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Ferns with important ethnomedicinal value and chemical and biological aspects of *Nephrolepis cordifolia*: brief review

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ABSTRACT. The Atlântic Forest comprises native forest formations which make it one of the main biomes in Brazil while the Cerrado is a strategical biome due to its diversity and economic resource. Ferns play important roles in both ecosystems and in the social context. Even though there are few studies of Pteridophytes, they have become fundamental not only to phytoremediation, but also to chemical and pharmaceutical industries. Ferns have different forms of life since they may be terrestrial, epiphytic, rupicolous, aquatic, hemiepiphyte and climbing plants which range from tiny herbaceous plants to arborescent ones. *Nephrolepis cordifolia* (L.) C. Presl, which is mostly found in the world's tropical and subtropical regions, is an ornamental fern that belongs to the Nephrolepidaceae family and whose young fronds and tubers are edible in some countries. Besides, it has medicinal properties against certain diseases, such as rheumatism and anorexia, and symptoms, such as nasal congestion. This brief report aims at compiling results of studies of chemical and biological applications of ferns, mainly the ones exhibited by the *N. cordifolia* species, such as the main secondary metabolites it biosynthesizes, its lab-proven biological activities and its uses in folk medicine.

Keywords: Nephrolepidaceae; fern; medicinal plant; edible fern; herbal medicine.

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Introduction

Ferns are considered lower vascular plants that belong to Lomariopsidaceae, a small and little-known family which has 7 genera and 600 species (Hirai & Prado, 2012). The botanic family, which is typical of tropical regions, comprises epiphytic and hemiepiphyte plants that are occasionally terrestrial and characterized by either creeping or climbing rachises. Their petioles have half-moon shaped vascular bundles with whole or indented pinnate fronds, often articulate and auriculate in some genera (Kaur, 1974). Lomariopsidaceae consists of the following genera: *Cyclopeltis, Lomariopsis, Thysanosoria* and *Nephrolepis*; the last one has just recently been added to the list because its exact phylogenetic position was uncertain. Before that, *Nephrolepis* had its own family – Nephrolepidaceae – with a single genus and 20-25 species (Smith & Kessler, 2018).

Plants that belong to the Nephrolepidaceae family may be terrestrial, rupicolous or epiphytic. Erect stem, ascendant or reptant, little developed with persistent scales (Viveros & Salino, 2017). Monomorphic fronds. Petiole with scales or glabrescent. Lanceolate, elliptic-lanceolate or linear blade, 1-pinna, glabrous, with trichomes or scales. Whole, lobed, serrate or crenulate pinnae, sometimes auriculate in the superior part of the basis, inequilateral, more developed acroscopically. Free veins, 1-4 furcate, ending in submarginal hydathodes. Round sori. Reniform or lunulate indusium. Monolete spores. Monogeneric and pantropical family with 19 species. Several species that belong to this family grow fast in tropical and subtropical climate. As a result, they have become popular and have had their ornamental value acknowledged (Figure 1). Due to cultivation practices, many species disseminated beyond their original habitats (Macedo & Nonato, 2018).

The genus was named *Nephrolepis* because its indusium has the shape of a nephron or kidney (from Greek *nephros*) (Maciel, 2016). *Nephrolepis* species are commonly referred to as macho ferns or Boston ferns; in Brazilian Portuguese, they are called *escadinha do céu*, *samambaias* and *fetos*. Some authors have reported 19 *Nephrolepis* species that are mainly found in tropical regions; nine out of them are found in Brazil (Maciel, 2016).

Besides their biological importance, ferns have several applications since they render certain compounds that are used as medication and others, such as sugars, proteins and essential oils, that are used in food and

cosmetics industries (Gomes, & Martins, 2017). About 220 fern species have been used by folk medicine and approximately 60 have been used in Brazil (Leite et al., 2021). In the Amazon region, their main use is medicinal. There are records of their uses not only to cure diarrhea and the flu, heal wounds, unswell hematomas, soothe pain in the body, stomach, teeth and kidneys but also to cure animals (veterinary uses) (Gomes, & Martins, 2017).

Figure 1. Ornamental ferns grown for their beauty.

In the field of Chemistry of Natural Products, flavonoids biosynthesized by ferns are basically restrited to four main classes: flavonoids, glycosylflavones, flavones and flavanones. Other flavonoids, such as anthocyanins, xanthones and biflavones, are seldom found in ferns (Gomes, & Martins, 2017).

Ferns, mainly *Nephrolepis pectinata*, *Trichomanes membranaceum* L., *Selaginella praestans* Alston and *Adiantum obliquum* Willd, have also been used by folk medicine for treating snakebites. The la+st species has also been used for treating diarrhea and rheumatism by *Chácobo* indigenous people in Bolivia. In the Amazon region, ferns have been used in religious rituals, such as happiness baths, indigenous practices and afro-Brazilian cults, by traditional peoples (Leite et al., 2021).

Therefore, this report aimed at compiling some literature findings that deeply describe chemical and biological aspects of the *Nephrolepis cordifolia* species.

Material and methods

This report is a brief literature review which consists of a methodological approach that aims at providing theme-based knowledge (Xavier et al., 2022). Therefore, it was classified into six steps: theme identification, hypothesis development, criterion determination for literature search, definition of contents to be extracted from chosen studies, result interpretation and, finally, reviewed knowledge synthesis.

Papers were collected from indexed databases – PubMed, SciELO, ScienceDirect, LILACS – and CAPES journals with the use of the following descriptors: fern, Lomariopsidaceae family, Nephrolepidaceae family, *Nephrolepis cordifolia*, chemical composition of *Nephrolepis* and biological activities of *Nephrolepis*. In sum, the study was carried out qualitatively since information on the research object was interpreted. This brief review did not consider any specific period to choose papers. It should be highlighted that they were carefully selected in agreement with the prudence of their means of scientific communication.

Results and discussion

The beginning of this section addresses two subthemes: ferns as medication and their ecological importance. Then, particularities of chemical and biological aspects of the *Nephrolepis cordifolia* species are introduced.

Ferns as medication

Medicinal plants have been used by humans for as long as they have existed, a fact that has been shown by trial and error experiments. In Brazil, the use of medicinal plants has been connected to indigenous peoples

and related to higher vascular plants, but little is known about the use of ferns. Even though they are often relegated to be mere ornaments in the Amazon region, there are records of their medicinal uses not only to treat intestine pain and gastrointestinal diseases, but also to act as cicatrizing, antiseptic and anti-inflammatory agents. Ferns take part in the chemical composition of a syrup that is sold in drugstores to treat respiratory diseases while buds of *Teridium arachnoideum* (Kaulf.) Maxon are used as an antirheumatic drug (Barbosa, Queiroz, Miranda, & Siqueira, 2018).

Polypodium species (Figure 2) have been used by indigenous peoples in Honduras for treating malignant tumors, rheumatoid arthritis and psoriasis (Das & Einstein, 2007). The Boras (in the Peruvian Amazon) use their leaves to prepare a drink against cough. The Witotos (in northwestern Amazon) use their rhizome for treating cough. Peruvian indigenous tribes use their rhizome against pancreas disorders. Indigenous groups in Latin America use their rhizome and leaves for treating several maladies, such as cancer, psoriasis, peptic ulcers, kidney disorders, diarrhea, arthritis and pain in joints and tendons. In the Amazon, they are considered a general tonic to detoxify the body and support the immune system (Das & Einstein, 2007).

Figure 2. Four species of the *Polypodium* genus.

In traditional medicine, ferns are considered alterative, antirheumatic, tonic, pectoral and expectorant. They have been widely used against cough, bronchitis, upper respiratory disorders, rheumatism and skin problems. In Peruvian herbal medicine, their rhizome is used for treating cough, fever, urinary infection and skin affections, such as psoriasis, boils, ulcers and abscesses (Reinaldo, Santiago, Medeiros, & Albuquerque, 2015).

Figure 3 shows the processes of fern preparation for medicinal use, dosage of the remedy and how often people take it. (Figure 3) was based on data described by Das and Einstein (2007).

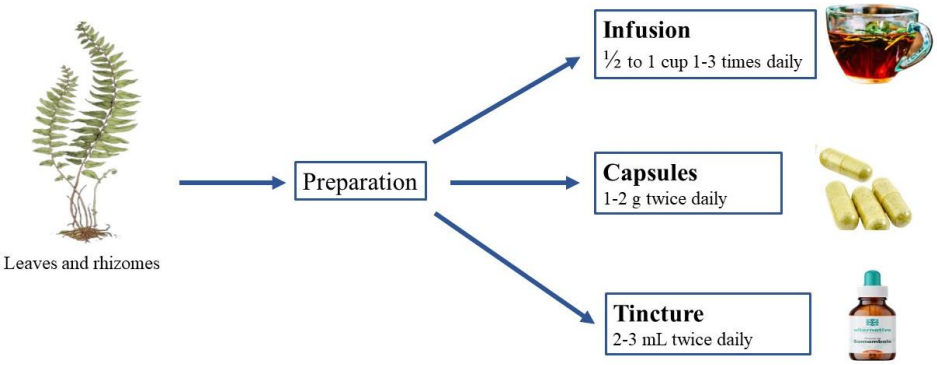

Figure 3. Medicinal use of ferns: processes, dosages and dosing regimen.

Ecological importance of ferns

Ferns play a very important role in maintaining moisture in forests since their roots absorb water and distribute it gradually over the soil and the air. It favors the development of substrate microfauna and microflora, which are extremely important to the ecological balance in the environment. In fact, ferns have played a significant role in people's lives for decades. They have been tools of environmental control, ornaments, instruments in religious rituals and amusement, ways to maintain the fauna in many places, food and shelter to several species; thus, they affect microclimate in many areas directly (Barbosa et al., 2018; Roger Anderson, 2021).

Ferns have economic and nutritional importance, besides their value as ornamental plants. They also have great cultural value worldwide. Some fern species are considered invaders and treated as if they were plagues because they threaten biodiversity. Some species, mainly arborescent ones, are good examples of their interaction with other organisms since several species of other plants, such as bryophytes, Pteridophytes species and orchidaceous ones, may be found around their rachises, along with several little animals, such as ants and macro- and microscopic fungi. Ferns may be indicators of types of soil and damaged environment, thus, showing their preservation levels. As a result, several species may be important to carry out studies of environmental monitoring (Barbosa et al., 2018; Roger Anderson, 2021).

The main environmental risk faced by ferns is habitat fragmentation, which hinders reproduction, deforestation, increase in edge effects and competition with exotic plants. Ferns have currently been threatened by some factors, such as habitat fragmentation. Due to the fact that they are susceptible to anthropic disturbance, ferns are important biological indicators; thus, they contribute to biodiversity preservation (Barbosa et al., 2018; Roger Anderson, 2021).

Nephrolepis cordifolia (L.) C. Presl

This fern species is only found in two Brazilian states, i. e., Pará and Mato Grosso (Maciel, 2016), where it is found in the Cerrado, hillside forests, waterfalls and riparian forests, mainly growing among stones at altitudes from 350 to 620 m. It is characterized by pale brown rachis scales, from slightly to strongly unequal pinnate fronds, underground rhizome in the form of several small tubers and petiole covered with bicolored pale brown scales (Figure 4).

Figure 4. *Nephrolepis cordifolia* (L.) C. Presl.

Nephrolepis cordifolia tubers are boiled with salt and eaten while fronds and rhizomes are used against amnesia in eastern Nigeria. Useful phytochemical constituents of *Nephrolepis* species are tannins, saponins

and flavonoids (Adebola, Adedayo, Adekanye, & Ayinke, 2019). Extracts from *N. cordifolia* rhizomes have been used in India as a contraceptive agent. Adebola et al. (2019) showed that the tubers exhibit nutrients and phytochemicals that are nutritionally important to human health and as feed for livestock.

Tuberous roots are used against indigestion, cold, cough, fever, jaundice and burning urination. They are also eaten to cure hypertension and inflammation (Bajracharya & Bajracharya, 2022). Root paste is applied to boils and skin problems. Tuber juice is useful against dehydration. The whole plant is used for curing kidney, liver and skin disorders, besides chest congestion, rheumatism, jaundice and wounds. Cough is cured by decoction of fresh fronds. Fronds have antibacterial and antifungal potential. Fruit and fronds are evaluated for 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging, α-amylase inhibition and glucose diffusion inhibition activities (Bajracharya & Bajracharya, 2022). Anthelmintic activity of the aqueous extract from fronds is said to paralyze earthworms (*Pheretima posthuma*) at the concentration of 10 mg mL^{-1}. Diuretic potential of rhizome juice is shown. Proximate analysis of different parts of *N. cordifolia* grown in Nepal and Nigeria has been reported. Tannins (11.5 mg 100 g^{-1}), alkaloids (9.1 mg 100 g^{-1}), flavonoids (16.5 mg 100 g^{-1}), phenols (8.3 mg 100 g^{-1}), saponin (1.2 mg 100 g^{-1}) and glycosides (5.4 mg 100 g^{-1}) are estimated in leaflets (Bajracharya & Bajracharya, 2022). Essential oil from aerial parts exhibits nonanal (10.6%, 1), β-ionone (8%, 2), eugenol (7.2%, 3) and anethol (4.6%, 4) (Figure 5). Sequoyitol (5), β-sitosterol (6), fern-9(11)-ene (7), oleanolic acid (8), myristic acid (9), hentriacontanoic acid (10) and triacontanol (11) are isolated from the plant material (Figure 6). *Nephrolepis cordifolia* is a less-explored wild plant that offers chances for researchers to discover novel phytochemicals concealed within it, but it requires more study effort to determine its phytochemical makeup (Mary, Kumar, Leelavathi, Lokesh, & Mahalakshmi, 2021).

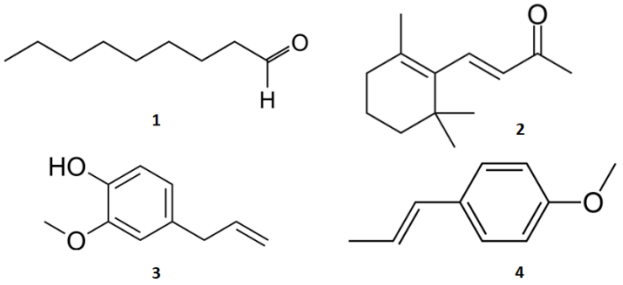

Figure 5. Chemical constituents of essential oil from aerial parts of *Nephrolepis cordifolia*.

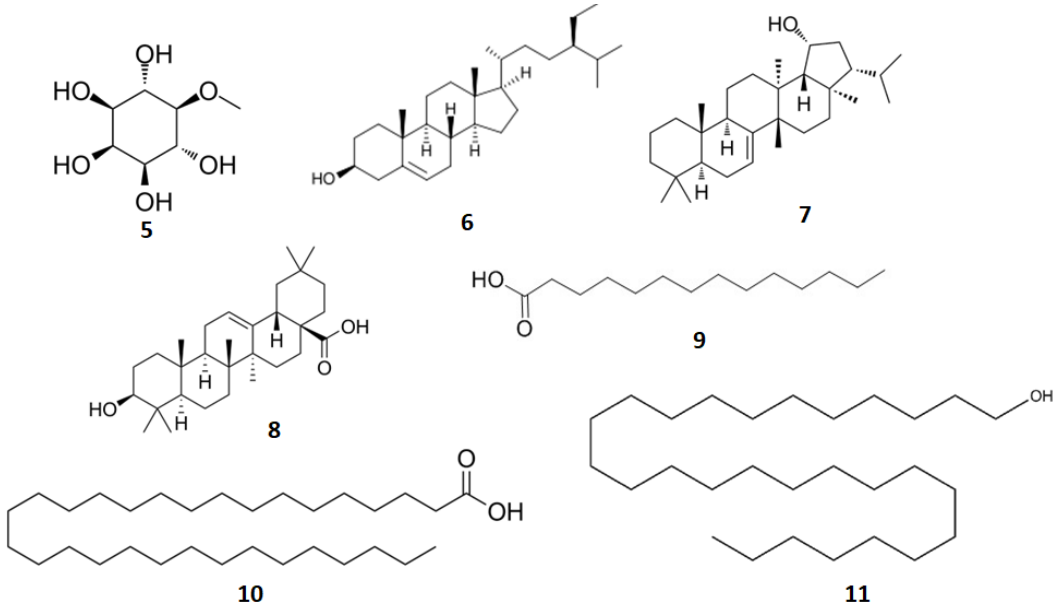

Figure 6. Secondary metabolites isolated of *Nephrolepis cordifolia.*

Boonmee, Suwitchayanon, Krumsri, and Kato-Noguchi, (2020) confirmed the allelopathic potential of crude extract from *N. cordifolia* aerial and underground parts which was capable of inhibiting growth of cress, lettuce, barnyard grass and Italian ryegrass. Essential oil from *N. cordifolia* aerial part grown in Egypt exhibited promising antimicrobial activity; thus, it may used for treating dermatophytosis. It also showed high

cytotoxicity against human cancer cell lines: colon (HCT-116), breast (MCF7) and lung (A-549) (El-Tantawy, Shams, & Afifi, 2016). The ethanol extract of *N. cordifolia* was effective against *Proteus mirabilis*, *Enterobacter aerogenes*, *E. coli* and *Klebsiella pneumonia*. Aqueous extract of *N. cordifolia* inhibited antifungal activity against *Microsporum gypseum*, *Trichophyton mentagrophytes* and *Trichophyton rubrum* (Rani, Khare, & Dantu, 2010).

Oyeyemi, Adebiyi, and Ojo, (2019) reported that *N. cordifolia* leaflets exhibit great nutritional potential and may contribute to food supplementation significantly. The species is rich in phytoconstituents, proteins, carbohydrates, vitamin C and essential minerals. Since it has low toxicity, by comparison with established limits, it may be consumed by humans and herbivorous animals.

Finally, a recent study carried out in Brazil reported that *N. cordifolia* fronds are excellent natural biodegradable insecticides, the so-called green insecticides; crude extract from dry fronds exhibited not only insecticide activity against *Oncopeltus fasciatus* but also terpenoids and phenolic compounds (De Souza, Lima, Feder, Lancellotti, & Santos, 2020).

Conclusion

This report of the *N. cordifolia* species showed its broad application worldwide as the result of its different biological applications. Researchers have studied the *N. cordifolia* species and compared them to other fern species to make sure that its use is as viable and healthy as possible. They have stated that new findings are relevant to the health area and to people who have already used ferns as therapeutic resources. Preliminary phytochemical assays described by the literature showed assertiveness to secondary metabolites, which are not only responsible for plant protection and adequacy but also explain biological activities that the species exerts on the human body, such as treatment and mitigation of diseases. The few studies found in the literature bestow antioxidant, anti-inflammatory, antidiarrhetic, antiseptic and antiulcerogenic activities on *N. cordifolia*. Besides, folk medicine has attributed other benefits. However, this brief literature review shows that further research is needed and that in-depth assays must be carried out with this botanic species in order to study its advantages and disadvantages to health.

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