which makes it a promising option in the treatment of various diseases.

Discussions

The significance of *D. furfuracea* lies in the abundance of phenolic compounds, flavonoids, and flavonols found in its leaves, particularly in the methanolic extract. These findings point to its medicinal potential as a source of bioactive, antioxidant, and anti-inflammatory substances [9]. The crude extract of *D. furfuracea* (HEDF) exhibits higher antioxidant activity compared to the methanolic and ethyl acetate fractions. However, there was no beneficial relationship between this activity and the overall quantity of phenols and flavonoids found. Furthermore, both the crude extract and its fractions demonstrated synergistic activity with fluconazole against a variety of fungal strains, indicating they could be effective antifungal medications [10].

[11] identified α-santalene and α-santalene-11-one for the first time from a plant of the Annonaceae family, emphasizing the rarity of these santalane sesquiterpenes. It also highlights the previous absence of reports of ishwarane in plants of the genus *Duguetia*. The isolation of these compounds, along with biclogermacrene, (-)-spathulenol, β-caryophyllene oxide, and the rare (-)-ishwarane, strengthens the chemotaxonomic linkage between Annonaceae and Aristolochiaceae, where these compounds were also discovered [12]. The isolated extract from the leaves of *Duguetia furfuracea* showed no genotoxicity, i.e., it did not damage cell DNA. However, a reduction in the number of bacteria and alterations in the proportion of blood cell types were observed, suggesting possible cellular toxicity.

[13] indicated the toxicity of *Duguetia furfuracea* in *Drosophila melanogaster*, with the plant extract causing adverse effects, including changes in cellular stress and neurobehavioral markers. This toxicity may be attributed to the phytochemicals present in the plant, with oxidative stress emerging as the main underlying mechanism. According to [14], the lyophilized extract of *D. furfuracea* leaves reduced the induction of genetic damage in all assays, regardless of the dose. This discovery indicates that the extract possesses antigenotoxic properties, suggesting it may prevent or mitigate genetic damage produced by genotoxic chemicals.

[15] isolated and identified twelve isoquinoline alkaloids from the aerial parts of a plant, including (-)-asimilobine. Tests against *Trypanosoma cruzi* revealed that only (-)-asimilobine was successful, killing about 72% of the parasites. This shows it may be useful in treating Chagas disease. According to [16], a lethality spectrum for *A. salina* was defined, corresponding to larvicidal toxicity testing against mosquitoes. The essential oil of *D. lanceolata* and its improved fraction contain α-selinene, aristolochene, (E)-caryophyllene, and (E)-calamenene. The underground sections of *D. furfuracea* included (E)-asarone, 2,4,5-trimethoxystyrene, and spathulenol, while the aerial parts contained biclogermacrene.

According to [17], the chemical composition of the aerial sections of the *Duguetia furfuracea* plant was investigated, resulting in the isolation and discovery of two new aporphinic alkaloids: N-nitrosoanonaine and N-nitrosoxylopine. The researchers used techniques such as NMR, elemental analysis, CD spectroscopy, infrared, and mass spectrometry to determine the chemical structure of these substances. [18] identified and structured five compounds in the plant's roots: α-asarone (1), asaraldehyde (2), staudine (3), β-sitosterol 3-O-β-D-glucoside (4), and stigmasterol 3-O-β-D-glucoside (5). Compounds (4) and (5) are found in many plants but are described for the first time in *D. furfuracea*. Staudine (3) is extremely rare and was previously discovered only in *Pachypodanthium staudtii*.

Additionally, the stem bark of *D. furfuracea* has anti-inflammatory qualities and benefits in relieving pain in the central and peripheral nervous systems, as evidenced by in vivo tests with animal models. Previous research on the chemical composition of the essential oil of *D. furfuracea* found the presence of various chemicals, including phenylpropanoid compounds and sesquiterpenes, in varying quantities [19]. Several compounds were discovered in the *Duguetia furfuracea* plant. From the alkaloidal extract of the stem bark, (-)-duguetine β-N-oxide, (-)-duguetine, dicentrinone, and others were obtained. Allantoin was extracted from the stem core. In the volatile oil of the barks, substances such as 2,4,5 -trimethoxystyrene and α-gurjunene were found, demonstrating the bioactive diversity of the plant [6].

According to [20], Annonaceae species like *D. furfuracea* and *Xylopia aromatica* are well known for their cytotoxic, larvicidal, and molluscicidal activities. In 1988, the use of these plants as insecticides was patented. Additionally, the present study demonstrates significant larvicidal activity of Annonaceae species such as *Annona*, *Duguetia*, and *Xylopia*. According to [21], the extracts and essential oils isolated from the aerial parts of *D. furfuracea* did not show significant activity. In contrast, the essential oil extracted from the underground stem bark exhibited exceptional activity. Additionally, α-asarone, a chemical compound isolated from the underground stem bark, was characterized in the literature as possessing insecticidal properties.

According to [22], an enriched fraction of the extract of *Duguetia furfuracea* plant oil demonstrated anti-inflammatory and antinociceptive properties. These effects were attributed to the presence of α-asarone and 2,4,5-trimethoxystyrene. The enriched fraction was observed to prevent edema, leukocyte migration, and synthesis of pro-inflammatory chemicals. It is suggested that this fraction acts on the adenosinergic and opioidergic systems to relieve pain, validating the traditional use of *D. furfuracea* root against inflammations. On the other hand, [23] investigated the antitumor, trypanocidal, and leishmanicidal properties of alkaloids extracted from the stem bark of the plant. Dicentrinone showed high leishmanicidal activity, while Duguetin and Duguetin β-N-oxide exhibited anticancer activity, especially against trypomastigote forms.

Conclusion

The result of the bibliographical review emphasizes the enormous medicinal potential of *Duguetia furfuracea*, being rich in chemical and bioactive substances in both its leaves, roots, aerial and underground parts, making it a useful source of constituents with possible therapeutic uses. Although there are concerns about toxicity in specific situations, these findings highlight the continued need for research to improve our understanding of the mechanisms of action and optimize the safe and effective use of these chemicals. There is an obvious need to continue research and develop extraction and isolation procedures in order to maximize the role of this plant as an ally in herbal medicine and in the development of new medicines.

Conflict of Interest

The authors declare no conflict of interest.

Acknowledgement

The Regional University of Cariri (URCA).

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Citation: Moreira FC, Filho AM, Albuquerque ES, de Sousa FFS, de Souza DL, dos Santos MAF, de Souza JH, Bezerra CF, de Alcântara BM, de Souza MA, Leandro CDS, Pereira ALG, da Anunciação JAO, Figueroa MEV, Fernandes PA, de S Ribeiro AM, Luciano BH, Almeida-Bezerra JW. Phytochemistry and Bioactivities of *Duguetia furfuracea* (A.St.-Hil.) Saff. *SVOA Microbiology 2024,* 5:3, 49-56. doi. 10.58624/SVOAMB.2024.05.043