UNIVERSIDADE FEDERAL DE PERNAMBUCO
CENTRO DE BIOCIÊNCIAS
DEPARTAMENTO DE BOTÂNICA
PROGRAMA DE PÓS-GRADUAÇÃO EM BIOLOGIA VEGETAL

JOSÉ JAILSON LIMA BEZERRA

POTENCIAL MEDICINAL DA FAMÍLIA CYPERACEAE E AVALIAÇÃO DAS ATIVIDADES ANTI-INFLAMATÓRIA, ANTINOCICEPTIVA E ANTIPIRÉTICA DE *Rhynchospora nervosa* (Vahl) Boeckeler

RECIFE - PE
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Tese apresentada ao Programa de Pós-Graduação em Biologia Vegetal da Universidade Federal de Pernambuco, como requisito parcial para obtenção do título de Doutor em Biologia Vegetal.

Área de concentração: Ecologia e Conservação.
Linha de pesquisa: Botânica Aplicada e Etnobotânica.

Orientador: Prof. Dr. Antônio Fernando Morais de Oliveira

RECIFE - PE

2022

Catalogação na Fonte:
Bibliotecário Bruno Márcio Gouveia, CRB4/1788

Bezerra, José Jailson Lima
Potencial medicinal da família Cyperaceae e avaliação das atividades anti-inflamatória, antinociceptiva e antipirética *Rhynchospora nervosa* (Vahl) Boeckeler / José Jailson Lima Bezerra. – 2022.

180 f. : il.

Orientador: Prof. Dr. Antônio Fernando Morais de Oliveira.
Tese (doutorado) – Universidade Federal de Pernambuco. Centro de Biociências. Programa de Pós-graduação em Biologia Vegetal, Recife, 2022.
Inclui referências e anexos.

1. Plantas medicinais. 2. Etnobotânica. 3. Flavonóides. I. Oliveira, Antônio Fernando Morais de (orientador). II. Título.

581.634 CDD (22.ed.) UFPE/CB – 2022-247

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Aprovado em: 29/11/2022

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Dedico este trabalho a minha família, em especial, ao meu sobrinho, Heitor Bezerra.

AGRADECIMENTOS

A Deus, por ter me dado forças para realizar todos os meus sonhos até aqui.

Ao Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), pela concessão da bolsa de Doutorado, sendo essencial para o financiamento e desenvolvimento desta pesquisa.

A Universidade Federal de Pernambuco (UFPE), pelo acolhimento e oportunidades únicas ao longo dos últimos anos.

Ao Programa de Pós-Graduação em Biologia Vegetal da Universidade Federal de Pernambuco (PPGBV/UFPE), pelo amadurecimento acadêmico e conhecimento oferecido durante a realização do curso de Doutorado.

Ao meu orientador, Prof. Dr. Antonio Fernando, por todos os ensinamentos, incentivos e paciência ao longo desses últimos anos, para que juntos pudéssemos desenvolver este trabalho da melhor forma possível.

Aos secretários do PPGBV, Felipe Costa e Soraya Melo, que sempre me atenderam da melhor forma possível todas as vezes que precisei de informações sobre o SIGAA, matrículas, disciplinas, enfim. Sou muito grato por todo o apoio que me deram ao longo do Doutorado.

Aos laboratórios e instituições parceiras pelas importantes contribuições em algumas etapas deste estudo. Deixo registrada aqui a minha gratidão ao Laboratório de Ecologia Aplicada e Fitoquímica (LEAF-UFPE), Laboratório de Lipídios e Aplicações de Biomoléculas em Doenças Prevalentes e Negligenciadas (LAB-DPN-UFPE), Laboratório de Produtos Naturais (LPN-UFPE), Instituto Nacional do Semiárido (INSA), Herbário do Instituto Agronômico de Pernambuco (IPA), e Laboratório de Imunopatologia Keizo Asami (LIKA-UFPE).

Aos professores Alisson Oliveira, Kiriaki Silva, Jarcilene Almeida, Laise Andrade, Maria Medeiros e Ulysses Albuquerque por terem aceitado fazer parte da minha banca examinadora da Tese.

Aos meus pais, Jailza Lima e Sebastião Bezerra, por todos os ensinamentos sobre a vida. Serei eternamente grato pela educação que me deram e por sempre me incentivarem a correr atrás dos meus objetivos.

A minha irmã, Jaelza Lima, e as minhas primas, Maria Dalva, Wennir Lira, Joanne Dantas, Viviane Bezerra e Lucia Dantas, pelo companheirismo e amizade de sempre. Obrigado por tudo!

Ao meu querido sobrinho, Heitor Bezerra, por ter alegrado meus dias nos momentos mais difíceis.

Aos demais familiares e amigos que torcem por mim. A força que vocês me deram foi essencial para o meu desenvolvimento pessoal e profissional.

As minhas grandes amigas, Ruana Carolina e Fernanda Souza, que sempre estiveram ao meu lado compartilhando momentos bons e ruins desde a graduação. A amizade de vocês é extremamente importante para mim.

Aos meus amigos que, independente da distância, sempre se mostraram presentes. Muito obrigado, Amanda Dias, Ariane Dantas, Dioginys César, Kelly Moreira, Luana Magalhães e Lucas Araújo.

Aos meus amigos que conheci na época do mestrado em Maceió e se tornaram pessoas muito especiais em minha vida. Alex Nascimento, Amanda Barbosa, Ariana Santos, Daniel Santos, Erasmo Ribeiro, Euclides Neto, Janaina Santos e Michalison Ferreira, sou muito grato pela amizade de vocês.

Ao excelente amigo pesquisador João Ricardhis, pela grande contribuição na realização das atividades biológicas *in vivo* e por todos os ensinamentos sobre o desenvolvimento de pesquisas utilizando animais.

Ao meu amigo, Anderson Pinheiro, pela parceria no desenvolvimento e publicação de trabalhos científicos.

Aos meus colegas do Laboratório de Ecologia Aplicada e Fitoquímica (LEAF), pelo compartilhamento de experiências vivenciadas ao longo desses últimos anos.

Aos revisores anônimos pelas valiosas contribuíção para a melhoria dos manuscritos.

A todos que, de forma direta ou indireta, contribuíram com esta pesquisa. Muito obrigado!

“O que vale na vida não é o ponto de partida e sim a caminhada. Caminhando e semeando, no fim terás o que colher”.

Cora Coralina

RESUMO

Espécies da família Cyperaceae são utilizadas na medicina tradicional de vários países para o tratamento de algumas enfermidades. O potencial farmacológico de extratos brutos e suas frações, do óleo essencial e de compostos químicos isolados de Cyperaceae tem sido averiguado e corroborado com algumas indicações de uso relatadas pelas comunidades tradicionais. Nesta perspectiva, o presente estudo teve como objetivo: 1) Revisar as espécies de Cyperaceae utilizadas como medicinais no Brasil; 2) Identificar as plantas da família Cyperaceae indicadas especificamente para o tratamento da inflamação incluindo seus prováveis constituintes bioativos; e 3) Avaliar o potencial anti-inflamatório, antinociceptivo e antipirético *in vivo* de *Rhynchospora nervosa* (Vahl) Boeckeler. Os estudos de revisão foram realizados por meio da análise de dados coletados nas plataformas Google Scholar, PubMed, Medline, ResearchGate, SciELO, ScienceDirect, Scopus e Web of Science. Para os estudos de bioatividade, o extrato hidroalcoólico de *R. nervosa* foi avaliado quanto ao seu efeito anti-inflamatório em camundongos Swiss através dos métodos de edema de pata e peritonite aguda induzida por carragenina. Também foram analisadas as atividades antinociceptiva (induzida por ácido acético), antipirética (induzida por leveduras) e toxicidade aguda nos animais. Quimicamente, o teor de flavonoides e fenóis totais do extrato de *R. nervosa* também foi determinado por métodos espectrofotométricos. Verificou-se que 28 espécies de Cyperaceae são utilizadas na medicina popular no Brasil. No entanto, apenas 36% tiveram seus constituintes químicos e/ou suas atividades biológicas investigadas. Tradicionalmente, as espécies de Cyperaceae têm sido empregadas para o tratamento de diferentes enfermidades, sobretudo, inflamações. Plantas inteiras e raízes são as partes mais utilizadas nas preparações tradiconais. Dez espécies de Cyperaceae são utilizadas para o tratamento da inflamação em diferentes países, incluindo o Brasil. Nos documentos científicos analisados, observou-se ainda que os sesquiterpenos e compostos fenólicos foram os principais constituintes químicos isolados a partir de diferentes espécies de Cyperaceae. O extrato hidroalcóolico de *R. nervosa* apresentou baixa toxicidade aguda nos testes pré-clínicos (DL50 = 3807 mg/kg), além de significativa atividade anti-inflamatória nos ensaios de edema de pata e peritonite aguda induzida por carragenina. Também foi verificada uma significativa atividade antinociceptiva com redução de até 86,53% das contorções abdominais nos animais. Quanto a atividade antipirética, não foram observados efeitos positivos do referido extrato. O extrato hidroalcóolico de *R. nervosa* apresentou um alto teor de flavonoides (440.50 μg EQ/mg) e de compostos fenólicos (322.47 μg EAG/mg). O efeito anti-inflamatório e antinociceptivo *in vivo* do extrato hidroalcóolico de *R. nervosa* em

camundongos corroboram as indicações de uso desta espécie na medicina popular brasileira para o tratamento da inflamação. Apesar de seu amplo espectro de uso, a maioria das espécies de Cyperaceae carecem de estudos químicos e farmacológicos.

Palavras-chave: Bioatividade *in vivo*; Etnobotânica; Flavonoides; Plantas medicinais; Revisão sistemática.

ABSTRACT

Species of the Cyperaceae family are used in traditional medicine in several countries for the treatment of some diseases. The pharmacological potential of crude extracts and their fractions, essential oil and chemical compounds isolated from Cyperaceae has been investigated and corroborated with some indications of use reported by traditional communities. In this perspective, the present study aimed to: 1) Review the Cyperaceae species used as medicinal in Brazil; 2) Identify the plants of the Cyperaceae family specifically indicated for the treatment of inflammation, including their probable bioactive constituents; and 3) To evaluate the *in vivo* anti-inflammatory, antinociceptive and antipyretic potential of *Rhynchospora nervosa* (Vahl) Boeckeler. Review studies were performed by analyzing data collected on Google Scholar, PubMed, Medline, ResearchGate, SciELO, ScienceDirect, Scopus and Web of Science platforms. For bioactivity studies, the hydroalcoholic extract of *R. nervosa* was evaluated for its anti-inflammatory effect in Swiss mice through the methods of paw edema and carrageenan-induced acute peritonitis. The antinociceptive activities (induced by acetic acid), antipyretic (induced by yeasts) and acute toxicity in the animals were also analyzed. Chemically, the total flavonoids and phenols content of the *R. nervosa* extract was also determined by spectrophotometric methods. It was found that 28 species of Cyperaceae are used in folk medicine in Brazil. However, only 36% had their chemical constituents and/or their biological activities investigated. Traditionally, Cyperaceae species have been used to treat different diseases, especially inflammation. Whole plants and roots are the most used parts in traditional preparations. Ten species of Cyperaceae are used for the treatment of inflammation in different countries, including Brazil. In the analyzed scientific documents, it was observed that sesquiterpenes and phenolic compounds were the main chemical constituents isolated from different species of Cyperaceae. The hydroalcoholic extract of *R. nervosa* showed low acute toxicity in preclinical tests (LD50 = 3807 mg/kg), in addition to significant anti-inflammatory activity in paw edema and carrageenan-induced acute peritonitis tests. It was also verified a significant antinociceptive activity with a reduction of up to 86.53% of the abdominal contortions in the animals. As for the antipyretic activity, no positive effects of said extract were observed. The hydroalcoholic extract of *R. nervosa* showed a high content of flavonoids (440.50 μg EQ/mg) and phenolic compounds (322.47 μg EAG/mg). The *in vivo* anti-inflammatory and antinociceptive effect of the hydroalcoholic extract of *R. nervosa* in mice corroborates the indications for the use of this species in Brazilian folk medicine for the

treatment of inflammation. Despite its broad spectrum of use, most Cyperaceae species lack chemical and pharmacological studies.

Keywords: Bioactivity *in vivo*; Ethnobotany; Flavonoids; Medicinal plants; Systematic review.

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LISTA DE ABREVIATURAS E SIGLAS

AA	Arachidonic acid
ActF	Active fraction
ADAMTS5	A disintegrin and metalloproteinase with thrombospondin motifs
AE	Aqueous extract
$AlCl_3$	Aluminium chloride
ANOVA	Analysis of variance
BF	*n*-Butanol fraction
BSA	Bovine serum albumin
CAPES	Coordenação de Aperfeiçoamento de Pessoal de Nível Superior
CE	Chloroform extract
CEUA	Animal Care and Use Committee
CH	Crude hydrodistillate
CNPq	Conselho Nacional de Desenvolvimento Científico e Tecnológico
COX	Cyclooxygenase
COX-2	Cyclooxygenase-2
DPPH	2,2-diphenyl-1-picrylhydrazyl
EAE	Ethyl acetate extract
EAF	Ethyl acetate fraction
EDTA	Ethylenediaminetetraacetic acid
EE	Ethanol extract
EO	Essential oil;
GAE	Gallic acid equivalents
HAE	Hydroalcoholic extract
HepG2	Cell line
HF	*n*-Hexane fraction
HO-1	Heme oxygenase-1
HPLC	High performance liquid chromatography
IC_{50}	Half the maximal inhibitory concentration
IFN-γ	Interferon-γ
IL-1β	Interleukin-1β
IL-6	Interleukin-6

iNOS	Inducible nitric oxide synthase
IPA	Agronomic Institute of Pernambuco
LD_{50}	Lethal dose required to kill 50% of a group of animals
LHERn	Lyophilized hydroalcoholic extract of *Rhynchospora nervosa*
LIKA	Keizo Asami Immunopathology Laboratory
5-LOX	5-Lipoxygenase
LPS	Lipopolysaccharides
LTC4	Leukotriene C4
LTD4	Leukotriene D4
LTE4	Leukotriene E4
MAPKs	Mitogen-activated protein kinase
ME	Methanol extract
MF	Methanol fraction
MMPs	Metalloproteinases
N	Total number of documents
Na_2CO_3	Sodium carbonate
ND	Number of documents per state
NF-κB	Factor nuclear kappa B
NO	Nitric oxide
Pb	Lead acetate
PBS	Phosphate buffer solution
PGE2	Prostaglandin E2
QE	Quercetin equivalents
RAGE	Receptor for advanced glycation end-products
RAW 264.7	Cells lines
RF	Relative frequency
SD	Standard deviation
SH-SY5Y	Cells lines
SisGen	National System of Management of Genetic Heritage and Associated Traditional Knowledge
THP-1	Cell line
TNF-α	Tumor necrosis factor-α
TOF	Extract enriched with total oligomer flavonoids

TPA	12-O-tetradecanoylphorbol-13-acetate
UFPE	Federal University of Pernambuco

SUMÁRIO

1 INTRODUÇÃO

Cyperaceae Juss. agrupa cerca de 5.500 espécies distribuídas em 90 gêneros (GOVAERTS et al., 2018; SEMMOURI et al., 2019). Esta família é considerada cosmopolita e desempenha um papel dominante na vegetação de zonas úmidas (LARRIDON et al., 2013). Nos trópicos e subtrópicos, *Cyperus* é o maior gênero de Cyperaceae com cerca de 700 espécies (GOVAERTS et al. 2011; LARRIDON et al., 2011). Segundo Schneider et al. (2020), foram catalogadas 647 espécies de Cyperaceae no Brasil, destas 196 são endêmicas, distribuídas em 30 gêneros, sendo os mais representativos: *Rhynchospora* (64), *Cyperus* (29), *Eleocharis* (20), *Scleria* (18), *Bulbostylis* (17) e *Hypolytrum* (11). Apesar de serem amplamente identificadas em várias regiões do Brasil, na região Nordeste, os estudos com Cyperaceae são escassos e raramente fornecem descrições botânicas das espécies (RIBEIRO et al., 2014)

Algumas das espécies de Cyperaceae que ocorrem no Brasil têm sido utilizadas para fins medicinais. Representantes do gênero *Cyperus* (ROQUE et al., 2010; BRANDÃO et al., 2012; RIBEIRO et al., 2017; MESSIAS et al., 2015), *Fimbristylis* (ROQUE et al., 2010), *Eleocharis* (ZENI; BOSIO, 2011), *Bulbostylis* (BIESKI et al., 2012), *Hypolytrum* (MOTTA et al., 2016), *Kyllinga* (PINTO et al., 2017), *Rhynchospora* (SANTANA et al., 2016), *Schoenoplectus* (CASTRO et al., 2016) e *Scleria* (ROMANUS et al., 2018), são amplamente utilizados para o tratamento de várias doenças, tais como inflamação, infecção, dores em geral, febre, diurese, hemorroidas, resfriado, gripe e problemas menstruais. *Cyperus rotundus* L., utilizada como medicinal no Brasil, também tem destaque como medicinal em vários países asiáticos, principalmente na Índia (BHUSHAN; KUMAR, 2013; RAMANATHAN et al., 2014; DATTA et al., 2014; GHULAM et al., 2015; GANESAN; XU, 2017). Uma revisão sobre as espécies de Cyperaceae utilizadas no Brasil como medicinais é mostrada no **Artigo 1** intitulado "Ethnobotanical uses of Cyperaceae species in Brazilian traditional medicine".

Investigações fitoquímicas a partir de espécies de Cyperaceae têm identificado substâncias de interesse farmacológico. Os terpenos (SEO et al., 2011; TSOYI et al., 2011; VILHENA et al., 2014; XU et al., 2015; AL-HAZMI et al., 2018; BRILLATZ et al., 2020), compostos fenólicos (ITO et al., 2012; ELSHAMY et al., 2017; CHO et al., 2018), glicosídeos iridóides (ZHOU et al., 2013; ZHOU; ZHANG, 2013), benzenoides (RABELO et al., 2014), fitoesteroides (MOHAMMED et al., 2014), ácidos graxos insaturados (SHIN et al., 2015), diterpenoides (DONG et al., 2016), triterpenos (KAKARLA et al., 2016), norterpenoides (IBRAHIM et al., 2018) e glicosídeos macrocíclicos (PENG et al., 2019) são as principais classes químicas de constituintes que ocorrem nesta família. Essas classes de compostos estão

diretamente relacionadas com o amplo espectro de atividades biológicas e farmacológicas relatadas para as espécies da família Cyperaceae.

Dentro de Cyperaceae, as espécies pertencentes aos gêneros *Cyperus* (DANG et al., 2011; PHAM et al., 2017; DATTA et al., 2018; NOGUEIRA et al., 2020), *Lagenocarpus* (MARTINS et al., 2014), *Pycreus* (ADEONIPEKUN et al., 2014), *Bulbostylis* (OWOYELE et al., 2015), *Carex* (GIRI et al., 2015; WANG et al., 2019), *Scleria* (KARUNASREE et al., 2015), *Scirpoides* (POPESCU et al., 2016), *Remirea* (DÓRIA et al., 2016), *Actinoscirpus* (SUBEDI et al., 2016), *Kyllinga* (JARAMILLO-COLORADO et al., 2016; AHMED; CHAKRAVARTHY, 2017), *Carpha* (CHO et al., 2018), *Eleocharis* (ROSYIDAH et al., 2018), *Fimbristylis* (MIA et al., 2019; MUKTA et al., 2020), *Bolboschoenus* (CAO et al., 2020) e *Schoenoplectus* (PENG et al., 2019), tiveram suas atividades antioxidante, antimicrobiana, anti-inflamatória, anticancerígena, antinociceptiva, antidiabética, antidiarreica, anti-helmíntica, neuroprotetora e gastroprotetora investigadas em estudos *in vitro* e *in vivo*.

Apesar de ser vista como uma família subutilizada para fins terapêuticos, esses trabalhos citados anteriormente indicam que alguns representantes de Cyperaceae apresentam um real potencial farmacológico, com destaque para investigações relacionadas a atividade anti-inflamatória *in vivo* e *in vitro*. Com base nestas informações obtidas em diferentes bases de dados *online*, o **Artigo 2** intitulado "Cyperaceae species used for the treatment of inflammation: a review of ethnomedicinal, pharmacological, toxicological, and phytochemical evidence" foi elaborado na forma de uma revisão sistemática abordando o tema nos últimos 30 anos. Neste, foi revisado o uso tradicional, potencial anti-inflamatório, toxicidade e compostos químicos isolados com potencial anti-inflamatório.

Alguns estudos investigaram as atividades biológicas de espécies do gênero *Rhynchospora* Vahl (MARTINS et al., 2013; PAGNING et al., 2016; BEZERRA et al., 2019). Este gênero é amplamente distribuído nas Américas, principalmente em ambientes quentes, zonas temperadas (sudeste dos Estados Unidos) e neotrópicos. O gênero possui cerca de 270 espécies descritas agrupadas em dois subgêneros e 27 seções (STRONG, 2006; ARGUELHO et al., 2012). No Brasil, o gênero *Rhynchospora* é amplamente representado, agrupando 168 espécies, dessas, 64 são endêmicas e ocorrem em todas as regiões geográficas brasileiras (THOMAS et al., 2020).

Rhynchospora nervosa (Vahl) Boeckeler é uma espécie nativa e endêmica do Brasil. Caracteriza-se por ser uma planta perene com cerca de 30-50 cm de altura, além disso, apresenta manchas alvas basais na face adaxial das brácteas involucrais, capítulo congesto apical, com glumas alvas ou alvo-rubescentes (RIVAS, 2007; SCHNEIDER et al., 2017). Esta planta é

utilizada por algumas comunidades brasileiras, localizadas no estado da Bahia, para o tratamento e cura de algumas doenças, tais como: gripe, febre, inflamação, inchaço, malária, congestão nasal e doença venérea. Geralmente, a planta inteira é utilizada na forma de chá, banhos ou xarope (MOREIRA et al., 2002; COSTA et al., 2006; RODRIGUES et al., 2006; GOMEZ et al., 2016; SANTANA et al., 2016; LISBOA et al., 2017; RAMÍREZ; BLAIR, 2017).

Esses relatos incentivam o desenvolvimento de estudos científicos para validar o potencial medicinal de *R. nervosa* relatados pela medicina popular, principalmente quando se trata dos seus efeitos relacionados aos processos inflamatórios. As investigações sobre o potencial anti-inflamatório de *R. nervosa* foram conduzidos pela primeira vez e são descritos no **Artigo 3** intitulado "Evaluation of the anti-inflammatory, antipyretic, and antinociceptive activities of the hydroalcoholic extract of *Rhynchospora nervosa* (Vahl) Boeckeler (Cyperaceae)". Em síntese, a tese encontra-se dividida em três capítulos.

2 OBJETIVOS

2.1 OBJETIVO GERAL

Realizar revisões abrangentes e sistemáticas das espécies de Cyperaceae utilizadas na medicina tradicional e investigar o potencial anti-inflamatório, antinociceptivo e antipirético *in vivo* de *Rhynchospora nervosa* (Vahl) Boeckeler.

2.2 OBJETIVOS ESPECÍFICOS

- Revisar as espécies de Cyperaceae utilizadas como medicinais no Brasil;
- Identificar as plantas da família Cyperaceae indicadas especificamente para o tratamento da inflamação incluindo seus prováveis constituintes bioativos;
- Avaliar a segurança biológica do extrato hidroalcoólico de *R. nervosa* por meio do teste de toxicidade aguda;
- Quantificar o teor de fenólicos e os flavonoides totais do extrato hidroalcoólico de *R. nervosa*;
- Avaliar a atividade anti-inflamatória do extrato hidroalcoólico de *R. nervosa* por meio dos testes de peritonite aguda e edema de pata induzida por carragenina;

- Avaliar a atividade antinociceptiva do extrato hidroalcoólico de *R. nervosa* por meio do teste de contorções abdominais induzidas por ácido acético;
- Avaliar a atividade antipirética do extrato hidroalcoólico de *R. nervosa* por meio do teste de pirexia induzida por leveduras de cerveja.

3 ARTIGO 1

Ethnobotanical uses of Cyperaceae species in Brazilian traditional medicine

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Abstract

Introduction: Species of Cyperaceae occur in all regions of Brazil and have been used in folk medicine by some communities in the country, as well as in other parts of the world. In this perspective, the present study aimed to review, for the first time, the herbal medicine of Cyperaceae species used in Brazil, making distinction between species with and without experimental data available in the literature. *Methods*: Data on the medicinal use of Cyperaceae species in Brazil were obtained from different databases. After major revision, a total number of 604 publications were retrieved and those that did not meet the search criteria were excluded. A total of 159 articles were selected and used in this review. *Results*: According to the analyzed documents, a total of twenty-seven species of Cyperaceae have reports of folk medicinal use in fifteen states of the country. Of these, 44% have had their chemical constituents and/or biological activities scientifically investigated. Sesquiterpenes were the main constituents isolated from different species. The species are used to treat different health problems, especially inflammation, and the roots are the most frequently used parts. *Conclusions*: *Cyperus rotundus* is the species with the highest number of medicinal indications and pharmacological and phytochemical studies. However, despite the wide spectrum of use of Cyperaceae species, experimental evidence to validate the indications mentioned by traditional communities is lacking for most of them.

Keywords: Cyperus; Ethnobotany; Ethnopharmacology; Medicinal plants; Volatile oil.

1. Introduction

A large number of reports of traditional uses of plants for medicinal purposes are published every year (Bitu et al., 2015; Ahmad et al., 2016; Pagani et al., 2017; Heinrich et al., 2018; Süntar, 2019; Yeung et al., 2020). Ethnopharmacological studies often document the traditional knowledge and the possible therapeutic potential of plants. In general, these publications provide indications about their use, forms of preparation and dosages, and make significant contributions to the planning and implementation of experimental research (Leonti et al., 2017; Süntar, 2019). As a result, natural products with potential to become sources of new drugs are eventually discovered (Weckerle et al., 2018).

Potentially medicinal plants are usually pharmacologically tested, and if any evidence of biological activity is detected, extracts are fractionated so as to isolate and identify the active compounds (Jamshidi-Kia et al., 2018). However, nothing prevents the chemical studies from being carried out concurrently or before any pharmacological evidence. Thus, ethnopharmacological studies together with pharmacological and phytochemical experiments have the ultimate goal of validating traditional preparations through the bioassay and isolation of bioactive substances for the development of new drugs (Pushpangadan et al., 2017).

In Brazil, different traditional communities, such as indigenous, quilombola, and gypsy peoples, use many native species as therapeutic resources. Local traditional knowledge of antimalarial plants, for example, is widespread in the indigenous communities of the Upper Rio Negro, in the Amazonas (Frausin et al., 2015; Kffuri et al., 2016). The Quilombo da Fazenda community, in Picinguaba, São Paulo State, takes into account some environmental and climatic factors when choosing plants to be used in the treatment of certain diseases (Yazbek et al., 2019). The gypsy community of the Calon ethnicity located in the state of Pernambuco, Northeast Brazil, uses several species for veterinary purposes. *Apodanthera congestiflora* Cogn. (Cucurbitaceae) and *Heliotropium indicum* L. (Boraginaceae), for example, stand out in the prophylaxis and treatment of Newcastle disease in poultry (Lobo et al., 2020).

Several botanical families have had their medicinal potential reported in Brazil and in the world (Bitu et al., 2015; Ahmed et al., 2015; Güneş et al., 2017; Sadat-Hosseini et al., 2017). Cyperaceae, for example, which includes grass-like monocots, is a cosmopolitan family comprising 95-100 genera and around 5,600 species. The family is widespread over all continents (Larridon et al., 2021; Taheri et al., 2021; Griffiths et al., 2022). Species of Cyperaceae are indicated in ethnopharmacological studies for the medicinal treatment of various diseases (Roque et al., 2010; Bieski et al., 2012; Brandão et al., 2012; Bersan et al.,

2014; Vásquez et al., 2014; Mesquita et al., 2018; Silva et al., 2020). In Brazil, 678 species of Cyperaceae distributed in 42 genera are recorded (Alves et al., 2009).

In the Brazilian medicinal flora, *Cyperus rotundus* L. is a species of Cyperaceae widely cited in ethnobotanical and ethnopharmacological studies (Fenner et al., 2006; Duarte et al., 2007; Monteles and Pinheiro, 2007; Staniski et al., 2014; Rego et al., 2016). This species has shown a wide spectrum of biological activities in both *in vivo* and *in vitro* studies (Dang et al., 2011; Kabbashi et al., 2015; Lin et al., 2019; Simorangkir et al., 2019). There are also other species of Cyperaceae in Brazil, such as *Bulbostylis capillaris* (L.) C.B. Clarke and *Rhynchospora nervosa* (Vahl) Boeckeler, with numerous indications in popular medicine (Rodrigues et al., 2006; Bieski et al., 2012; Santana et al., 2016). However, no chemical constituents and/or pharmacological activities have been reported for *B. capillaris*. Recently, the anti-inflammatory, antipyretic and antinociceptive activities of *R. nervosa* were described, but the chemical constituents of the species are not well characterized (Bezerra et al., 2022a).

The present study aimed to review the representatives of Cyperaceae with reports of medicinal use in Brazil. Ethnomedicinal findings regarding geographic region and state of citation, therapeutic indication, plant organ used, and pharmacological and chemical studies when available~~,~~ were summarized, making distinction between species with and without pharmacological and chemical studies in the literature to confirm the efficacy and safety of their uses.

2. Methodology

Data on the medicinal use of Cyperaceae species in Brazil were collected through search in the Google Scholar (https://scholar.google.com), PubMed® (https://pubmed.ncbi.nlm.nih.gov/), PubMed Central® (https://www.ncbi.nlm.nih.gov/pmc/), SciELO (https://scielo.org/), Scopus® (http://www.scopus.com/), and Web of Science™ (https://www.webofknowledge.com) databases. Patent databases were not consulted. The survey included documents in English and Portuguese and covered articles available until November 07, 2022. Initially, the keywords “Cyperaceae” AND “medicinal” AND “Brazil” were searched and then associated with the following terms: “bioactive”, “biological activity”, “ethnomedicinal use”, “ethnobotany”, “ethnopharmacology”, “local community”, “local medicine”, “local use”, “medicinal”, “medicinal use”, “natural products”, “pharmacology”, “phytochemistry”, phytoconstituents”, “toxicity”, “traditional community”, and “traditional use”. After major revision, a total of 604 publications were obtained. Duplicated articles and

those that did not meet the search criteria were excluded using the Mendeley Desktop software version 1.19.4 (Mendeley Ltd., United Kingdom). End-of-course papers, dissertations, theses, and abstracts published in congress proceedings were also excluded. Book chapters (digital and printed) were not included because they are previous publications already covered in published articles. Scientific articles that cited plants only at the genus level or that did not provide sufficient ethnopharmacological information such as the parts of the plants used in herbal medicines or their preparation method were also excluded. Finally, 159 articles were selected and used in this review.

The origin of the Cyperaceae species listed in the present study was checked according to information available on the "Flora do Brasil 2020" database. If pertinent, the species names, synonyms and authors were corrected. Data were categorized according to geographic region and state, indication of use, plant organ used, pharmacological activities, and chemical constituents identified. The species surveyed were then assigned to three groups: "Cyperaceae species used in folk medicine in Brazil and subject to scientific investigation", "Cyperaceae species used in folk medicine in Brazil without pharmacological and/or chemical studies", and "Cyperaceae species used in folk medicine in Brazil and other countries".

The relative frequency (RF) of ethnopharmacological information by geographic region and Brazilian state was calculated using the formula of Sadat-Hosseini et al. (2017) by dividing the number of documents per state (ND) by the total number of documents (N), according to the formula: RF = (ND/N) x 100. The values obtained were multiplied by one hundred (x 100) to express the RF in percentage (%).

3. Results and discussion

In total, twenty-seven (27) species of Cyperaceae used for medicinal purposes in Brazil were identified (Table 1). *Cyperus* was the genus with the largest number of species (12). *Bulbostylis* (3), *Rhynchospora* (3), *Scleria* (3), *Carex* (1), *Eleocharis* (1), *Fimbristylis* (1), *Hypolytrum* (1), *Kyllinga* (1), and *Schoenoplectus* (1) were less frequently cited. Only 44% of the species have had their chemical constituents and/or biological activities scientifically investigated. Therefore, most species (56%) depend on further studies to have their medicinal potential indicated in folk medicine validated.

According to the scientific documents analyzed, different uses of Cyperaceae species have been reported in all geographical regions of Brazil (Midwest, North, Northeast, South, and Southeast). These reports were made in fifteen (15) of the twenty-six (26) states of the country

(Table 2). The state with the highest number of indications (RF value) was Bahia (14.30%), followed by Mato Grosso and Rio Grande do Sul (11.90% each). The other states had a low RF of information due to the fewer or non-existent records to this date. Table 2 shows the number of documents (ND) and RF value of Cyperaceae species used in folk medicine by geographic region and state of Brazil. According to Alves et al. (2009), the regions with higher richness of species are the Southeast and North, with about 350 species each. These numbers indicate that there are many species of Cyperaceae with still unknown and consequently unexplored medicinal potential.

Regarding medicinal applications, Cyperaceae species are indicated in Brazil mainly for the treatment of inflammation (28%). Fever (15%), diarrhea (9%) and flu (9%) appear in second, third and fourth place, respectively. Other indications are present in less than 8% of the citations (Fig. 1). Several scientific studies using different species of Cyperaceae have proven the anti-inflammatory effects of the species through *in vitro* and *in vivo* experiments (Chaulya et al., 2012; Rabelo et al., 2013; Kakarla et al., 2014; Owoyele et al., 2015; Sukjamnong and Santiyanont, 2015; Dong et al., 2016; Upadhyay and Jain, 2017; Kim et al., 2020; Rocha et al., 2020; Udefa et al., 2020). According to Bezerra et al. (2022b), only 10 species of Cyperaceae are used for the treatment of inflammation in the traditional medicine of some countries and 13 species have been targeted in *in vivo* and *in vitro* studies for the bioprospecting of anti-inflammatory agents. Despite the low number of studies compared to that developed with species of other families, it is likely that further scientific studies will corroborate some indications of the use of Cyperaceae in the treatment of inflammation in folk medicine in Brazil.

In the present study, it was found that the plant organs most used in homemade medicinal preparations were the roots (27%) followed by the whole plant (22%) and the leaves (19%). It is important to note that, in citations such “whole plant” or “aerial parts”, the authors did not specify to which organs they were referring (Fig. 2). According to some studies, the roots, or roots associated with the rhizome, or even the whole plant, were the targets of several pharmacological and chemical studies (Oladosu et al., 2011; Majumder, 2018; Peerzada et al., 2015; Dhar et al., 2017; Alif et al., 2018). As shown in Table 1, tea (decoction or infusion) was the most common form of preparation using different parts of the plants. Sesquiterpene compounds were the main constituents isolated from different species, but flavonoids were also isolated from some species. The main chemical constituents isolated from Cyperaceae species used in the traditional medicine of Brazil are shown in Table 3.

3.1. Cyperaceae species used in folk medicine in Brazil and subject to scientific investigation

Cyperus aggregatus (Willd.) Endl. (Syn. *Cyperus flavus* (Vahl) Nees)

Cyperus aggregatus has been used by Tiriyó indigenous communities in the Brazilian Amazon for the treatment of fever. The whole plant is usually used in the preparation of decoctions (baths) (Cavalcante and Frikel, 1973). Chemically, flavonoid conjugates such as luteolin 7-glucoside, luteolin 7-glucuronide, tricin 7-glucoside, tricin 7-glucuronide, and tricin 7-glucoside sulphate have been recorded in *Cyperus flavus* (Syn. *C. aggregatus*) leaves (Harborne et al., 1982). However, no pharmacological study has been conducted on this species.

Cyperus articulatus L.

Popularly known as "priprioca", *C. articulatus* has been widely used in folk medicine in Brazil. Underground structures (roots, tubers and rhizomes) are the parts usually used in the preparation of decoctions, infusions, macerates, and teas. The plant is used for the treatment of fever, back pain, deep wounds, "quebranto" (weariness attributed to the evil influence of spells) and asthma (Milliken and Albert, 1996; Roque et al., 2010; Palheta et al., 2017; Mesquita and Tavares-Martins, 2018). "Priprioca" also stands out as an important anti-infective and anti-inflammatory agent (Duarte et al., 2007; Bersan et al., 2014).

Scientific studies have evaluated the medicinal potential of rhizomes of *C. articulatus*. Antibacterial (Oladosu et al., 2011; Azzaz et al., 2014), anti-Onchocerca (Metuge et al., 2014), antimalarial (Silva et al., 2019), and anticancer (Nogueira et al., 2020) activities are some examples reported in the literature. Silva et al. (2019) reported that the essential oil from the rhizomes of *C. articulatus* grown in Santarém, Pará, exhibited a low IC_{50} against two strains of *Plasmodium falciparum* (W2 and 3D7). The sesquiterpene mustakone was identified as the main constituent.

According to Zoghbi et al. (2006a), the volatile constituents from the stems and rhizomes of *C. articulatus*, also cultivated in the state of Pará, had the sesquiterpenes caryophyllene oxide (4.6-28.5%) and mustakone (7.3-14.5%) and the monoterpene α-pinene (0.7-12.9%) as major constituents. In the rhizomes of *C. articulatus* cultivated in the municipality of Santarém, Pará, mustakone (9.9%), cyclocolorenone (7.4%), α-copaene (4.4), α-selinene (4.4) and cis-thujopsenal (4.0%) were identified as major compounds (Silva et al., 2019).

Nogueira et al. (2020) observed that the essential oil from the rhizomes of samples of *C. articulatus* from the state of Amazonas caused cell cycle arrest in the G_2/M phase and cell

death of hepatocellular carcinoma (HepG2) *in vitro* and presented anti- liver cancer potential in an *in vivo* xenograft model. The essential oil of the species had sesquiterpenes (muskatone, cyclocolorenone, pogostol, *α*-copaene, and caryophyllene oxide) and a monoterpene (*α*-pinene) in its composition (Nogueira et al., 2020).

Cyperus brevifolius (Rottb.) Endl. ex Hassk.

Based on ethnographic indications of native plants in Southern Brazil, Avancini and Wiest (2008) reported that the flowering parts of *C. brevifolius* are indicated for the treatment of skin mycoses. In a review of the useful Brazilian plants listed in the field books of the French naturalist Auguste de Saint-Hilaire (1779-1853), Brandão et al. (2012) found that the roots of *C. brevifolius* were indicated in cases of snake bites. The method of preparation using the vegetative or reproductive parts of this species was not described in any of the documents analyzed.

Scientific findings revealed that *C. brevifolius* has already had its antioxidant activity and phenolic content investigated. In a study developed by Uy and Garcia (2015), the ethanolic extract of the fresh leaves of this species presented low phenol content and weak antioxidant activity by the free radical 2,2-diphenyl-1-picrylhydrazyl (DPPH) and phosphomolybdenum methods.

To our knowledge, no data have been reported on the chemical composition of *C. brevifolius* in Brazil. However, flavonol (quercetin) and flavone (luteolin) were isolated from Australian samples (Harborne et al., 1982). In addition, the essential oil of this species collected in Manoa, Hawaii, contained 58% of *n*-paraffins and, in smaller amounts, sesqui- and monoterpenes (Komai and Tang, 1989).

Cyperus compressus L.

Ribeiro et al. (2017) observed that the infusion of the whole plant of *C. compressus* was used as a diuretic agent by riverside dwellers in the microregion of the North of Araguaia, Mato Grosso. Different extracts obtained from this species had their antioxidant activity evaluated by Datta et al. (2018). According to these authors, the ability to scavenge free radicals varied from 4 to 22% by the DPPH method, and from 5 to 55% using the 2,2’-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS) method. The best antioxidant activity was observed for the 70% ethanolic extract.

To the best of our knowledge, the chemical composition of *C. compressus* has not yet been investigated in samples from Brazil. Nevertheless, the essential oil from the roots of samples of this species collected in Southern India was characterized by the predominance of sesquiterpenoids (89.9%), with caryophyllene oxide (34.0%) and cyperene (25.6%) being the major constituents (Rameshkumar et al., 2011).

Cyperus esculentus L.

In Brazil, specifically in some states such as Amazonas, Maranhão, Paraíba, Rio Grande do Norte, and Minas Gerais, several popular names such as "tiririca", "junça", "junco", "manufa", and "alho-brabo" are used to refer to *C. esculentus*. Different authors have observed the use of roots, leaves, rhizomes or even the whole plant of *C. esculentus* in different forms of preparation for treating diseases of the respiratory system (e.g. influenza). There are also reports of its indication as emmenagogue, analgesic and anti-inflammatory agent, as well as to reduce symptoms of hemorrhoids and diarrhea (Monteles and Pinheiro, 2007; Paulino et al., 2011; Santos et al., 2012; Vásquez et al., 2014; Messias et al., 2015).

The pharmacological potential of *C. esculentus* has been demonstrated through antibacterial (Prakash and Ragavan, 2009; Jing et al., 2016), antiobesity, hypolipidemic (Moon et al., 2012), antioxidant (Oloyede et al., 2014), antidiarrheal (Majumder, 2014; Shorinwa and Dambani, 2020), antidiabetic (Onyenibe and Udogadi, 2019), and antiproliferative (Achoribo and Ong, 2019) activities in *in vivo* and *in vitro* assays. Sucrose, oleic acid glyceryl ester, oleamide, linoleic acid glyceryl ester, stigmasterol, quercetin, myricetin, tyramine, and *N*-feruloyltyramine were some chemical compounds isolated from the rhizomes (Vega-Morales et al., 2019).

Cyperus giganteus Vahl

Popularly known as "papiro" in a Cerrado area in Prudente de Morais, Minas Gerais, *C. giganteus*, specifically the stem, is indicated in folk medicine for the treatment of bronchitis and influenza (Silva et al., 2015). The essential oils obtained from the rhizomes of *C. giganteus* grown in the North of Brazil had the sesquiterpenes cyperotundone and cyperene as the main compounds. Caryophyllene oxide, patchoulenone, trans-pinocarveol, α-cyperone, and the monoterpenes myrtenol, and β-pinene were minor constituents (Zoghbi et al., 2006b). To date, no data have been found on the biological activities of *C. giganteus*.

Cyperus iria L.

Residents of the municipality of Quissamã in the state of Rio de Janeiro reported that the whole plant of *C. iria* is used as a stimulant and diuretic, but data on the method of preparation was not mentioned (Boscolo and Valle, 2008).

In a recent study, Vera et al. (2022) reported that the ethanolic extract of *C. iria* roots showed *in vitro* anti-inflammatory activity by the egg albumin denaturation method. According to them, the concentration of 1000 µg/mL of the extract was sufficient to inhibit albumin denaturation by up to 63.07% and no toxic effects of the extract were detected in the toxicological evaluation using *Artemia salina*. model. According to Bezerra et al. (2022c), the chloroform phase of the hydroalcoholic extract of the underground parts of *C. iria* showed a significant bacteriostatic and fungistatic effect against *Staphylococcus aureus* and *Candida albicans*, respectively, with a minimum inhibitory concentration of only 31.2 µg/mL.

Cyperus odoratus L.

Popularly known as "capim-santo", *C. odoratus* has been used on the coast of Paraná in the form of infusion of roots to treat infections of the uterus, of the urinary tract, and myoma (Silva et al., 2020). According to Alif et al. (2018), the ethanolic extract of the whole plant showed significant analgesic activity, reducing 36.23% and 61.32% of writhing in mice at doses of 250 and 500 mg/kg, respectively. It also showed potent antioxidant activity by the DPPH method and anthelmintic activity against *Pheretima posthuma*.

No chemical study of *C. odoratus* has been conducted in Brazil. However, flavone (luteolin) and aurone (aureusidin) were identified in leaves and inflorescences of this species occurring in Australia (Harborne et al., 1982).

Cyperus rotundus L.

Cyperus rotundus is one of the best studied species of Cyperaceae. In the form of infusion, decoction, maceration, tincture, tea and "garrafada" (mixture of medicinal herbs kept in water or brandy in a bottle) of roots, tubers, seeds and stems, *C. rotundus* has been indicated for the treatment of wounds, general pain, memory problems, inflammation, diseases of the circulatory and urogenital system, and diseases associated with blood and hematopoietic organs (Fenner et al., 2006; Barros et al., 2007; Duarte et al., 2007; Monteles and Pinheiro, 2007; Borges and Bautista, 2010; Bieski et al., 2012; Staniski et al., 2014; Rego et al., 2016).

A wide range of biological activities of extracts, essential oils and fractions obtained from the leaves, rhizomes, roots, and tubers of *C. rotundus* is described in the literature (Peerzada et al., 2015; Dhar et al., 2017). The main activities include anti-inflammatory (Dang et al., 2011; Tsoyi et al., 2011; Zhou et al., 2013), anti-diarrheal (Daswani et al., 2011), antioxidant (Lydia and Sundarsanam, 2012), anticancer (Park et al., 2014; Lin et al., 2019; Simorangkir et al., 2019), antimicrobial (Kabbashi et al., 2015), antidiabetic (Singh et al., 2015), lactogenic (Badgujar and Bandivdekar, 2015), gastroprotective (Thomas et al., 2015), anti-hepatitis B (Xu et al., 2015), and anthelmintic (Kasala et al., 2016) activities.

In relation to phytochemical findings, several compounds, mainly sesquiterpenes, have been isolated from *C. rotundus*, mainly from the rhizomes. However, in representatives occurring in Brazil, studies were based on presence or absence of classes of compounds. On the other hand, in other parts of the world, the sesquiterpenes valencene and nootkatone (Jin et al., 2011), *α*-cyperone (Jung et al., 2013), 14-hydroxy-*α*-cyperone (Ahn et al., 2015), cyperene-3, 8-dione, 14-hydroxy cyperotundone, 14-acetoxy cyperotundone, 3*β*-hydroxycyperenoic acid and sugetriol-3, 9-diacetate (Xu et al., 2015), isocyperol (Seo et al., 2016), sugetriol triacetate (Mohamed-Ibrahim et al., 2018), 4*α*, 5*α*-Oxidoeudesm-11-en-3-one, cyper-11-ene-3,4-dione, cyperotundone, caryophyllene *α*-oxide, *α*-cyperone, and isocyperol (Park et al., 2019) have been identified from the rhizomes of the species. In addition to sesquiterpenes, iridoid glycosides such as rotunduside A, B and C (Zhou and Yin, 2012; Zhou and Zhang, 2013; Zhang et al., 2014), several stilbenes such as cyperotundol A, B, C, and D, methoxycyperotundol A, and cyperusphenol (Ito et al., 2012), phenolic compounds such as 1*α*-methoxy-3*β*-hydroxy-4*α*-(3′,4′-dihydroxyphenyl)-1, 2,3,4-tetrahydronaphthalin, 1*α*,3*β*-dihydroxy-4*α*-(3′,4′-dihydroxyphenyl)-1,2,3,4-tetrahydronaphthalin, salicylic acid, caffeic acid, protocatechuic acid, p-coumaric acid, pongamone A, and biochanin A (Zhou and Yin, 2012), pungenin, salidroside (Zhang et al., 2014), norterpenoid cyperalin A (Mohamed-Ibrahim et al., 2018), and chlorogenic acid (Rocha et al., 2020) have also been identified.

Kyllinga odorata Vahl [Syn. *Cyperus sesquiflorus* (Torr.) Mattf. & Kük.]

Kyllinga odorata is popularly known as “capim-cheiroso”, “cidreira”, “marinho”, “acapé”, “jarapé”, “coquerinho-do-banhado”, and “capim-cidreira” in some regions of Brazil. Folk uses have been described in the states of Mato Grosso and Rio Grande do Sul. According to ethnopharmacological research, the aerial parts of *K. odorata* are indicated for the treatment of diarrhea (Vendruscolo et al., 2005; Vendruscolo and Mentz, 2006) and are used as

carminative, antispasmodic, diaphoretic, and diuretic agent (Ricardo et al. 2017). In addition, the tea from its leaves, rhizomes and/or stems is indicated for the treatment of influenza and used as a tranquilizer (Souza et al., 2011; Pinto et al., 2017).

Chemical and pharmacological studies confirming the effectiveness of the ethnomedicinal use of *K. odorata* are few. According to Bezerra et al. (2019), the chloroform phase of the underground parts of this species showed antimicrobial activity against the pathogens *C. albicans*, *S. aureus*, and *Pseudomonas aeruginosa*. In contrast, the hydroalcoholic extracts obtained from the aerial and underground parts showed a weak antioxidant activity in the DPPH assay. Although no phytochemical study of this plant has been conducted in Brazil, the analysis of the essential oil of *K. odorata* collected in Mississippi indicated dihydrokaranone (53.1%) and aristolochene (11.3%) as major components (Tucker et al., 2006).

Rhynchospora nervosa (Vahl) Boeckeler

Popularly known as “capim-estrela”, *R. nervosa* has been widely used in some regions of Brazil. According to some authors, the whole plant is used in the form of teas, baths or syrups to treat inflammation, fever, flu, swelling, venereal diseases, and nasal congestion (Moreira et al., 2002; Costa et al., 2006; Rodrigues et al., 2006; Gomez et al., 2016; Santana et al., 2016; Lisboa et al., 2017). Ramírez and Blair (2017) reported the empirical use of *R. nervosa* by the community of Villa Cachoeira in, Ilhéus, Bahia, as a plant with anti-inflammatory potential.

According to Bezerra et al. (2022a), the lyophilized hydroalcoholic extract of *R. nervosa* showed significant anti-inflammatory activity in mice, reducing paw edema by up to 96.37%. Furthermore, at the highest dose (400 mg/kg), a reduction of 86.53% in abdominal constrictions was observed, indicating that this plant has analgesic and antinociceptive properties. The authors reported that the high content of phenols and flavonoids in *R. nervosa* may be responsible for the pharmacological activities found.

Scleria hirtella Sw.

Scleria hirtella is known as “capim-santo” because its scent resembles lemongrass and other aromatic herbs. According to Maia et al. (2005), the major constituents of the oil from whole plants of *S. hirtella* were nonanal (42.0%), geranial (25.3%), and neral (15.3%). Ethnopharmacologically, leaf and stem decoction (bath and ablutions) is used by indigenous people (Tiriyó ethnic group in the Brazilian Amazon) as remedy against epileptic seizures in

children (Cavalcante and Frikel, 1973). To date, no pharmacological data has been reported for this species.

3.2. Cyperaceae species used in folk medicine in Brazil without pharmacological and/or chemical studies

Bulbostylis capillaris (L.) C.B.Clarke

Bulbostylis capillaris is popularly known in Brazil as “barba-de-bode” due to the morphological aspects of the plant. According to Vila Verde et al. (2003), the population of Mossâmedes in the state of Goiás uses the whole plant for the treatment of cold and high fever. Borba and Macedo (2006) reported that the leaves and roots of this species are used in the form of decoction to treat colds in a community in the Santa Cruz neighborhood in Chapada dos Guimarães, Mato Grosso. In the Pantanal region, also in Mato Grosso, *B. capillaris* is used as infusion for diuretic purposes and is indicated for problems of the stomach, kidneys, and worm infections (Bieski et al., 2012).

Bulbostylis junciformis (Kunth) C.B.Clarke

Cavalcante and Frikel (1973) reported that leaf and stem decoction (bath and ablutions) of *B. junciformis* is used to treat fever by Tiriyó indigenous communities in the Brazilian Amazon. No phytochemical and pharmacological studies have been conducted on this species.

Bulbostylis lanata (Kunth) Lindm.

The whole plant of *B. lanata* is used by the Tiriyó indigenous people abovementioned as herbal medicine to treat fever and headache. The medicine is made from the decoction of the whole plant (bath). Similarly to the previous species, no phytochemical and pharmacological studies have been performed with this species (Cavalcante and Frikel, 1973).

Carex sororia Kunth

The aerial parts of *C. sororia* were reported by residents of the Ponta Grossa neighborhood, Porto Alegre, Rio Grande do Sul, as being efficient in the treatment of diarrhea, but the method of preparation was not informed (Vendruscolo et al., 2005; Vendruscolo and Mentz, 2006).

Cyperus eragrostis Lam.

According to Vendruscolo and Mentz (2006), residents of the Ponta Grossa neighborhood indicated the aerial parts of *C. eragrostis* for the treatment of hemorrhoids. The method of preparation was not informed.

Cyperus sesquiflorus (Torr.) Mattf. & Kük.

Based on a review by Mentz et al. (1997) of Manuel Cypriano D'Ávila's work on the medicinal flora of Rio Grande Sul (1910), the infusion of leaves and rhizomes of *C. sesquiflorus* could serve as a substitute for *Melissa officinalis* L. (Lamiaceae) in the treatment of gastritis.

Cyperus uncinulatus Schrad. ex Nees

According to a survey of medicinal plants used by rural communities in Oeiras, in the semi-arid region of Piauí, Oliveira et al. (2010) reported that the roots of *C. uncinulatus* were used in cases of irregular menstruation.

Eleocharis montana (Kunth) Roem. & Schult.

Zeni and Bosio (2011) reported in their work that a rural community in Nova Russia, Santa Catarina, uses *E. montana* leaves to regulate blood pressure. The method of preparation and the form of use were not mentioned.

Fimbristylis vahlii (Lam.) Link

Popularly known as "barba-de-bode" in the rural community of Laginhas, municipality of Caicó, Rio Grande do Norte, Roque et al. (2010) reported that infusions of the root of this species can be prepared to be used in the treatment of kidney disease.

Hypolytrum pungens (Vahl) Kunth [Syn. *Hypolytrum pulchrum* (Rudge) H.Pfeiff.]

A survey of medicinal plants conducted by Motta et al. (2016) in a Child Education Center in Goiânia, state of Goiás, found that the leaves of *H. pungens* are used in the preparation of teas and indicated for the relief of headaches and as a tranquilizer.

Rhynchospora barbata (Vahl) Kunth

Decoction (bath) and smoke of leaves and stems of *R. barbata* are used for the treatment of fever by Tiriyó indigenous communities in the Brazilian Amazon (Cavalcante and Frikel, 1973). No phytochemical and pharmacological studies have been reported on this species.

Rhynchospora pubera (Vahl) Boeckeler

The medicinal use of *R. pubera* was reported in Abaetetuba, a quilombola community in the Eastern Amazon, in the state of Pará. According to Pereira and Coelho-Ferreira (2017), the leaves of this species are used in the preparation of teas and indicated for the treatment of urinary infection.

Schoenoplectus californicus (C.A.Mey.) Soják

The fresh roots of "junco", as *S. californicus* is popularly known, are empirically indicated by the community of Bom Princípio do Piauí, in the state of Piauí, for cases of snake bite (Castro et al., 2016).

Scleria distans Poir.

A study by Romanus et al. (2018) on migrants from rural areas of Northeastern Brazil to a metropolitan region of Southeastern Brazil pointed out the use of the whole plant of *S. distans*, among several other species used for medicinal purposes, in the preparation of infusions to relieve pain.

Scleria gaertneri Raddi

Ribeiro et al. (2017) reported in their study that riverside dwellers in the northern region of Araguaia, state of Mato Grosso, used the roots or the whole plants of *S. gaertneri* in the form of decoction and maceration for the treatment of urinary infection, throat infection, and throat inflammation.

3.3. Cyperaceae species used in folk medicine in Brazil and other countries

Of the 27 species of Cyperaceae used for medicinal purposes in Brazil, only eight have reports of uses in other countries such as Algeria, Bangladesh, Benin, China, Colombia, Philippines, Gabon, Ghana, India, Iran, Iraq, Morocco, Nepal, Papua New Guinea, Pakistan, Peru, Turkey, and Yemen (Table 4). The species are mainly indicated for the treatment of scabies, rheumatism, urolithiasis, malaria, tuberculosis, helminthiasis, fever, menstrual problems, measles, chickenpox, diarrhea, dysentery, leprosy, liver disease, diuretic problems, worms, dermatitis, pain, and hypersplenism, and as a galactagogue (Dangol and Gurung, 1991; Adhikari et al., 2010; Mati and Boer, 2011; Yetein et al., 2013; Sivasankari et al., 2014; Ong and Kim, 2014; Nguta et al., 2015; Ndob et al., 2016; Ganesan and Xu, 2017; Umair et al., 2017). *Cyperus rotundus* and *C. esculentus* were the species with the greatest number of studies and indications of use. Comparatively, *C. rotundus* is the most widespread and well-studied species in Brazil, followed by *C. articulatus*. *Cyperus esculentus* comes in the third place in number of studies.

4. Conclusion and recommendations

In this review, we compiled ethnobotanical data on Cyperaceae species used in Brazilian traditional medicine. Twenty-seven species of Cyperaceae with ethnopharmacological indications in different regions of Brazil were presented. In the Brazilian traditional medicine, Cyperaceae species are mainly used for the treatment of inflammation. Other indications include the treatment of fever, diarrhea and flu. The roots or the whole plant are the most used parts, prepared in the form of decoction or infusion. Among the twenty-seven species recorded, only twelve have had their chemical constituents and/or biological activities investigated. Sesquiterpenes were the predominant class of compounds identified. *Cyperus rotundus* stood out as the species with the highest number of medicinal indications and pharmacological and phytochemical studies. Although the other fifteen species of Cyperaceae are reported as medicinal in Brazil, scientific research to confirm their effectiveness and safety is still needed. It is recommended that the pharmacological, toxicological, and chemical properties of these species be evaluated to validate or refute their medicinal indications in Brazil.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

Acknowledgments

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES) - Finance Code 001. The first author is grateful to the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq - Brazil) for a PhD scholarship. The second author is grateful to the CNPq for the research grant (310811/2019-8).

References

Achoribo, E.S., Ong, M.T., 2019. Antioxidant screening and cytotoxicity effect of tigernut (*Cyperus esculentus*) extracts on some selected cancer-origin cell lines. EuroMediterranean Biomed. J. 14, 001-006. https://doi.org/10.3269/1970-5492.2019.14.01

Adhikari, B.S., Babu, M.M., Saklani, P. L., Rawat, G.S., 2010. Medicinal plants diversity and their conservation status in Wildlife Institute of India (WII) campus, Dehradun. Ethnobot. Leafl. 14, 46-83.

Ahmad, M., Khan, M.P.Z., Mukhtar, A., Zafar, M., Sultana, S., Jahan, S., 2016. Ethnopharmacological survey on medicinal plants used in herbal drinks among the traditional communities of Pakistan. J. Ethnopharmacol. 184, 154-186. https://doi.org/10.1016/j.jep.2016.02.039

Ahmed, N., Mahmood, A., Mahmood, A., Sadeghi, Z., Farman, M., 2015. Ethnopharmacological importance of medicinal flora from the district of Vehari, Punjab province, Pakistan. J. Ethnopharmacol. 168, 66-78. https://doi.org/10.1016/j.jep.2015.02.048

Ahn, J.H., Lee, T.W., Kim, K.H., Byun, H., Ryu, B., Lee, K.T., et al., 2015. 6-Acetoxy cyperene, a patchoulane-type sesquiterpene isolated from *Cyperus rotundus* rhizomes induces caspase-dependent apoptosis in human ovarian cancer cells. Phytother. Res. 29, 1330-1338. https://doi.org/10.1002/ptr.5385

Al-Fatimi, M., 2019. Ethnobotanical survey of medicinal plants in central Abyan governorate, Yemen. J. Ethnopharmacol. 241, 111973. https://doi.org/10.1016/j.jep.2019.111973

Alif, A.H., Hossain, A., Hossain, M.A., Madhu, T.M., Sumi, S.A., Rahman, M.M., 2018. Phytochemical and pharmacological evaluation of *Cyperus odoratus* extract. Bangladesh Pharm. J. 21, 150-159. https://doi.org/10.3329/bpj.v21i2.37927

Alves, M., Araújo, A.C., Prata, A.P., Vitta, F., Hefler, S., Trevisan, R., Giol, A.S.B., Martins, S., Thomas, W., 2009. Diversity of Cyperaceae in Brazil. Rodriguésia 60, 771-782. https://doi.org/10.1590/2175-7860200960405

Avancini, C.A.M., Wiest, J.M., 2008. Etnomedicina veterinária, etnonosotaxia e etnoterapêutica de doenças de pele como referência para seleção e avaliação preliminar da atividade antibacteriana de plantas nativas no sul do Brasil. Rev. Bras. Plantas Med. 10, 21-28.

Azzaz, N.A., El-Khateeb, A.Y., Farag, A.A., 2014. Chemical composition and biological activity of the essential oil of *Cyperus articulatus*. Int. J. Acad. Res. 6, 265-269. https://doi.org/10.7813/2075-4124.2014/6-5/A.37

Badgujar, S.B., Bandivdekar, A.H., 2015. Evaluation of a lactogenic activity of an aqueous extract of *Cyperus rotundus* Linn. J. Ethnopharmacol. 163, 39-42. https://doi.org/10.1016/j.jep.2015.01.019

Barros, F.M., Pereira, K.N., Zanetti, G.D., Heinzmann, B.M., 2007. Plantas de uso medicinal no município de São Luiz Gonzaga, RS, Brasil. Lat. Am. J. Pharm. 26, 652-662.

Benarba, B., Belabid, L., Righi, K., amine Bekkar, A., Elouissi, M., Khaldi, A., Hamimed, A., 2015. Ethnobotanical study of medicinal plants used by traditional healers in Mascara (North West of Algeria). J. Ethnopharmacol. 175, 626-637. https://doi.org/10.1016/j.jep.2015.09.030

Bersan, S.M., Galvão, L.C., Goes, V.F., Sartoratto, A., Figueira, G.M., Rehder, V.L., et al., 2014. Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms. BMC Complement. Altern. Med. 14, 451. https://doi.org/10.1186/1472-6882-14-451

Bezerra, J.J.L., Nascimento, T.G., Kamiya, R.U., Prata, A.P.N., Medeiros, P.M., Silva, S.A.S., Mendonca, C.N., 2019. Phytochemical screening, chromatographic profile and evaluation of antimicrobial and antioxidant activities of three species of the Cyperaceae Juss. Family. J. Med. Plants. Res. 13, 312-320. https://doi.org/10.5897/JMPR2019.6796

Bezerra, J.J.L., Oliveira, J.R.S., Lima, V.L.M., Silva, M.V., Araújo, D.R.C., Oliveira, A.F.M., 2022a. Evaluation of the anti-inflammatory, antipyretic and antinociceptive activities of the hydroalcoholic extract of *Rhynchospora nervosa* (Vahl) Boeckeler (Cyperaceae). J. Ethnopharmacol. 284. http://doi:10.1016/j.jep.2021.114811

Bezerra, J.J.L., Pinheiro, A.A.V., Oliveira, A.F.M., 2022b. Cyperaceae species used for the treatment of inflammation: A review of ethnomedicinal, pharmacological, toxicological, and phytochemical evidence. S. Afr. J. Bot. 150, 1138-1158. https://doi.org/10.1016/j.sajb.2022.09.020

Bezerra, J.J.L., Nascimento, T.G., Kamiya, R.U., Prata, A.P.N., Medeiros, P.M., Silva, S.A.S., Melo, N.E., 2022c. Phytochemical profile, evaluation of antimicrobial and antioxidant activity *in vitro* of the hydroalcoholic extract of two species of the genus *Cyperus* (Cyperaceae). Braz. J. Pharm. Sci. 58, e20205. https://doi.org/10.1590/s2175-97902022e20205

Bieski, I.G.C., Santos, F.R., Oliveira, R.M., Espinosa, M.M., Macedo, M., Albuquerque, U.P., Martins, D.T.O., 2012. Ethnopharmacology of medicinal plants of the pantanal region (Mato Grosso, Brazil). Evid. Based Complement. Alternat. Med. 2012, 1-36. https://doi.org/10.1155/2012/272749

Bitu, V.C.N., Bitu, V.C.N., Matias, E.F.F., Lima, W.P., Portelo, A.C., Coutinho, H.D.M., Menezes, I.R.A., 2015. Ethnopharmacological study of plants sold for therapeutic purposes in public markets in Northeast Brazil. J. Ethnopharmacol. 172, 265-272. https://doi.org/10.1016/j.jep.2015.06.022

Borba, A.M., Macedo, M., 2006. Plantas medicinais usadas para a saúde bucal pela comunidade do bairro Santa Cruz, Chapada dos Guimarães, MT, Brasil. Acta Bot. Bras. 20, 771-782. https://doi.org/10.1590/S0102-33062006000400003

Borges, K.N., Bautista, H., 2010. Etnobotânica de plantas medicinais na comunidade de Cordoaria, litoral norte do estado da Bahia, Brasil. Plurais – Rev. Multidis. 1, 153-174.

Boscolo, O.H., Valle, L.S., 2008. Plantas de uso medicinal em Quissamã, Rio de Janeiro, Brasil. Iheringia Ser. Bot. 63, 263-278.

Brandão, M.G., Pignal, M., Romaniuc, S., Grael, C.F., Fagg, C.W., 2012. Useful Brazilian plants listed in the field books of the French naturalist Auguste de Saint-Hilaire (1779–1853). J. Ethnopharmacol. 143, 488-500. https://doi.org/10.1016/j.jep.2012.06.052

Burlakoti, C., Kunwar, R.M., 2008. Folk herbal medicines of Mahakali watershed Area, Nepal. Med. Plants Nepal: An Anthology of Contemporary Res. 187-193.

Bussmann, R.W., Glenn, A., 2010. Cooling the heat-Traditional remedies for malaria and fever in Northern Peru. Ethnobot. Res. Appl. 8, 125-134.

Bussmann, R.W., Ashley, G., Sharon, D., Chait, G., Diaz, D., Pourmand, K., et al., 2011. Proving that traditional knowledge works: the antibacterial activity of Northern Peruvian medicinal plants. Ethnobot. Res. Appl. 9, 067-096.

Carbonó-Delahoz, E., Dib-Diazgranados, J.C., 2013. Plantas medicinales usadas por los Cogui nn el Río Palomino, Sierra Nevada de Santa Marta (Colombia). Caldasia 35, 333-350.

Castro, K.N.C., Wolschick, D., Leite, R.R.S., Andrade, I.M., Magalhães, J.A., Mayo, S.J., 2016. Ethnobotanical and ethnoveterinary study of medicinal plants used in the municipality of Bom Princípio do Piauí, Piauí, Brazil. J. Med. Plants Res. 10, 318-330. https://doi.org/10.5897/JMPR2015.6038

Cavalcante, P.B., Frikel, P., 1973. A farmacopéia Tiriyó: estudo etnobotânico. Museu Paraense Emílio Goeldi: Belém, p. 157.

Chaulya, N.C., Haldar, P.K., Mukherjee, A., 2012. Anti-inflammatory and analgesic activity of methanol extracts of *Cyperus tegetum* Roxb. rhizome. J. PharmaSciTech 1, 27-29.

Costa, L.C.B., Rocha, E.A., Silva, L.A.M., Jardim, J.G., Silva, D.C., Gaião, L.O., Moreira, R.D.C.T., 2006. Levantamento preliminar das espécies vegetais com potencial econômico no Parque Municipal da Boa Esperança, Ilhéus, Bahia, Brasil. Acta Farm. Bonaerense 25, 184-191.

Costa, I.V., Farisco, F., Gandolfi, P.E., Morais, E.R., 2021. Ethnopharmacological study of medicinal plants used by population in district of Travessão De Minas, Minas Gerais. Int. J. Herb. Med., 9, 127-139.

Dang, G.K., Parekar, R.R., Kamat, S.K., Scindia, A.M., Rege, N.N., 2011. Antiinflammatory activity of *Phyllanthus emblica*, *Plumbago zeylanica* and *Cyperus rotundus* in acute models of inflammation. Phytother. Res. 25, 904-908. https://doi.org/10.1002/ptr.3345

Dangol, D.R., Gurung, S.B., 1991. Ethnobotany of the Tharu tribe of Chitwan district, Nepal. Int. J. Pharmacogn. 29, 203-209. https://doi.org/10.3109/13880209109082879

Daswani, P.G., Brijesh, S., Tetali, P., Birdi, T.J., 2011. Studies on the activity of *Cyperus rotundus* Linn. tubers against infectious diarrhea. Indian J. Pharmacol. 43, 340-344. https://doi.org/10.4103/0253-7613.81502

Datta, S., Seal, T., Sinha, B.K., Bhattacharjee, S., 2018. RP-HPLC based evidences of rich sources of phenolics and water-soluble vitamins in an annual sedge *Cyperus compressus*. J. Phytopharmacol. 7, 305-311.

Dhar, P., Dhar, D.G., Rawat, A.K.S., Srivastava, S., 2017. Medicinal chemistry and biological potential of *Cyperus rotundus* Linn.: An overview to discover elite chemotype (s) for industrial use. Ind. Crop. Prod. 108, 232-247. https://doi.org/10.1016/j.indcrop.2017.05.053

Dong, S.H., Zhang, J.F., Tang, Y.M., Li, J., Xiang, Y.R., Liang, Q.L., 2016. Chemical constituents from the tubers of *Scirpus yagara* and their anti-inflammatory activities. J. Asian Nat. Prod. Res. 18, 791-797. https://doi.org/10.1080/10286020.2016.1158166

Duarte, M.C.T., Leme, E.E., Delarmelina, C., Soares, A.A., Figueira, G.M., Sartoratto, A., 2007. Activity of essential oils from Brazilian medicinal plants on *Escherichia coli*. J. Ethnopharmacol. 111, 197-201. https://doi.org/10.1016/j.jep.2006.11.034

Fakir, H., Korkmaz, M., Güller, B., 2009. Medicinal plant diversity of western Mediterrenean region in Turkey. J. Appl. Biol. Sci. 3, 33-43.

Fenner, R., Betti, A.H., Mentz, L.A., Rates, S.M.K., 2006. Plantas utilizadas na medicina popular brasileira com potencial atividade antifúngica. Rev. Bras. Cienc. Farm. 42, 369-394. https://doi.org/10.1590/S1516-93322006000300007

Flora do Brasil 2020 em construção. Jardim Botânico do Rio de Janeiro. http://floradobrasil.jbrj.gov.br/. 23 dez. 2020.

Frausin, G., Hidalgo, A.F., Lima, R.B.S., Kinupp, V.F., Ming, L.C., Pohlit, A.M., Milliken, W., 2015. An ethnobotanical study of anti-malarial plants among indigenous people on the upper Negro River in the Brazilian Amazon. J. Ethnopharmacol. 174, 238-252. https://doi.org/10.1016/j.jep.2015.07.033

Ganesan, K., Xu, B., 2017. Ethnobotanical studies on folkloric medicinal plants in Nainamalai, Namakkal District, Tamil Nadu, India. Trends Phytochem. Res. 1, 153-168.

Gomez, M., Rocha, E.A., Gomberg, E., 2016. Análise das publicações etnobotânicas sobre plantas medicinais da Mata Atlântica na Região Sul do Estado da Bahia, Brasil. Rev. Fitos 10, 115-140. https://doi.org/10.5935/2446-4775.20160010

Griffiths, M., Ralimanana, H., Rakotonasolo, F., Larridon, I., 2022. A monograph of the African and Madagascan species of *Cyperus* sect. Incurvi (Cyperaceae). Kew Bulletin, 1-32. https://doi.org/10.1007/s12225-022-10058-9

Güneş, S., Savran, A., Paksoy, M.Y., Koşar, M., Çakılcıoğlu, U., 2017. Ethnopharmacological survey of medicinal plants in Karaisalı and its surrounding (Adana-Turkey). J. Herb. Med. 8, 68-75. https://doi.org/10.1016/j.hermed.2017.04.002

Harborne, J.B., Williams, C.A., Wilson, K.L., 1982. Flavonoids in leaves and inflorescences of Australian *Cyperus* species. Phytochemistry 21, 2491-2507. https://doi.org/10.1016/0031-9422(82)85246-1

Heinrich, M., Lardos, A., Leonti, M., Weckerle, C., Willcox, M., 2018. Best practice in research: consensus statement on ethnopharmacological field studies – ConSEFS. J. Ethnopharmacol. 211, 329-339. https://doi.org/10.1016/j.jep.2017.08.015

Idm'hand, E., Msanda, F., Cherifi, K., 2020. Ethnobotanical study and biodiversity of medicinal plants used in the Tarfaya Province, Morocco. Acta Ecol. Sin. 40, 134-144. https://doi.org/10.1016/j.chnaes.2020.01.002

Ito, T., Endo, H., Shinohara, H., Oyama, M., Akao, Y., Iinuma, M., 2012. Occurrence of stilbene oligomers in *Cyperus* rhizomes. Fitoterapia 83, 1420-1429. https://doi.org/10.1016/j.fitote.2012.08.005

Jamshidi-Kia, F., Lorigooini, Z., Amini-Khoei, H., 2018. Medicinal plants: Past history and future perspective. J. Herbmed. Pharmacol. 7, 1-7. https://doi.org/10.15171/jhp.2018.01

Jin, J.H., Lee, D.U., Kim, Y.S., Kim, H.P., 2011. Anti-allergic activity of sesquiterpenes from the rhizomes of *Cyperus rotundus*. Arch. Pharm. Res. 34, 223-228. https://doi.org/10.1007/s12272-011-0207-z

Jing, S., Li, Q., Zheng, L., Yue, L., Fan, S., Tao, G., 2016. Dynamic high pressure microfluidization-assisted extraction and bioactivities of *Cyperus esculentus* (*C. esculentus* L.) leaves flavonoids. Food Chem. 192, 319-327. https://doi.org/10.1016/j.foodchem.2015.06.097

Jung, S.H., Kim, S.J., Jun, B.G., Lee, K.T., Hong, S.P., Oh, M.S., Jang, D.S., Choi, J.H., 2013. *α*-Cyperone, isolated from the rhizomes of *Cyperus rotundus*, inhibits LPS-induced COX-2 expression and PGE2 production through the negative regulation of NFκB signalling in

RAW 264.7 cells. J. Ethnopharmacol. 147, 208-214. https://doi.org/10.1016/j.jep.2013.02.034

Kabbashi, A.S., Mohammed, S.E.A., Almagboul, A.Z., Ahmed, I.F., 2015. Antimicrobial activity and cytotoxicity of ethanolic extract of *Cyperus rotundus* L. Am. J. Pharm. Pharm. Sci. 2, 1-13.

Kakarla, L., Mathi, P., Allu, P.R., Rama, C., Botlagunta, M., 2014. Identification of human cyclooxegenase-2 inhibitors from *Cyperus scariosus* (R. Br) rhizomes. Bioinformation 10, 637-646. https://doi.org/10.6026/97320630010637

Kasala, S., Ramanjaneyulu, K., Himabindhu, J., Alluri, R., Babu, R.R., 2016. Preliminary phytochemical screening and *in vitro* anthelmintic activity of *Cyperus rotundus* (L). J. Pharmacogn. Phytochem. 5, 407-409.

Kffuri, C.W., Lopes, M.A., Ming, L.C., Odonne, G., Kinupp, V.F., 2016. Antimalarial plants used by indigenous people of the Upper Rio Negro in Amazonas, Brazil. J. Ethnopharmacol. 178, 188-198. https://doi.org/10.1016/j.jep.2015.11.048

Kim, K.H., Bae, E.Y., Lim, H.G., Kim, M.H., Oh, T.S., Lee, S.W., 2020. *Eleocharis kuroguwai* Ohwi ameliorates LPS-mediated inflammation by suppressing MAPKs signaling. J. Life Sci. 30, 476-482.

Komai, K., Tang, C.S., 1989. Chemical constituents and inhibitory activities of essential oils from *Cyperus brevifolius* and *C. kyllingia*. J. Chem. Ecol. 15, 2171-2176. https://doi.org/10.1007/BF01014107

Larridon, I., Zuntini, A.R., Léveillé-Bourret, É., Barrett, R.L., Starr, J.R., Muasya, A.M., et al. 2021. A new classification of Cyperaceae (Poales) supported by phylogenomic data. J. Syst. Evol. 59, 852-895. https://doi.org/10.1111/jse.12757

Leonti, M., Stafford, G.I., Dal Cero, M., Cabras, S., Castellanos, M.E., Casu, L., Weckerle, C.S., 2017. Reverse ethnopharmacology and drug discovery. J. Ethnopharmacol. 198, 417-431. https://doi.org/10.1016/j.jep.2016.12.044

Li, D.L., Xing, F.W., 2016. Ethnobotanical study on medicinal plants used by local Hoklos people on Hainan Island, China. J. Ethnopharmacol. 194, 358-368. https://doi.org/10.1016/j.jep.2016.07.050

Lin, C.H., Peng, S.F., Chueh, F.S., Cheng, Z.Y., Kuo, C.L., Chung, J.G., 2019. The ethanol crude extraction of *Cyperus rotundus* regulates apoptosis-associated gene expression in hela human cervical carcinoma cells *in vitro*. Anticancer Res. 39, 3697-3709. https://doi.org/10.21873/anticanres.13518

Lisboa, M.S., Pinto, A.S., Barreto, P.A., Ramos, Y.J., Silva, M.Q., Caputo, M.C., Almeida, M.Z.D., 2017. Estudo Etnobotânico em Comunidade Quilombola Salamina/Putumujú em Maragogipe, Bahia. Rev. Fitos 11, 48-61. https://doi.org/10.5935/2446-4775.20170006

Lobo, R.A.A.M., Lobo, A.C.B.N.M., Oliveira, A.F.M., Andrade, L.H.C., 2020. Ethnomedicinal plants for veterinary use in gypsy communities of the Northeast of Brazil. Bol. Latinoam. Caribe Plant. Med. Aromat. 19, 179-187.

Lydia, J., Sundarsanam, D., 2012. Phytoconstituents of *Cyperus rotundus* L. that attribute to its medicinal value and antioxidant property. Int. J. Pharm. Sci. Res. 3, 3304-3308. http://dx.doi.org/10.13040/IJPSR.0975-8232.3(9).3304-08

Maia, J.G.S., Silva, M.H.L., Andrade, E.H.A., Rosa, N.A., 2005. Essential oil composition of *Scleria hirtella* swartz (Cyperaceae). Flavour Frag. J. 20, 472-473. https://doi.org/10.1002/ffj.1593

Majumder, P., 2014. Investigation of phytochemicals and anti-diarrhoeal potential of an ignored grass - *Cyperus esculentus* L. root. Indian J. Res. Pharm. Biotech. 2, 1158-1160.

Mati, E., Boer, H., 2011. Ethnobotany and trade of medicinal plants in the Qaysari Market, Kurdish Autonomous Region, Iraq. J. Ethnopharmacol. 133, 490-510. https://doi.org/10.1016/j.jep.2010.10.023

Mentz, L.A., Lutzemberger, L.C., Schenkel, E.P., 1997. Da flora medicinal do Rio Grande do Sul: notas sobre a obra de D'Avila (1910). Cad. Farm. 13, 25-47.

Mesquita, U.O., Tavares-Martins, A.C.C., 2018. Etnobotánica de plantas medicinales en la comunidad de Caruarú, Isla del Mosqueiro, Belém-PA, Brasil. Bol. Latinoam. Caribe Plant. Med. Aromat. 17, 130-159.

Messias, M.C.T.B., Menegatto, M.F., Prado, A.C.C., Santos, B.R.D., Guimarães, M.F.M., 2015. Uso popular de plantas medicinais e perfil socioeconômico dos usuários: um estudo em área urbana em Ouro Preto, MG, Brasil. Rev. Bras. Plantas Med. 17, 76-104. https://doi.org/10.1590/1983-084X/12_139

Metuge, J.A., Nyongbela, K.D., Mbah, J.A., Samje, M., Fotso, G., Babiaka, S.B., Cho-Ngwa, F., 2014. Anti-Onchocerca activity and phytochemical analysis of an essential oil from *Cyperus articulatus* L. BMC Complement. Altern. Med. 14, 223. https://doi.org/10.1186/1472-6882-14-223

Milliken, W., Albert, B., 1996. The use of medicinal plants by the Yanomami Indians of Brazil. Econ. Bot. 50, 10-25. https://doi.org/10.1007/BF02862108

Mohamed-Ibrahim, S.R.M., Mohamed, G.A., Khayat, M.T.A., Zayed, M.F., El-Kholy, A.A.E.S., 2018. Anti-inflammatory terpenoids from *Cyperus rotundus* rhizomes. Pak. J. Pharm. Sci. 31, 1449-1456.

Monteles, R., Pinheiro, C.U.B., 2007. Plantas medicinais em um quilombo maranhense: uma perspectiva etnobotânica. Rev. Biol. Cienc. Terra. 7, 1-11.

Moon, M.K., Ahn, J., Lee, H., Ha, T.Y., 2012. Anti-obesity and hypolipidemic effects of chufa (*Cyperus esculentus* L.) in mice fed a high-fat diet. Food Sci. Biotechnol. 21, 317-322. https://doi.org/10.1007/s10068-012-0042-0

Moreira, R.D.C.T., Costa, L.C.D.B., Costa, R.C.S., Rocha, E.A., 2002. Abordagem etnobotânica acerca do uso de plantas medicinais na Vila Cachoeira, Ilhéus, Bahia, Brasil. Acta Farm Bonaerense 21, 205-211.

Motta, A.O., Lima, D.C.S., Vale, C.R., 2016. Levantamento do uso de plantas medicinais em um Centro de Educação Infantil em Goiânia-GO. Rev. Univ. Vale Rio Verde 14, 629-646. http://dx.doi.org/10.5892/ruvrd.v14i1.2613

Ndob, I.B., Mengome, L.E., Bourobou, H.P.B., Banfora, Y.L., Bivigou, F., 2016. Ethnobotanical survey of medicinal plants used as anthelmintic remedies in Gabon. J. Ethnopharmacol. 191, 360-371. https://doi.org/10.1016/j.jep.2016.06.026

Nguta, J.M., Appiah-Opong, R., Nyarko, A.K., Yeboah-Manu, D., Addo, P.G., 2015. Medicinal plants used to treat TB in Ghana. Int. J. Mycobacteriol. 4, 116-123. https://doi.org/10.1016/j.ijmyco.2015.02.003

Nogueira, M.L., Lima, E.J., Adrião, A.A., Fontes, S.S., Silva, V.R., Santos, L.D.S., et al., 2020. *Cyperus articulatus* L. (Cyperaceae) rhizome essential oil causes cell cycle arrest in the G2/M phase and cell death in HepG2 cells and inhibits the development of tumors in a xenograft model. Molecules 25, 2687. https://doi.org/10.3390/molecules25112687

Oladosu, I.A., Usman, L.A., Olawore, N.O., Atata, R.F., 2011. Antibacterial activity of rhizomes essential oils of two types of *Cyperus articulatus* growing in Nigeria. Adv. Biol. Res. 5, 179-183.

Oliveira, F.C.S., Barros, R.F.M., Moita Neto, J.M., 2010. Plantas medicinais utilizadas em comunidades rurais de Oeiras, semiárido piauiense. Rev. Bras. Plantas Med. 12, 282-301. https://doi.org/10.1590/S1516-05722010000300006

Oloyede, G.K., Abimbade, S.F., Nwabueze, C.C., 2014. Antioxidant and toxicity screenings of extracts obtained from *Cyperus esculentus*. Academ. Arena 6, 77-83.

Ong, H.G., Kim, Y.D., 2014. Quantitative ethnobotanical study of the medicinal plants used by the Ati Negrito indigenous group in Guimaras island, Philippines. J. Ethnopharmacol. 157, 228-242. https://doi.org/10.1016/j.jep.2014.09.015

Onyenibe, N.S., Udogadi, N.S., 2019. Ameliorative potentials of *Cyperus esculentus* oil on type 2 diabetes induced by high fat diet and low dose streptozotocin in male Wistar rats. Int. J. Diabetes Res. 2, 33-39. https://doi.org/10.17554/j.issn.2414-2409.2019.02.16

Owoyele, B.V., Abioye, A.I.R., Oyewole, A.L., Ameen, M.O., Owemidu, I.O., Adewusi, M.O., 2015. Effects of the ethanolic extract of *Bulbostylis coleotricha* (Hochst. Exa. Rich.) on inflammation in adult Wistar rats. Niger. J. Nat. Prod. Med. 19, 101-105. http://dx.doi.org/10.4314/njnpm.v19i1.11

Pagani, E., Santos, J.F.L., Rodrigues, E., 2017. Culture-Bound Syndromes of a Brazilian Amazon Riverine population: Tentative correspondence between traditional and conventional medicine terms and possible ethnopharmacological implications. J. Ethnopharmacol. 203, 80-89. https://doi.org/10.1016/j.jep.2017.03.024

Palheta, I.C., Tavares-Martins, A.C.C., Lucas, F.C.A., Jardim, M.A.G., 2017. Ethnobotanical study of medicinal plants in urban home gardens in the city of Abaetetuba, Pará state, Brazil. Bol. Latinoam. Caribe Plant. Med. Aromat. 16, 206-262.

Park, S.E., Shin, W.T., Park, C., Hong, S.H., Kim, G.Y., Kim, S.O., et al., 2014. Induction of apoptosis in MDA-MB-231 human breast carcinoma cells with an ethanol extract of *Cyperus rotundus* L. by activating caspases. Oncol. Rep. 32, 2461-2470. https://doi.org/10.3892/or.2014.3507

Park, Y.J., Zheng, H., Kwak, J.H., Chung, K.H., 2019. Sesquiterpenes from *Cyperus rotundus* and 4*α*, 5*α*-oxidoeudesm-11-en-3-one as a potential selective estrogen receptor modulator. Biomed. Pharmacother. 109, 1313-1318. https://doi.org/10.1016/j.biopha.2018.10.186

Partha, P., 2014. Ethnobotany of the Laleng (Patra) Community in Bangladesh. J. Pharmacogn. Phytochem. 2, 173-184.

Paulino, R.C., Henriques, G.P.S.A., Coelho, M.F.B., Maia, S.S.S.S., 2011. Conhecimento sobre Plantas medicinais entre alunos da Universidade Federal do Semi-árido, Mossoró, RN. Rev. Verde Agroecol. Des. Sust. 6, 78-90.

Peerzada, A.M., Ali, H.H., Naeem, M., Latif, M., Bukhari, A.H., Tanveer, A., 2015. *Cyperus rotundus* L.: traditional uses, phytochemistry, and pharmacological activities. J. Ethnopharmacol. 174, 540-560. https://doi.org/10.1016/j.jep.2015.08.012

Pereira, M.G.S., Coelho-Ferreira, M., 2017. Uso e diversidade de plantas medicinais em uma comunidade quilombola na Amazônia Oriental, Abaetetuba, Pará. Biota Amazon. 7, 57-68. http://dx.doi.org/10.18561/2179-5746/biotaamazonia.v7n3p57-68

Pinto, J.S., Oliveira, A.K.M., Fernandes, V., Matias, R., 2017. Ethnobotany and popular culture in the use of plants in settlements on the southern edge of southern Pantanal Mato Grosso. Biosci. J. 33, 193-203. https://doi.org/10.14393/BJ-v33n1a2017-33106

Prakash, N., Ragavan, B., 2009. Phytochemical observation and antibacterial activity of *Cyperus esculentus* L. Anc. Sci. Life 28, 16-20.

Pushpangadan, P., George, V., Ijinu, T.P., Rajasekharan, S., 2017. Ethnopharmacology, traditional knowledge and intellectual property rights. In: Laladhas KP, Nilayangode P, Oommen OV. (eds.) Biodiversity for sustainable development. Switzerland, Springer International Publishing. 97-119. https://doi.org/10.1007/978-3-319-42162-9_6

Rabelo, A.S., Serafini, M.R., Rabelo, T.K., Melo, M.G.D., Prado, D.S., Gelain, D.P., Araújo, A.A.S., 2014. Chemical composition, antinociceptive, anti-inflammatory and redox properties *in vitro* of the essential oil from *Remirea maritima* Aubl. (Cyperaceae). BMC Complement. Altern. Med.14, 514. https://doi.org/10.1186/1472-6882-14-514

Rameshkumar, K.B., Sudheesh, N., George, V., Mohanan, N., 2011. Volatile constituents of the roots of *Cyperus compressus* Linn. J. Essent. Oil Res. 23, 39-41. https://doi.org/10.1080/10412905.2011.9700455

Ramírez, O., Blair, S., 2017. Ethnobotany of medicinal plants used to treat malaria by traditional healers from ten indigenous Colombian communities located in Waupes Medio. Biodivers. Int. J. 1, 151-167. https://doi.org/10.15406/bij.2017.01.00022

Rego, C.A.R.M., Rocha, A.E., Oliveira, C.A., Pacheco, F.P.F., 2016. Levantamento etnobotânico em comunidade tradicional do assentamento Pedra Suada, do município de Cachoeira Grande, Maranhão, Brasil. Acta Agron. 65, 284-291. https://doi.org/10.15446/acag.v65n3.50240

Ribeiro, R.V., Bieski, I.G.C., Balogun, S.O., Martins, D.T.O., 2017. Ethnobotanical study of medicinal plants used by Ribeirinhos in the North Araguaia microregion, Mato Grosso, Brazil. J. Ethnopharmacol. 205, 69-102. https://doi.org/10.1016/j.jep.2017.04.023

Ricardo, L.M., Paula-Souza, J., Andrade, A., Brandão, M.G., 2017. Plants from the Brazilian traditional medicine: species from the books of the Polish physician Piotr Czerniewicz (Pedro Luiz Napoleão Chernoviz, 1812–1881). Rev. Bras. Farmacogn. 27, 388-400. https://doi.org/10.1016/j.bjp.2017.01.002

Rocha, F.G., Brandenburg, M.M., Pawloski, P.L., Soley, B.S., Costa, S.C.A., Meinerz, C.C., et al., 2020. Preclinical study of the topical anti-inflammatory activity of *Cyperus rotundus* L. extract (Cyperaceae) in models of skin inflammation. J. Ethnopharmacol. 254, 112709. https://doi.org/10.1016/j.jep.2020.112709

Rodrigues, E., Mendes, F.R., Negri, G., 2006. Plants indicated by Brazilian Indians for disturbances of the central nervous system: a bibliographical survey. Cent. Nerv. Syst. Agents Med Chem. 6, 211-244. https://doi.org/10.2174/187152406778226725

Romanus, P.C., Mendes, F.R., Carlini, E.A., 2018. Factors affecting the use of medicinal plants by migrants from rural areas of Brazilian Northeast after moving to a metropolitan region in Southeast of Brazil. J. Ethnobiol. Ethnomed. 14, 72. https://doi.org/10.1186/s13002-018-0270-3

Roque, A.A., Rocha, R.M., Loiola, M.I.B., 2010. Uso e diversidade de plantas medicinais da Caatinga na comunidade rural de Laginhas, município de Caicó, Rio Grande do Norte (Nordeste do Brasil). Rev. Bras. Plantas Med. 12, 31-42. http://dx.doi.org/10.1590/S1516-05722010000100006

Sadat-Hosseini, M., Farajpour, M., Boroomand, N., Solaimani-Sardou, F., 2017. Ethnopharmacological studies of indigenous medicinal plants in the south of Kerman, Iran. J. Ethnopharmacol. 199, 194-204. https://doi.org/10.1016/j.jep.2017.02.006

Safa, O., Soltanipoor, M. A., Rastegar, S., Kazemi, M., Dehkordi, K.N., Ghannadi, A., 2013. An ethnobotanical survey on hormozgan province, Iran. Avicenna J. Phytomed. 3, 64–81.

Santana, B.F., Voeks, R.A., Funch, L.S., 2016. Ethnomedicinal survey of a maroon community in Brazil's Atlantic tropical forest. J. Ethnopharmacol. 181, 37-49. https://doi.org/10.1016/j.jep.2016.01.014

Santana, B.F.D., Voeks, R.A., Funch, L.S., 2022. Quilombola ethnomedicine: The role of age, gender, and culture change. Acta Bot. Bras. 36, e2020abb0500. https://doi.org/10.1590/0102-33062020abb0500

Santos, S.L.D.X., Alves, R.R.N., Santos, S.L.D.X., Barbosa, J.A.A., Brasileiro, T.F., 2012. Plantas utilizadas como medicinais em uma comunidade rural do semi-árido da Paraíba, Nordeste do Brasil. Rev. Bras. Farm. 93, 68-79.

Seo, Y.J., Jeong, M., Lee, K.T., Jang, D.S., Choi, J.H., 2016. Isocyperol, isolated from the rhizomes of *Cyperus rotundus*, inhibits LPS-induced inflammatory responses via suppression of the NF-κB and STAT3 pathways and ROS stress in LPS-stimulated RAW 264.7 cells. Int. Immunopharmacol. 38, 61-69. https://doi.org/10.1016/j.intimp.2016.05.017

Sharma, L., Khandelwal, S., 2010. Weeds of rajasthan and their ethno-botanical importance. Stud. EthnoMed. 4, 75-79. https://doi.org/10.1080/09735070.2010.11886363

Shorinwa, O.A., Dambani, D.T., 2020. Antidiarrheal activity of aqueous ethanol extract of *Cyperus esculentus* tuber in albino rats. J. Appl. Biol. Biotechnol. 8, 47-50. https://doi.org/10.7324/JABB.2020.80309

Silva, A.F., Rabelo, M.F.R., Enoque, M.M., 2015. Diversidade de angiospermas e espécies medicinais de uma área de Cerrado. Rev. Bras. Plantas Med. 17, 1016-1030. https://doi.org/10.1590/1983-084x/14_115

Silva, N.C.D., Goncalves, S.F., Araújo, L.S.D., Kasper, A.A.M., Fonseca, A.L.D., Sartoratto, A., Moraes, W.P., 2019. *In vitro* and *in vivo* antimalarial activity of the volatile oil of

Cyperus articulatus (Cyperaceae). Acta Amazon. 49, 334-342. https://doi.org/10.1590/1809-4392201804331

Silva, L.E.D., Amaral, W., Silva, M., Oliveira, A.L.D., 2020. Conservação de recursos genéticos: a pesquisa com plantas medicinais no litoral do Paraná. Ambient. Soc. 23, 1-20. https://doi.org/10.1590/1809-4422asoc20180299r1vu2020l1ao

Silva, A.F., Sousa, R.L., Silva, S.G., Costa, J.M., Albuquerque, L.C.S., Pereira, M.G.S., Mesquita, S.S., Silva, E.C., Cordeiro, Y.E.M., 2021. Etnobotânica de plantas medicinais aromáticas: preparações e usos da flora local em cinco comunidades rurais localizadas na região do Baixo Tocantins, Pará, Brasil. Res. Soc. Dev. 10, e9510111284. http://dx.doi.org/10.33448/rsd-v10i1.11284

Simorangkir, D., Masfria, M., Harahap, U., Satria, D., 2019. Activity anticancer n-hexane fraction of *Cyperus rotundus* L. rhizome to breast cancer MCF-7 cell line. Open Access Maced. J. Med. Sci. 7, 3904-3906. https://doi.org/10.3889/oamjms.2019.530

Singh, P., Khosa, R.L., Mishra, G., Jha, K.K., 2015. Antidiabetic activity of ethanolic extract of *Cyperus rotundus* rhizomes in streptozotocin-induced diabetic mice. J. Pharm. Bioall. Sci. 7, 289-292.

Sivasankari, B., Anandharaj, M., Gunasekaran, P., 2014. An ethnobotanical study of indigenous knowledge on medicinal plants used by the village peoples of Thoppampatti, Dindigul district, Tamilnadu, India. J. Ethnopharmacol. 153, 408-423. https://doi.org/10.1016/j.jep.2014.02.040

Soares, M.A.A., Braga, J.R.P., Mourão, A.E.B., Parente, K.M.S., Parente Filho, E.G., 2009. Levantamento etnobotânico das plantas medicinais utilizadas pela população do município de Gurinhém – Paraíba. Rev. Homem, Espaço e Tempo 3, 36-47.

Souza, M.D., Fernandes, R.R., Pasa, M.C., 2011. Estudo etnobotânico de plantas medicinais na comunidade São Gonçalo Beira Rio, Cuiabá, MT. Rev. Biodiversidade 9, 91-100.

Staniski, A., Floriani, N., Strachulski, J., 2014. Estudo etnobotânico de plantas medicinais na comunidade faxinalense Sete Saltos de Baixo, Ponta Grossa-PR. Terr@ Plural 8, 320-340. https://10.5212/TerraPlural.v.8i2.0004

Sukjamnong, S., Santiyanont, R., 2015. Effect of *Fimbristylis ovata* on receptor for advanced glycation end-products, proinflammatory cytokines, and cell adhesion molecule level and

gene expression in U937 and bEnd. 3 cell lines. Genet. Mol. Res. 14, 3984-3994. http://dx.doi.org/10.4238/2015.April.27.13

Süntar, I., 2019. Importance of ethnopharmacological studies in drug discovery: role of medicinal plants. Phytochem. Rev. 1-11. https://doi.org/10.1007/s11101-019-09629-9

Taheri, Y., Herrera-Bravo, J., Huala, L., Salazar, L.A., Sharifi-Rad, J., Akram, M., et al., 2021. *Cyperus* spp.: A Review on Phytochemical Composition, Biological Activity, and Health-Promoting Effects. Oxid. Med. Cell. Longev. 2021, 4014867. https://doi.org/10.1155/2021/4014867

Thomas, D., Govindhan, S., Baiju, E.C., Padmavathi, G., Kunnumakkara, A.B., Padikkala, J., 2015. *Cyperus rotundus* L. prevents non-steroidal anti-inflammatory drug-induced gastric mucosal damage by inhibiting oxidative stress. J. Basic Clin. Physiol. Pharmacol. 26, 485-490. https://doi.org/10.1515/jbcpp-2014-0093

Tsoyi, K., Jang, H.J., Lee, Y.S., Kim, Y.M., Kim, H.J., Seo, H.G., et al., 2011. (+)-Nootkatone and (+)-Valencene from rhizomes of *Cyperus rotundus* increase survival rates in septic mice due to heme oxygenase-1 induction. J. Ethnopharmacol. 137, 1311-1317. https://doi.org/10.1016/j.jep.2011.07.062

Tucker, A.O., Maciarello, M.J., Bryson, C.T., 2006. The essential oil of *Kyllinga odorata* Vahl (Cyperaceae) from Mississippi. J. Essent. Oil Res. 18, 381-382. https://doi.org/10.1080/10412905.2006.9699120

Udefa, A.L., Amama, E.A., Archibong, E.A., Nwangwa, J.N., Adama, S., Inyang, V.U., et al., 2020. Antioxidant, anti-inflammatory and anti-apoptotic effects of hydro-ethanolic extract of *Cyperus esculentus* L. (tigernut) on lead acetate-induced testicular dysfunction in Wistar rats. Biomed. Pharmacother. 129, 110491. https://doi.org/10.1016/j.biopha.2020.110491

Umair, M., Altaf, M., Abbasi, A.M., 2017. An ethnobotanical survey of indigenous medicinal plants in Hafizabad district, Punjab-Pakistan. PloS one. 12, e0177912. https://doi.org/10.1371/journal.pone.0177912

Upadhyay, A., Jain, S., 2017. Nephro protective, diuretic and anti-inflammatory evaluation of monocot grass *Kyllinga triceps* Rottb. IOSR J. Pharm. 7, 1-4.

Uy, M.M., Garcia, K.I., 2015. Evaluation of the antioxidant properties of the leaf extracts of Philippine medicinal plants *Casuarina equisetifolia* Linn, *Cyperus brevifolius* (Rottb)

Hassk, *Drymoglossum piloselloides* Linn, *Ixora chinensis* Lam, and *Piper abbreviatum* Opiz. Adv. Agric. Bot. 7, 71-79.

Vásquez, S.P.F., Mendonça, M.S., Noda, S.N., 2014. Etnobotânica de plantas medicinais em comunidades ribeirinhas do Município de Manacapuru, Amazonas, Brasil. Acta Amaz. 44, 457-472. https://doi.org/10.1590/1809-4392201400423

Vega-Morales, T., Mateos-Díaz, C., Pérez-Machín, R., Wiebe, J., Gericke, N.P., Alarcón, C., López-Romero, J.M., 2019. Chemical composition of industrially and laboratory processed *Cyperus esculentus* rhizomes. Food Chem. 297, 124896. https://doi.org/10.1016/j.foodchem.2019.05.170

Vendruscolo, G.S., Simões, C.M.O., Mentz, L.A., 2005. Etnobotânica no Rio Grande do Sul: análise comparativa entre o conhecimento original e atual sobre as plantas medicinais nativas. Pesq. Bot. 56, 285-320.

Vendruscolo, G.S., Mentz, L.A., 2006. Levantamento etnobotânico das plantas utilizadas como medicinais por moradores do bairro Ponta Grossa, Porto Alegre, Rio Grande do Sul, Brasil. Iheringia Ser. Bot. 61, 83-103.

Vera, P.J.D., Tayone, J.C., Las Llagas, M.C.S., 2022. *Cyperus iria* linn. Roots ethanol extract: its phytochemicals, cytotoxicity, and anti-inflammatory activity. J. Taibah Univ. Sci. 16, 854-862. https://doi.org/10.1080/16583655.2022.2123088

Vila Verde, G.M., Paula, J.R., Caneiro, D.M., 2003. Levantamento etnobotânico das plantas medicinais do cerrado utilizadas pela população de Mossâmedes (GO). Rev. Bras. Farmacogn. 13, 64-66. https://doi.org/10.1590/S0102-695X2003000300024

Waruruai, J., Sipana, B., Koch, M., Barrows, L.R., Matainaho, T.K., Rai, P.P., 2011. An ethnobotanical survey of medicinal plants used in the Siwai and Buin districts of the Autonomous Region of Bougainville. J. Ethnopharmacol. 138, 564-577. https://doi.org/10.1016/j.jep.2011.09.052

Weckerle, C.S., Boer, H.J., Puri, R.K., Van Andel, T., Bussmann, R.W., Leonti, M., 2018. Recommended standards for conducting and reporting ethnopharmacological field studies. J. Ethnopharmacol. 210, 125-132. https://doi.org/10.1016/j.jep.2017.08.018

Xu, H.B., Ma, Y.B., Huang, X.Y., Geng, C.A., Wang, H., Zhao, Y., et al., 2015. Bioactivity-guided isolation of anti-hepatitis B virus active sesquiterpenoids from the traditional

Chinese medicine: Rhizomes of *Cyperus rotundus*. J. Ethnopharmacol. 171, 131-140. https://doi.org/10.1016/j.jep.2015.05.040

Yaseen, G., Ahmad, M., Sultana, S., Alharrasi, A.S., Hussain, J., Zafar, M., 2015. Ethnobotany of medicinal plants in the Thar Desert (Sindh) of Pakistan. J. Ethnopharmacol. 163, 43-59. ttps://doi.org/10.1016/j.jep.2014.12.053

Yazbek, P.B., Matta, P., Passero, L.F., Santos, G., Braga, S., Assunção, L., et al., 2019. Plants utilized as medicines by residents of Quilombo da Fazenda, Núcleo Picinguaba, Ubatuba, São Paulo, Brazil: A participatory survey. J. Ethnopharmacol. 244, 112123. https://doi.org/10.1016/j.jep.2019.112123

Yetein, M.H., Houessou, L.G., Lougbégnon, T.O., Teka, O., Tente, B., 2013. Ethnobotanical study of medicinal plants used for the treatment of malaria in plateau of Allada, Benin (West Africa). J. Ethnopharmacol. 146, 154-163. https://doi.org/10.1016/j.jep.2012.12.022

Yeung, A.W.K., Heinrich, M., Kijjoa, A., Tzvetkov, N.T., Atanasov, A.G., 2020. The ethnopharmacological literature: An analysis of the scientific landscape. J. Ethnopharmacol. 250, 112414. https://doi.org/10.1016/j.jep.2019.112414

Zeni, A.L.B., Bosio, F., 2011. O uso de plantas medicinais em uma comunidade rural de Mata Atlântica-Nova Rússia, SC. Neotrop. Biol. Conserv. 6, 55-63. https://doi.org/10.4013/nbc.2011.61.07

Zhang, T.Z., Xu, L.J., Xiao, H.P., Zhou, X., Mo, S.M., Cai, S.M., Zhou, Z.L., 2014. A new iridoid glycoside from the rhizomes of *Cyperus rotundus*. Bull. Korean. Chem. Soc. 35, 2207-2209. https://doi.org/10.5012/bkcs.2014.35.7.2207

Zhou, Z., Yin, W., 2012. Two novel phenolic compounds from the rhizomes of *Cyperus rotundus* L. Molecules 17, 12636-12641. https://doi.org/10.3390/molecules171112636

Zhou, Z., Zhang, H., 2013. Phenolic and iridoid glycosides from the rhizomes of *Cyperus rotundus* L. Med. Chem. Res. 22, 4830-4835. https://doi.org/10.1007/s00044-013-0504-9

Zoghbi, M.G.B., Andrade, E.H.A., Oliveira, J., Carreira, L.M.M., Guilhon, G.M.S., 2006a. Yield and chemical composition of the essential oil of the stems and rhizomes of *Cyperus articulatus* L. cultivated in the state of Pará, Brazil. J. Essent. Oil Res. 18, 10-12. https://doi.org/10.1080/10412905.2006.9699371

Zoghbi, M.G.B., Andrade, E.H.A., Oliveira, J., Guilhon, G.M.S., Vilhena, K.S.S., 2006b. Analysis of the essential oil of the rhizome of *Cyperus giganteus* Vahl. (Cyperaceae) cultivated in north of Brazil. J. Essent. Oil Res. 18, 408-410. https://doi.org/10.1080/10412905.2006.9699127

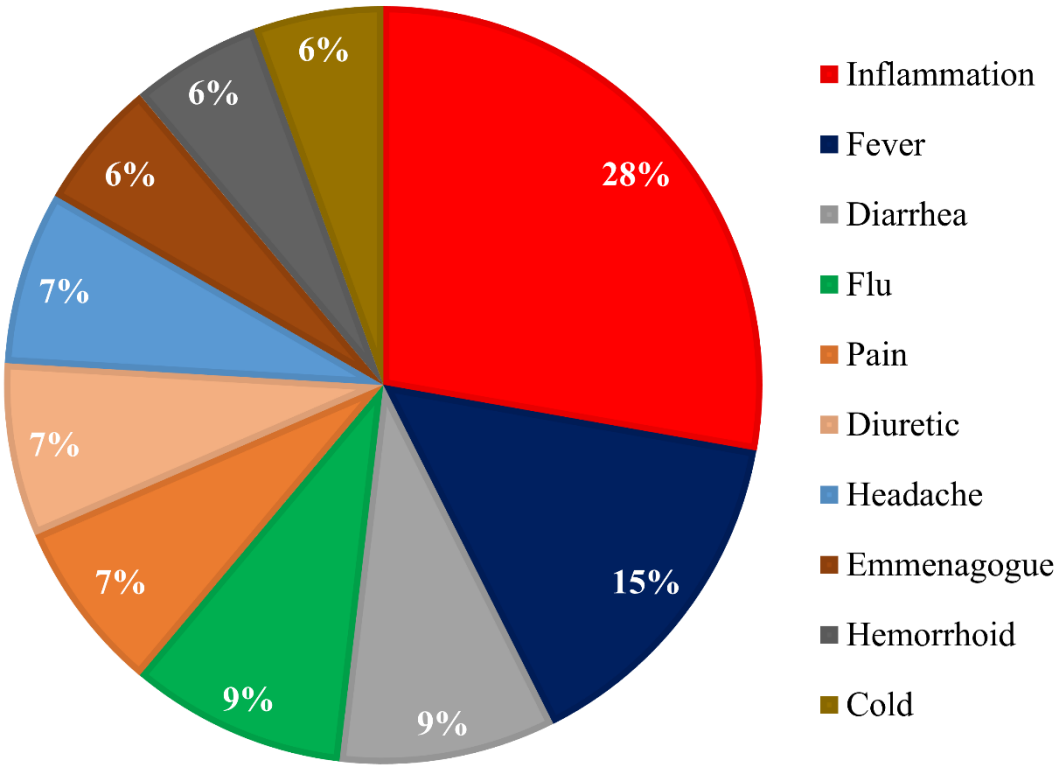


Fig. 1. Indications of use in folk medicine reported for Cyperaceae species in Brazil.

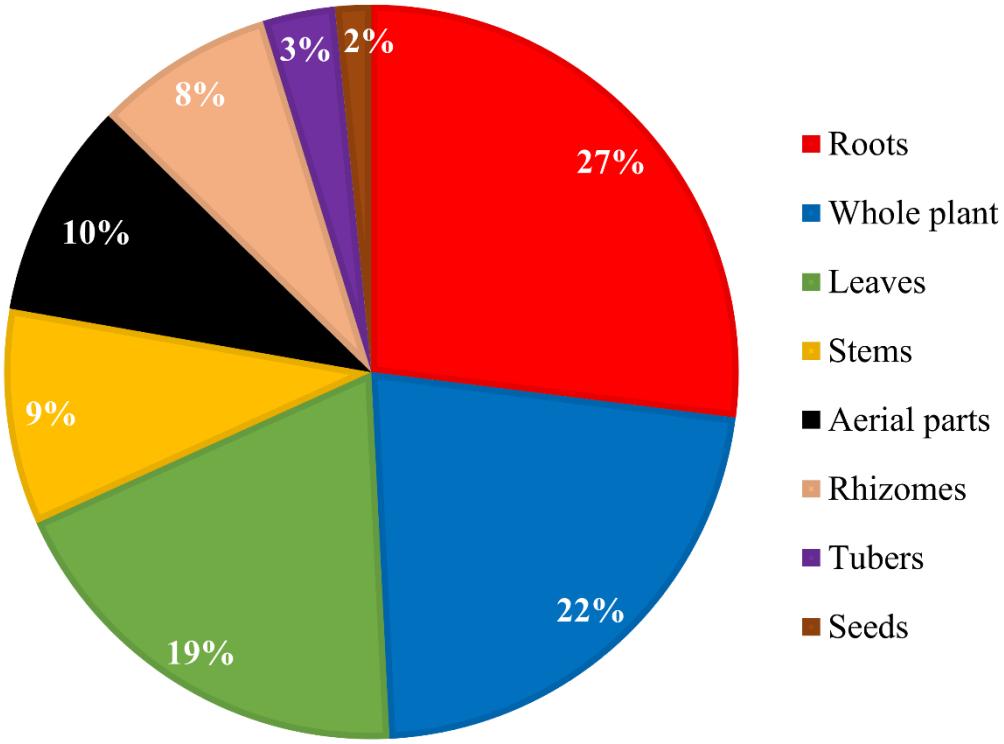


Fig. 2. Plant organs of Cyperaceae species used in folk medicine in Brazil. Aerial parts are not specified by the authors of the studies.

Table 1. Cyperaceae species used in folk medicine in Brazil.

Species*	Local name	Part used	Preparation mode	Mode of use	Medicinal use	References
Bulbostylis capillaris (L.) C.B.Clarke	Barba-de-bode	-	Infusion	Internal use	Diuretic, stomach, kidneys, worms	Bieski et al. (2012)
		Whole plant	-	-	Cold, high fever	Vila Verde et al. (2003)
		Leaves, roots	Warm bath, decoction	-	Cold	Borba and Macedo (2006)
Bulbostylis junciformis (Kunth) C.B.Clarke	Barba-de-bode	Leaves, stem	Decoction	External use	Fever	Cavalcante and Frikel (1973)
Bulbostylis lanata (Kunth) Lindm	-	Whole plant	Decoction	External use	Fever, headache	Cavalcante and Frikel (1973)
Carex sororia Kunth	-	Aerial parts	-	-	Diarrhea	Vendruscolo et al. (2005)
		Aerial parts	-	-	Diarrhea	Vendruscolo and Mentz (2006)

Cyperus aggregatus (Willd.) Endl.	Junquinho, três-quinas	Whole plant	Decoction	External use	Fever	Cavalcante and Frikel (1973)
Cyperus articulatus L.	Priprioca	Roots	Decoction	External use	Anti-infectious, anti-inflammatory	Duarte et al. (2007)
		Tubers	-	-	Anti-inflammatory	Bersan et al. (2014)
		Roots	Infusion	-	Back pain	Roque et al. (2010)
		-	Tea[1]	Oral use	Asthma	Mesquita and Tavares-Martins (2018)
		Roots	Maceration, bath	External use	"Quebranto"[2], deep wounds	Palheta et al. (2017)
		Rhizomes	Infusion	External use	Fever	Milliken and Albert (1996)
		Rhizomes	Maceration	External use	Fever	Silva et al. (2021)
Cyperus brevifolius (Rottb.) Endl. ex Hassk.	Chufa, sulfa, tunça	Flowery parts	-	-	Mycoses	Avancini and Wiest (2008)
		Roots	-	-	Snake bites	Brandão et al. (2012)
Cyperus compressus L.	Capim-baba-de-bode	Whole plant	Infusion	-	Diuretic	Ribeiro et al. (2017)

Cyperus eragrostis Lam.	Junção	Aerial parts	-	-	Hemorrhoids	Vendruscolo et al. (2005)
		Aerial parts	-	-	Hemorrhoids	Vendruscolo and Mentz (2006)
Cyperus esculentus L.	Tiririca, junça, junco	Whole plant	Decoction	-	Tonsillitis	Messias et al. (2015)
		Roots	Maceration	-	Headache	Santos et al. (2012)
		Leaves, roots	Tea, bath, maceration	Internal and external use	Flu, headache, hemorrhoid, diarrhea	Vásquez et al. (2014)
		Leaves	"Lambedor"[3]	-	Respiratory system diseases	Monteles and Pinheiro (2007)
		Rhizomes	Tea	Internal use	Emmenagogue	Paulino et al. (2011)
		Root	-	-	Helps in tooth birth in children	Costa et al. (2021)
Cyperus giganteus Vahl	Papiro	Stems	-	-	Bronchitis, flu	Silva et al. (2015)
Cyperus iria L.	Tiririca	Whole plant	-	-	Stimulant, diuretic	Boscolo and Valle (2008)
Cyperus odoratus L.	Capim-santo	Roots	Infusion	-	Uterus infections,	Silva et al. (2020)

					uterine fibroids (myoma), urinary infections	
Cyperus rotundus L.	Tiririca, junça-aromática, dandá	-	Infusion	Internal use	Pain	Bieski et al. (2012)
		Roots	Decoction	External use	Anti-infectious, anti-inflammatory	Duarte et al. (2007)
		Tubers	-	-	Wounds	Fenner et al. (2006)
		Whole plant	Tea	-	Regularizes menstrual cycle	Staniski et al. (2014)
		Seeds	Dye	-	Diseases of the circulatory system	Monteles and Pinheiro (2007)
		Roots	Tea	-	Diseases associated with blood and	Rego et al. (2016)

					hematopoietic organs	
		Stems	Decoction	-	Diuretic, anti-inflammatory	Borges and Bautista (2020)
		Roots	Maceration	-	Memory problems	Barros et al. (2007)
		Roots	"Garrafada"[4]	-	Pain in general	Soares et al. (2009)
Cyperus sesquiflorus (Torr.) Mattf. & Kük.	Capim-de-cheiro, jaçapé	Leaves, rhizomes	Infusion	-	Gastritis	Mentz et al. (1997)
Cyperus uncinulatus Schrad. ex Nees	Barba-de-bode	Roots	Infusion	-	Irregular menstruation	Oliveira et al. (2010)
Eleocharis montana (Kunth) Roem. & Schult.	Cavalinha	Leaves	-	-	Regulates pressure	Zeni and Bosio (2011)
Fimbristylis vahlii (Lam.) Link	Barba-de-bode	Roots	Infusion	-	Kidney disease	Roque et al. (2010)

Hypolytrum pungens (Vahl) Kunth [Syn. *Hypolytrum pulchrum* (Rudge) H.Pfeiff.]	Capim-santo	Leaves	Tea	-	Soothing, headache	Motta et al. (2016)
Kyllinga odorata Vah [Syn. *Cyperus sesquiflorus* (Torr.) Mattf. & Kük.]	Capim-cheiroso, capim-de-cheiro, Capim-cidreira	Aerial parts	-	-	Diarrhea	Vendruscolo et al. (2005)
		Aerial parts	-	-	Diarrhea	Vendruscolo and Mentz (2006)
		Leaves	Tea	-	Flu	Souza et al. (2011)
		Leaves, rhizomes, stem	Tea	-	Soothing	Pinto et al. (2017)
Rhynchospora barbata (Vahl) Kunth	-	Leaves, stem	Decoction, smoke	-	Fever	Rodrigues et al. (2006)

Rhynchospora nervosa (Vahl) Boeckeler	Capim-estrela	Whole plant	Tea	-	Inflammation	Moreira et al. (2002)
		Whole plant	Tea	-	Swelling, inflammation, venereal disease	Gomez et al. (2016)
		Whole plant, only the part of the star	Tea, syrup	-	Flu	Lisboa et al. (2017)
		Whole plant	Infusion (bath and ablutions)	External use	Fever	Rodrigues et al. (2006)
		Whole plant	Syrup, tea	-	Dental inflammation, flu, nasal congestion	Santana et al. (2022)
Rhynchospora pubera (Vahl) Boeckeler	Barba-de-paca	Leaves	Tea	-	Urinary infection	Pereira and Coelho-Ferreira (2017)
	Junco	Roots	*In natura*	-	Snake bites	Castro et al. (2016)

Schoenoplectus californicus (C.A.Mey.) Soják						
Scleria distans Poir.	Junço, dandá	Whole plant	Infusion	External use	Pain	Romanus et al. (2018)
Scleria hirtella Sw.	-	Leaves, stem	Decoction	External use	Epileptic seizures in children	Cavalcante and Frikel (1973)
Scleria gaertneri Raddi	Capim-navalha, navalha-de-macaco	Whole plant, roots	Decoction, maceration	-	Infections, urinary infection, sore throat	Ribeiro et al. (2017)

*All species are native and not endemic, except *Rhynchospora nervosa* and *Cyperus odoratus* which are native and endemic and *Cyperus esculentus* which is naturalized and not endemic. [1]Authors did not specify if infusion, decoction or maceration; [2]weariness attributed to the evil influence of spells; [3]plants immersed in sweetened substances to obtain decoctions; [4]mixture of medicinal herbs kept in water or brandy in a bottle; - = not informed.

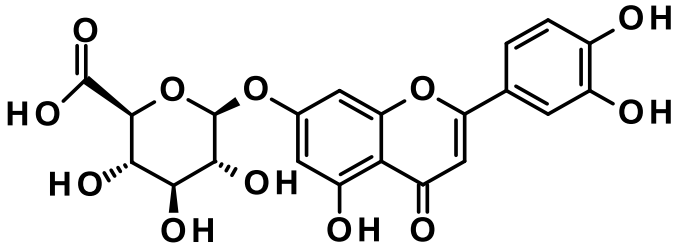
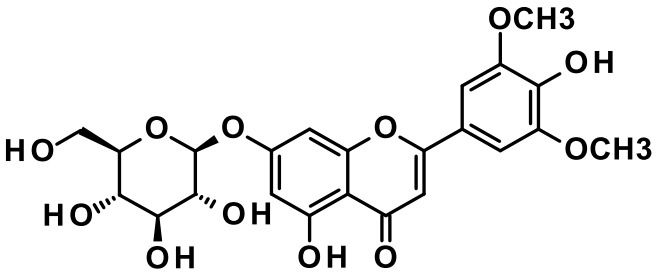
Table 2. Cyperaceae species used in folk medicine by geographic region and state of Brazil. ND = Document numbers per state and RF = Relative frequency.

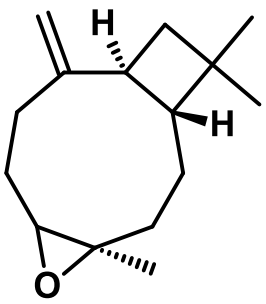
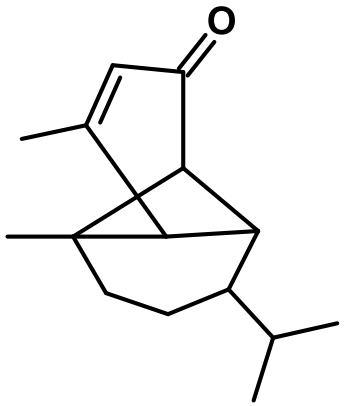
Species	Geographic region	Brazilian state	DN	RF (%)
Bulbostylis capillaris (L.) C.B.Clarke	Midwest	Goiás - GO	2	4.76
Hypolytrum pungens (Vahl) Kunth [Syn. *Hypolytrum pulchrum* (Rudge) H.Pfeiff.]				
Bulbostylis capillaris (L.) C.B.Clarke		Mato Grosso - MT	5	11.90
Cyperus articulatus L.				
Cyperus compressus L.				
Cyperus rotundus L.				
Kyllinga odorata Vah [Syn. *Cyperus sesquiflorus* (Torr.) Mattf. & Kük.]				
Scleria gaertneri Raddi				
Cyperus articulatus L.	North	Amazonas - AM	3	7.15
Cyperus esculentus L.				
Cyperus articulatus L.		Pará - PA	4	9.52
Rhynchospora pubera (Vahl) Boeckeler				
Cyperus rotundus L.	Northeast	Bahia - BA	6	14.30
Rhynchospora nervosa (Vahl) Boeckeler				
Cyperus esculentus L.		Maranhão - MA	2	4.76

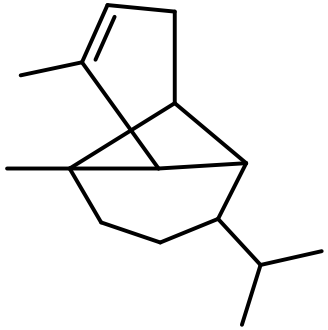
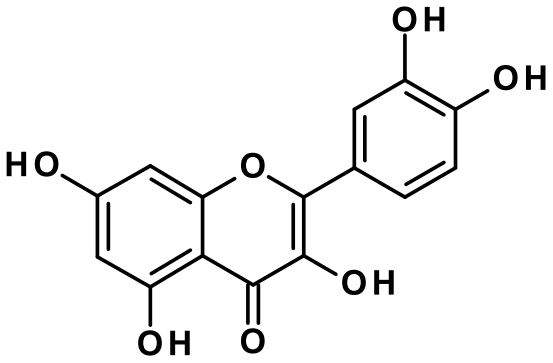
Cyperus rotundus L.				
Cyperus esculentus L.		Paraíba - PB	2	4.76
Cyperus rotundus L.				
Cyperus uncinulatus Schrad. ex Nees		Piauí - PI	2	4.76
Schoenoplectus californicus (C.A.Mey.) Soják				
Cyperus articulatus L.		Rio Grande do Norte - RN	2	4.76
Cyperus esculentus L.				
Fimbristylis vahlii (Lam.) Link				
Cyperus odoratus L.	**S**outh	Paraná - PR	2	4.76
Cyperus rotundus L.				
Carex sororia Kunth		Rio Grande do Sul - RS	5	11.90
Cyperus brevifolius (Rottb.) Endl. ex Hassk.				
Cyperus eragrostis Lam.				
Cyperus esculentus L.				
Cyperus rotundus L.				
Kyllinga odorata Vah [Syn. *Cyperus sesquiflorus* (Torr.) Mattf. & Kük.]				
Eleocharis montana (Kunth) Roem. & Schult.		Santa Catarina - SC	1	2.38
Cyperus esculentus L.	**S**outheast	Minas Gerais - MG	3	7.15
Cyperus giganteus Vahl				
Cyperus iria L.		Rio de Janeiro - RJ	1	2.38

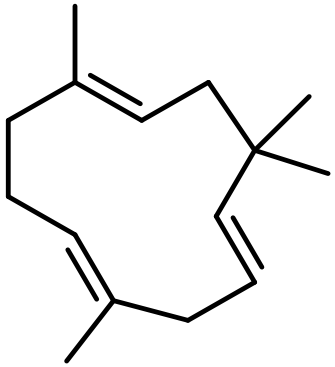
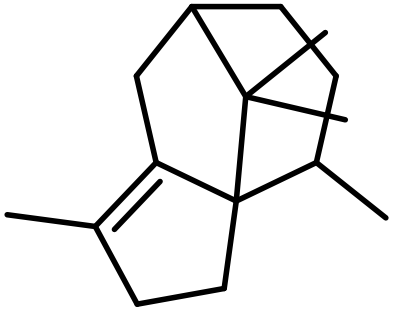
Cyperus articulatus L.		São Paulo - SP	2	4.76
Cyperus rotundus L.				
Scleria distans Poir.				
	Total		42	100

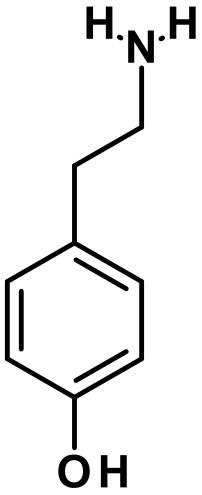
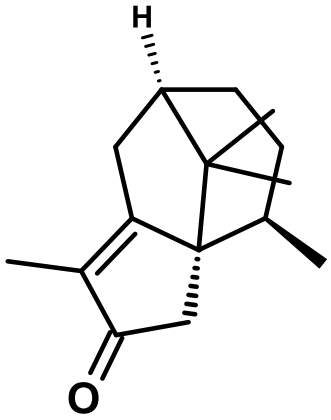
Table 3. Main constituents isolated from different Cyperaceae species used in the traditional medicine of Brazil. Name of the chemical structure is shown in bold.

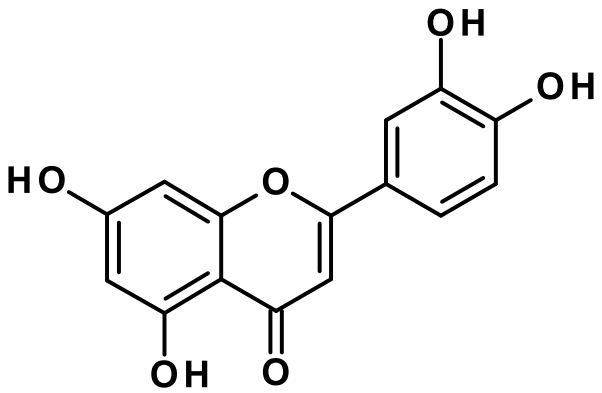
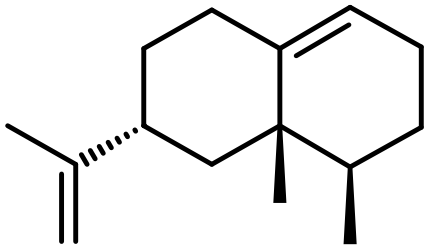
Species	Compounds	Plant organ	References
Cyperus aggregatus (Syn. *Cyperus flavus*)	Flavonoids	Leaves	Harborne et al. (1982)
	Lutein 7- glucuronide		
			
	Tricin 7-glucoside		
			

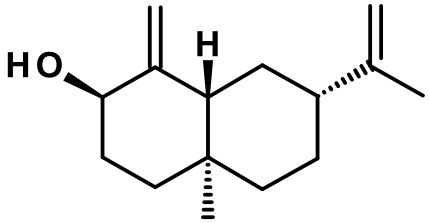
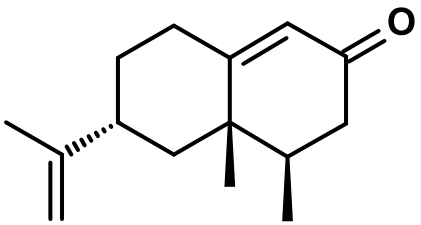
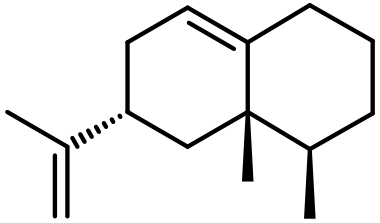
Cyperus articulates 	Sesquiterpenes (**caryophyllene oxide**, and mustakone); monoterpene (α-pinene)	Stems and rhizomes	Zoghbi et al. (2006a)
	Sesquiterpenes (**muskatone**, cyclocolorenone, pogostol, α-copaene and caryophyllene oxide); monoterpene (α-pinene)	Rhizomes	Nogueira et al. (2020)

	Sesquiterpenes (mustakone, cyclocolorenone, ***α*-copaene**, *α*-selinene and cis-thujopsenal)	Rhizomes	Silva et al. (2019)
Cyperus brevifolius. 	Flavonoids (**quercetin** and luteolin)	Leaves and inflorescences	Harborn et al. (1982)

	*n*-Paraffins (heneicosane and nonadecane) and sesquiterpenes (*δ*-cadinene and ***α*-humulene**)	Rhizomes and roots	Komai and Tang (1989)
Cyperus compressus 	Sesquiterpenes (caryophyllene oxide and **cyperene**)	Roots	Rameshkumar et al. (2011)
Cyperus esculentus	Sugar (sucrose), fatty acids (oleic acid glyceryl ester, oleamide, linoleic acid and glyceryl ester), phytosteroids (stigmasterol), flavonols	Rhizomes	Vega-Morales et al. (2019)

	(quercetin and myricetin) and amines (**tyramine** and N-feruloyltyramine)		
Cyperus giganteus 	Sesquiterpenes (**cyperotundone**, and cyperene)	Rhizomes	Zoghbi et al. (2006b)

Cyperus odoratus. 	Flavonoids (**luteolin** and aureusidin)	Leaves and inflorescences	Harborne et al. (1982)
Cyperus rotundus 	Sesquiterpenes (**valencene** and nootkatone)	Rhizomes	Jin et al. (2011)
	Sesquiterpenes (**isocyperol**)	Rhizomes	Seo et al. (2016)

 	Sesquiterpenes (***α*-cyperone**)	Rhizomes	Park et al. (2019)
Kyllinga odorata 	Sesquiterpenes (dihydrokaranone and **aristolochene**)	Whole plant	Tucker et al. (2006)
Scleria hirtella	Aliphatic aldehydes	Whole plant	Maia et al. (2005)

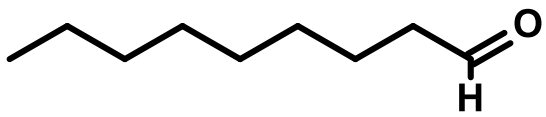
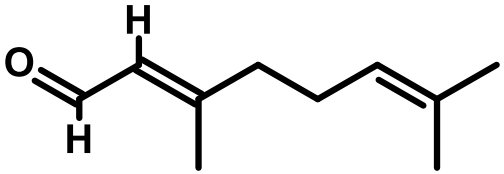
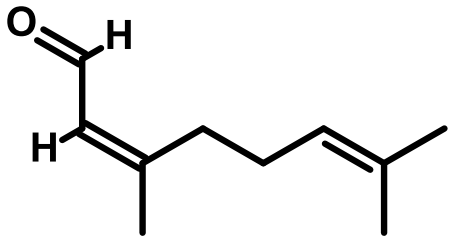
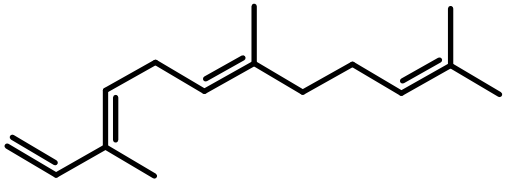
	(octanal, **nonanal,** and decanal)
	Monoterpenes **(geranial** and **neral)**
	Sesquiterpenes **((E,E)-*α*-Farnesene)**
	

Table 4. Cyperaceae species used in folk medicine in Brazil and other countries.

Species	Uses reported in other countries	References
Cyperus articulatus L.	In Ghana, roots are indicated for the treatment of tuberculosis.	Nguta et al. (2015)
	In Gabon, root macerates are administered orally for the treatment of helminthiasis.	Ndob et al. (2016)
Cyperus compressus L.	The paste prepared from the whole plant is applied to treat scabies by traditional communities in Nepal.	Dangol and Gurung (1991)
Cyperus esculentus L.	For cases of urolithiasis, traditional Iraqi communities recommend boiling the tubers in water and drinking a cup a day until recovery.	Mati and Boer (2011)
	The leaves are used in the form of decoction to treat the symptoms of malaria in the Allada plateau in Benin.	Yetein et al. (2013)
	It is indicated by traditional Algerian healers to help with weight gain and due to its aphrodisiac properties.	Benarba et al. (2015)
	In India, tubers are used to treat helminthiasis, diarrhea, dysentery, leprosy, and liver disease.	Ganesan and Xu (2017)

Cyperus iria L.	The roots are indicated for the treatment of rheumatism in India.	Adhikari et al. (2010)
Cyperus rotundus L.	In Asian countries such as India, Pakistan, Bangladesh, Nepal, Iran, Yemen, China, and Turkey, the rhizomes, roots, leaves, and the whole plant are used for the treatment of numerous diseases, such as tonsillitis, dysentery, diarrhea, fever, pain, menstruation problems, wounds, itching, leprosy, cough, cold, worms, dermatitis, hemorrhoids, hair loss, cholera, female infertility, hypersplenism, and it is used as a diuretic agent, galactagogue, digestive tonic, heart tonic.	Burlakoti and Kunwar (2008); Fakir et al. (2009); Sharma and Khandelwal (2010); Safa et al. (2013); Partha (2014); Sivasankari et al. (2014); Yaseen et al. (2015); Li and Xing (2016); Umair et al. (2017); Al-Fatimi (2019)
	In Morocco, on the African continent, the paste prepared from the leaves is indicated for cases of hair loss.	Idm'hand et al. (2020)
	The infusion of the roots is used by traditional communities in Papua New Guinea to treat toothache.	Waruruai et al. (2011)
Kyllinga odorata Vah [Syn. *Cyperus sesquiflorus* (Torr.) Mattf. & Kük.]	The Ati Negrito indigenous group on the Guimaras island, Philippines, reported that the decoction of the whole plant can be used to treat measles and chickenpox.	Ong and Kim (2014)
Rhynchospora pubera (Vahl) Boeckeler	It is used by indigenous people in the Palomino River basin, Colombia, as a potent antacid for the stomach.	

		Carbonó-Delahoz and Dib-Diazgranados (2013)
Schoenoplectus californicus (C.A.Mey.) Soják [Syn. *Scirpus californicus* (C.A.Mey.) Steud.]	In Peru, the whole plant is boiled and given orally for eight days to treat fever.	Bussmann and Glenn (2010); Bussmann et al. (2011)

4 ARTIGO 2

Cyperaceae species used for the treatment of inflammation: a review of ethnomedicinal, pharmacological, toxicological, and phytochemical evidence

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Abstract

Species of the family Cyperaceae are used in traditional medicine in several countries for the treatment of some illnesses. The indications of some representatives for the treatment of inflammation have been experimentally evaluated, suggesting that Cyperaceae has chemical compounds with anti-inflammatory activity. The present work aimed to carry out a systematic review of the traditional uses, anti-inflammatory potential, toxicity, and chemical compounds isolated from species of this family. Scientific articles were obtained through searches in the Google Scholar, PubMed®, SciELO, and Scopus® databases. Only works published in the last 31 years (1991-2022) were eligible. After application of the inclusion and exclusion criteria, a total of 82 articles were used in this review. Ten species of Cyperaceae are traditionally used to treat inflammation in different countries. *In vitro* and *in vivo* assays with the essential oil, extracts and its fractions exhibited potent anti-inflammatory action. Relevant preclinical toxicity was not found for different formulations. A total of 50 compounds belonging to the classes of sesquiterpenes, phenolic compounds, benzenoids, phytosterols, unsaturated fatty acids, diterpenoids, triterpenes, and norterpenoids presented anti-inflammatory potential. *Cyperus rotundus* stood out for the high amount of information on its traditional use, anti-inflammatory potential, and phytochemical studies. Bioprospecting other species indicated in

traditional medicine for the treatment of inflammation is essential to validate or refute the suggested ethnopharmacological information.

Keywords

Anti-inflammatory; Bioactive compounds; Ethnopharmacology; Medicinal plants; Phytoteraphy

Abbreviations

AA, Arachidonic acid; ActF, Active fraction; ADAMTS5, A disintegrin and metalloproteinase with thrombospondin motifs; AE, Aqueous extract; BF, *n*-butanol fraction; BSA, Bovine serum albumin; CE, Chloroform extract; CH, Crude hydrodistillate; COX, Cyclooxygenase; COX-2, Cyclooxygenase-2; EAE, Ethyl acetate extract; EAF, Ethyl acetate fraction; EE, Ethanol extract; EO, Essential oil; HAE, Hydroalcoholic extract; HF, *n*-hexane fraction; HO-1, Heme oxygenase-1; HPLC, High performance liquid chromatography; IC_{50}, Half the maximal inhibitory concentration; IFN-γ, Interferon-γ; IL-1β, Interleukin-1β; IL-6, Interleukin-6; iNOS, Inducible nitric oxide synthase; 5-LOX, 5-lipoxygenase; LPS, Lipopolysaccharide; LTC4, Leukotriene C4; LTD4, Leukotriene D4; LTE4, Leukotriene E4; MAPKs, Mitogen-activated protein kinase; ME, Methanol extract; MF, Methanol fraction; MMPs, Metalloproteinases; NF-κB, Factor nuclear kappa B; NO, Nitric oxide; Pb, Lead acetate; PGE2, Prostaglandin E2; RAGE, Receptor for advanced glycation end-products; RAW 264.7, Cell line; THP-1, Cell line; TNF-α, Tumor necrosis factor-α; TOF, extract enriched with total oligomer flavonoids; TPA, 12-O-tetradecanoylphorbol-13-acetate.

1. Introduction

Inflammation is a highly dynamic process that can be characterized as the first protective response of the immune system (Tasneem et al., 2019). This clinical condition is triggered by factors such as injuries and infections (Agarwal et al., 2019) and is characterized by five main symptoms: redness, swelling, heat, pain and loss of tissue function (Takeuchi and Akira, 2010). Inflammatory lesions induce the release of a variety of systemic mediators that cause the resolution of the inflammatory response and restoration of the integrity of the affected tissue (Maione et al., 2015). The treatment of inflammation is done by administration of steroidal (corticosteroids) and non-steroidal anti-inflammatory drugs (Brune and Patrignani, 2015; Juthani et al., 2017; Oguntibeju, 2018), which, in most cases, cause side effects.

In several countries, some representatives of the family Cyperaceae have been used in traditional medicine for the treatment of inflammation. Medicinal plants are known for their therapeutic potential, including anti-inflammatory activity, with little or no side effects (Recio et al., 2012; Kazemi, et al., 2018; Oguntibeju, 2018). Cyperaceae species such as *Cyperus rotundus* L. (Qureshi et al., 2008; Borges and Bautista, 2010; Napagoda et al., 2018; Penchala et al., 2018), *Scirpoides holoschoenus* (L.) Soják (Parada et al., 2009), *Cyperus glomeratus* L. (Ikram et al., 2014), *Rhynchospora nervosa* Boeckeler (Santana et al., 2016; Gomez et al., 2016), *Scleria gaertneri* Raddi (Ribeiro et al., 2017), *Cyperus articulatus* L. (Pompermaier et al., 2018; Oliveira et al., 2019), *Cyperus distans* L.f (Mir et al., 2018), *Cyperus papyrus* L. (Mhlongo and Wyk, 2019), *Cyperus scariosus* R. Br. (Kumari et al., 2019), and *Cyperus alopecuroides* Rottb. (Ali and Ahmed, 2020), for example, are popularly indicated for anti-inflammatory purposes. For some *Cyperus* species, notably *C. rotundus*, the anti-inflammatory potential has been demonstrated through *in vivo* and *in vitro* studies (Dang et al., 2011; Tsoyi et al., 2011; Kumar et al., 2012; Jung et al., 2013; Kakarla et al., 2014; Mohammed et al., 2014; Rocha et al., 2020).

The anti-inflammatory potential observed in Cyperaceae species is directly related to their chemical constituents. Sesquiterpenes (Khan et al., 2011; Kim et al., 2013; Seo et al., 2016; Azimi et al., 2016), phenolic compounds (Rabelo et al., 2013; Elshamy et al., 2017), benzenoids (Rabelo et al., 2014), phytosterols (Mohammed et al., 2014), unsaturated fatty acids (Shin et al., 2015), diterpenoids (Dong et al., 2016), triterpenes (Kakarla et al., 2016), and norterpenoids (Mohamed-Ibrahim et al., 2018a) have been identified in representatives of this family. The *in vitro* anti-inflammatory mechanism of action of two sesquiterpenes, *α*-cyperone and isocyperol, isolated from the rhizomes of *C. rotundus*, for example, has already been described (Jung et al., 2013; Azimi et al., 2016; Seo et al., 2016; Gao et al., 2021).

To our knowledge, there are no records in the literature of any review on the anti-inflammatory potential of representatives of Cyperaceae conducted exclusively with this family. In this sense, the present study aimed to carry out a systematic review of ethnobotanical, pharmacological, toxicological, and chemical studies conducted with species of Cyperaceae focusing on the treatment of inflammation. In addition to cataloging the species used to treat inflammatory disorders, the likely bioactive constituents of these species were illustrated.

2. Methodology

2.1. Database search

Searches for scientific articles in Google Scholar (https://scholar.google.com, PubMed® (https://pubmed.ncbi.nlm.nih.gov), SciELO (https://search.scielo.org), and Scopus® (https://www.scopus.com) were performed. The keywords used were: "Cyperaceae AND traditional use AND inflammation", "Cyperaceae AND medicinal use AND inflammation", "Cyperaceae AND ethnobotany AND inflammation", "Cyperaceae AND ethnopharmacology AND inflammation", "Cyperaceae AND anti-inflammatory", "Cyperaceae AND toxicity", "Cyperaceae AND toxicology", "Cyperaceae AND phytochemistry AND anti-inflammatory", and "Cyperaceae AND chemical compounds AND anti-inflammatory".

2.2. Inclusion and exclusion criteria

Only scientific articles that addressed specific information on the use of Cyperaceae species in traditional medicine for inflammation, anti-inflammatory activity in *in vivo* and *in vitro* models, and reports on the toxicity of extracts, fractions and the essential oil of the species in addition to isolated chemical compounds with anti-inflammatory potential were selected. Only papers published in the last 31 years (1991-2022) were included in the review. As for exclusion criteria, publications in e-books, book chapters, undergraduate theses, master's theses, doctoral dissertations, and abstracts published in congress proceedings were excluded because these means of communication often present data already published elsewhere. All scientific names were confirmed using World Flora Online (http://www.worldfloraonline.org/).

2.3. Data screening and categorization of information

Two hundred and thirty-four (235) scientific documents were found through the database search. After an initial analysis of titles and abstracts, 114 documents were excluded for not falling within the scope of this review. A total of 121 articles were analyzed in full and 82 articles containing data on traditional use, anti-inflammatory activity, toxicity, and chemical compounds of Cyperaceae species were considered in the present work (Fig. 1, Table S1). The information found was categorized into: 1) "Cyperaceae species traditionally used for the treatment of inflammation"; 2) "Anti-inflammatory potential of Cyperaceae species"; 3) "Toxicity of Cyperaceae species"; and 4) "Phytochemicals of Cyperaceae species with anti-inflammatory potential".

3. Results and discussion

3.1. Cyperaceae species traditionally used for the treatment of inflammation

A total of 10 species of Cyperaceae used in traditional medicine in several countries for the treatment of inflammation were found (Table 1). The species traditionally referred to as medicinal plants belong to the genera *Cyperus* (7), *Rhynchospora* (1), *Scirpoides* (1), and *Scleria* (1). *Cyperus rotundus* (Fig. 2A) was the species with the highest number of indications in folk medicine for the treatment of inflammation and has been widely evaluated for this purpose through *in vitro* and *in vivo* assays (Dang et al., 2011; Tsoyi et al., 2011; Kumar et al., 2012; Jung et al., 2013; Soumaya et al., 2013; Rocha et al., 2020). In Brazil, *R. nervosa* (Fig. 2B) is a native and endemic species with some indications for the treatment of inflammation. Recently, we demonstrated that the lyophilized hydroalcoholic extract of *R. nervosa* showed significant anti-inflammatory and antinociceptive activity *in vivo* using heterogenic Swiss mice (Bezerra et al., 2022).

The whole plant (34%) is more often used by traditional communities in the preparation of herbal medicines based on Cyperaceae species for the treatment of inflammation. The following plant organs were also mentioned in the articles: roots (23%), rhizomes (13%), tubers (10%), stems (7%), bulbs (7%), corms (3%), and leaves (3%). The traditional pharmaceutical formulations most used in the treatment of inflammation were teas (Moreira et al., 2002; Duarte et al., 2007; Parada et al., 2009; Gomez et al., 2016; Napagoda et al., 2018; Ali and Ahmed, 2020), powder (Qasim et al., 2014; Tufail et al., 2020), paste (Kumar et al., 2015; Penchala et al., 2018), macerate (Ribeiro et al., 2017), extract (Amjad et al., 2017), and essential oil (Oliveira et al., 2019).

The use of Cyperaceae species for inflammation was reported in countries on the Asian (India, Pakistan, Sri Lanka), African (Angola, South Africa, Sudan), European (Spain), and South American (Brazil) continents (Fig. 3). *Cyperus rotundus*, the most studied species of this family, stands out for its wide traditional use in Asian countries (Khalid and Siddiqui, 2014; Peerzada et al., 2015; Dhar et al., 2017). In India and Pakistan, the whole plant and the roots, tubers, rhizomes, and bulbs of *C. rotundus* are used in the form of decoction, infusion, powder, paste, and extract (Qureshi et al., 2008; Ahmad et al., 2014a; Ajaib et al., 2014; Qasim et al., 2014; Kumar et al., 2015; Ghulam et al., 2015; Maitreya, 2015; Parul, 2015; Amjad et al., 2017; Vijayashalini et al., 2017; Penchala et al., 2018; Fatima et al., 2019; Rehman et al., 2020; Tufail et al., 2020).

In South America, specifically in Brazil, there are records of indications of *C. articulatus* and *C. rotundus* to treat cases of inflammation. The roots and bulbs of *C. articulatus*, for example, are used in the preparation of decoctions and for the extraction of essential oil (Duarte et al., 2007; Bersan et al., 2014; Oliveira et al., 2019). The stem of *C. rotundus* is usually used in the preparation of decoctions by traditional peoples in the state of Bahia, in the Northeast region of the country (Borges and Bautista, 2010). In addition to these two species, *R. nervosa* also stands out for being used by communities in Bahia, where it is popularly known as star grass, to treat inflammation; the whole plant is used in the preparation of teas to this end (Moreira et al., 2002; Gomez et al., 2016; Santana et al., 2016). Other Cyperaceae species with a lower number of indications for the treatment of inflammation in some regions of the world are *C. alopecuroides* in Sudan (Ali and Ahmed, 2020), *C. distans* in India (Mir et al., 2018), *C. glomeratus* in Pakistan (Ikram et al., 2014), *C. papyrus* in South Africa (Mhlongo and Wyk, 2019), *S. holoschoenus* in Spain (Parada et al., 2009), and *S. gaertneri* in Brazil (Ribeiro et al., 2017).

The number of indications of Cyperaceae species for the treatment of inflammation is low compared to that of species of others botanical families frequently reported in ethnopharmacological surveys to present this application. According to Namsa et al. (2009); Bussa and Belayneh (2019); Khumalo et al., (2021), Asteraceae, Fabaceae, Euphorbiaceae, and Apocynaceae have several representatives used medicinally for the treatment of inflammatory disorders. However, it is worth noting that the number of species belonging to the family Cyperaceae is drastically smaller when compared to Asteraceae and Fabaceae, for example.

3.2. Anti-inflammatory potential of Cyperaceae species

In vivo and *in vitro* anti-inflammatory activity was reported for 13 species of Cyperaceae (Table 2). The genus with the highest number of studies was *Cyperus* (7), followed by *Bulbostylis*, *Bolboschoenus*, *Eleocharis*, *Fimbristylis*, *Remirea*, and *Rhynchospora*, with only one species studied each. Among the species belonging to the genus *Cyperus*, *C. rotundus* stood out with the largest number of studies on anti-inflammatory potential (Biradar et al., 2010; Dang et al., 2011; Tsoyi et al., 2011; Kumar et al., 2012; Mohammed et al., 2014; Ahmad et al., 2014b; Rajamanickam and Rajamanickam, 2016; Rocha et al., 2020), which is in line with the significant number of indications in traditional medicine for the treatment of inflammation.

3.2.1. In vitro anti-inflammatory activity

Regarding the *in vitro* assays conducted with *C. rotundus*, Seo et al. (2001) reported that the methanol extract of the rhizomes of this species significantly reduced the production of nitric oxide (NO) in lipopolysaccharide (LPS) and interferon-*γ* (IFN-*γ*) activated macrophages (RAW 264.7). Similar results were observed by Tsoyi et al. (2011), where the methanol extract of *C. rotundus* rhizomes significantly reduced the levels of inducible nitric oxide synthase (iNOS) and NO production in culture medium in LPS-stimulated macrophages. According to Jung et al. (2013), the ethanol extract and the *n*-hexane fraction of *C. rotundus* significantly inhibited NO production without any cytotoxicity in LPS-activated RAW 264.7 cells. Furthermore, these authors found, for the first time, that the extract from this species can suppress the production of prostaglandin E2 (PGE2), a key mediator in several inflammatory diseases. Kakarla et al. (2014) found that the methanol extract of *C. scariosus* rhizomes inhibited the denaturation of bovine serum albumin (BSA) *in vitro* in a dose-dependent manner at concentrations of 50–5000 µg/mL.

According to Elshamy et al. (2017), the ethanol extract and the methanol fraction of the aerial parts of *C. laevigatus* L. decreased NO accumulation in LPS-activated macrophages. Sukjamnong and Santiyanont (2015) reported that the polar and non-polar extracts of *F. ovata* (Burm.f.) J.Kern not only suppressed the secretion of the pro-inflammatory cytokine IL-6 in U937 cells and the cell adhesion molecule VCAM-1 in bEnd.3 cells *in vitro*, but also inhibited the activation of the receptor for advanced glycation end-products (RAGE), suggesting that this plant may be useful for treating chronic inflammation. From an *in vitro* study with LPS-induced RAW 264.7 cells, Kim et al. (2020) reported that the ethanol extract and sub-fractions of *E. kuroguwai* Ohwi significantly inhibited NO production.

3.2.2. In vivo anti-inflammatory activity

The *in vivo* anti-inflammatory potential of *C. rotundus* was investigated by the methods of carrageenan-induced paw edema and xylene-induced ear edema in rats and mice (Kumar et al., 2012; Soumaya et al., 2013; Rajamanickam and Rajamanickam, 2016). According to Kumar et al. (2012), the dose of 1000 mg/kg of the methanol extract of this species showed a maximum inhibition of 57.5% of paw edema in rats when compared to the control. Polar and non-polar extracts of *C. rotundus* administered at a dose of 300 mg/kg showed a significant inhibitory effect against xylene-induced ear edema in mice (Soumaya et al., 2013). Similar results were reported by Rajamanickam and Rajamanickam (2016), showing that different extracts of this species were effective in inhibiting carrageenan-induced paw edema in mice.

In a study by Chaulya et al. (2012), it was observed that the methanol extract of *C. pangorei* Rottb. at doses of 250 and 500 mg/kg reduced by 49.57% and 86.40%, respectively, the paw edema in mice. According to Owoyele et al. (2015), a dose equivalent to 50 mg/kg of ethanolic extract of *B. coleotricha* C.B.Clarke inhibited by 92% the carrageenan-induced paw edema in Wistar rats. Rabelo et al. (2013) observed that the aqueous extract of *R. maritima* Aubl. inhibited the migration of leukocytes in the peritoneal fluid of mice and suggested that a possible mechanism associated with this activity could be the inhibition of the synthesis of many inflammatory mediators involved in cell migration.

Recently, the anti-inflammatory activity of the hydroalcoholic extract of *R. nervosa* was investigated by our group (Bezerra et al., 2022). Our findings showed promising anti-inflammatory activity from the first to the fifth hour of observation, with an average of 96.37% inhibition of carrageenan-induced paw edema in mice. The observed effect was similar to that of indomethacin. A high content of phenolic compounds and total flavonoids was found in the extracts.

3.3. Toxicity of Cyperaceae species

A total of seven Cyperaceae species have been evaluated for their toxicity. Overall, no typical clinical signs of intoxication were observed in animal models treated with extracts and other products obtained from Cyperaceae species reported for the treatment of inflammation (Imam and Sumi, 2014; Badgujar and Bandivdekar, 2015; Okwu et al., 2015; Singh et al., 2015; Shakerin et al., 2020; Bezerra et al., 2022). According to Imam and Sumi (2014), the hydromethanolic extract of *C. rotundus* did not cause mortality, behavioral changes or allergic reactions in mice up to a dose of 3000 mg/kg. Badgujar and Bandivdekar (2015) observed no behavioral changes or deaths in rats when receiving a dose of 2000 mg/kg of the aqueous extract of this species. Similar results were observed by Singh et al. (2015) in the oral administration of the ethanol extract of *C. rotundus* rhizomes in mice.

The acute toxicity of the essential oil of *C. articulatus* rhizomes caused no mortality in mice during 14 days of follow-up (Metuge et al., 2014), and rough hair and weight loss were observed in only one of the six mice evaluated. In another study, no significant clinical changes or mortality were observed in mice that received a dose equivalent to 2,000 mg/kg of the essential oil of *C. articulatus* (Silva et al., 2019).

The acute toxicity of the aqueous extract of *C. esculentus* L. tubers was evaluated in mice at doses of 500, 1000, 1500, and 2000 mg/kg (Chukwuma et al., 2010). No abnormalities

were found. The hydroethanolic extract of this species, up to the dose of 5000 mg/kg, did not cause significant mortality or behavioral changes in rats either (Nwangwa et al., 2020).

Studies performed with *C. scariosus* did not find any type of toxicity when mice were subjected to treatment with the methanol and hexane extracts of this species (Alam et al., 2011; Ramesh et al., 2012). The acute toxicity of the methanol extract of *C. pangorei* did not cause mortality in mice either, however, a sedative effect was observed in the animals (Chaulya et al., 2011). Vanapatla et al. (2011) found that the fractions obtained from the roots of *Cyperus dubius* Rottb. showed no adverse effects and mortality in rats during the study period. According to Bezerra et al. (2022), the lyophilized hydroalcoholic extract of *R. nervosa* showed low acute toxicity in mice in preclinical tests (LD_{50} = 3807 mg/kg).

Based on the above studies, it appears that the use of Cyperaceae extracts for the treatment of inflammation and other diseases has some degree of safety due to the near absence of toxicity in the models tested.

3.4. Phytochemicals of Cyperaceae species with anti-inflammatory potential

A total of 50 chemical compounds were isolated from Cyperaceae species and they present potential to be used against inflammatory processes (Table 3). These substances belong to the classes of sesquiterpenes (Khan et al., 2011; Kim et al., 2013; Seo et al., 2016; Azimi et al., 2016), phenolic compounds (Rabelo et al., 2013; Elshamy et al., 2017), benzenoids (Rabelo et al., 2014), phytosterols (Mohammed et al., 2014), unsaturated fatty acids (Shin et al., 2015), diterpenoids (Dong et al., 2016), triterpenes (Kakarla et al., 2016), and norterpenoids (Mohamed-Ibrahim et al., 2018a).

Cyperus rotundus was the species with the highest number of isolated compounds (28) with anti-inflammatory potential. Sesquiterpenes from this species are the main substances used in assays to investigate anti-inflammatory activity *in vitro* (Khan et al., 2011; Kim et al., 2013; Jung et al., 2013; Seo et al., 2016; Azimi; et al., 2016; Mohamed-Ibrahim et al., 2018a). The sesquiterpenes nootkatone and α-cyperone, for example, isolated from *C. rotundus*, showed inhibition of iNOS and cyclooxygenase-2 (COX-2) expression in LPS-activated macrophages (Khan et al., 2011). α-Cyperone also downregulates nuclear factor-kappa B (NF-κB) signaling, the expression of metalloproteinases (MMPs) and thrombospondin motifs 5 (ADAMTS5), and decreases the phosphorylation of mitogen-activated protein kinase (MAPKs) in isolated rat chondrocytes (Zhang et al., 2021). Other sesquiterpene compounds with anti-inflammatory activity are shown in Table 3.

In addition to sesquiterpenes, phenolic compounds, mainly flavonoids, with anti-inflammatory potential have been identified in different species of Cyperaceae, especially in the genus *Cyperus* (Table 3). According to the literature, flavonoids, are the main anti-inflammatory agents found in plant extracts. These compounds have a broad spectrum of action and the ability to intervene at various levels of the immune response (Talhouk et al., 2007; Salaritabar et al., 2017).

According to Lee et al. (1998), the *in vitro* anti-inflammatory activity exhibited by *α*-viniferin, the stilbene trimer isolated from the roots of *C. humilis* Kunth, could be related to the inhibitory effects on the activities of cyclooxygenase and protein kinase C. Sparstolonin B, an anthracene compound, and other compounds isolated from *Bolboschoenus yagara* (Ohwi) Y.C.Yang & M.Zhan showed significant anti-inflammatory activity on tumor necrosis factor-*α* (TNF-*α*) and interleukin-6 (IL-6) levels in LPS- or Pam3csk4-stimulated macrophages, with IC_{50} values varying between 0.34-16.57 μM (Dong et al., 2016).

The flavonoids orientin, quercetin 3-O-*β*-D-glucopyranoside, cyperaflavoside, and myrcetin 3-O-*β*-D -glucopyranoside isolated from the aerial parts of *C. rotundus* exhibited 5-LOX (5-lipoxygenase) inhibitory activities with IC_{50} values of 4.5, 4.0, 3.7, and 2.3 μM, respectively (Mohamed-Ibrahim et al., 2018b). Chemical compounds with inhibitory activity on 5-LOX are important, considering that this enzyme plays an important role in the formation of leukotrienes (LTC4, LTD4, and LTE4), which are reported as potent bronchoconstrictors and pro-inflammatory mediators (Masferrer et al., 2010; Lin et al., 2014). Rocha et al. (2020) found a topical anti-inflammatory activity in rats using models of irritative dermatitis and cutaneous hyperproliferation after administration of the ethanol extract of *C. rotundus* rhizomes. HPLC analyses identified 45 μg/g of chlorogenic acid in the extracts. According to Francisco et al. (2013), chlorogenic acid has anti-inflammatory activity and its effect is possibly related to down-regulation of the NF-κB pathway. Synthetic aureusidin, a flavonoid, also showed significant anti-inflammatory activity by blocking the NF-κB signaling pathways and activating the MAPKs signaling pathways (Ren et al., 2020). Aureusidin is found in several genera of Cyperaceae, such as *Lepironia*, *Eleocharis*, *Scirpus*, *Schoenus*, *Gahnia*, *Ptilanthelium*, and *Cyperus* (Clifford and Harborne, 1969; Harborne et al., 1982).

Lupeol, a triterpene isolated from the rhizomes of *C. rotundus* and *C. scariosus*, showed potent inhibition of interleukin-1β (IL-1β) activity in THP-1 monocytic cells and significant anti-inflammatory activity *in vivo* (Kakarla et al., 2016). Compounds belonging to the benzenoid class such as dihydroremirol, iso-evodionol, and remirol may be associated with the *in vitro* and *in vivo* anti-inflammatory potential of *C. pedunculatus* (R.Br.) J.Kern and *R.*

maritima (Siani et al., 2001; Rabelo et al., 2014). The anti-inflammatory activity of fulgidic acid, an unsaturated trihydroxy C18 fatty acid isolated from the rhizomes of *C. rotundus*, inhibited the production of NO, PGE2, TNF-α, and IL-6 in LPS-activated RAW264.7 macrophages (Shin et al., 2015).

The anti-inflammatory activity of natural compounds and their molecular targets based on non-Cyperaceae plants has been summarized by Gupta et al. (2021).

4. Concluding remarks and future perspectives

In this study, the traditional use of Cyperaceae species against inflammation, *in vivo* and *in vitro* anti-inflammatory assays conducted with these plants, the toxicity of the extracts, and the chemical compounds isolated from the species were reviewed based on works published in the last 30 years. Although Cyperaceae species are traditionally used as medicines in several countries around the world, it is noteworthy that of the nearly 5,000 species hitherto known to science, only 10 are used for the treatment of inflammation and 13 have been the target of pharmacological studies. This number is much lower than that observed for species of other families. This may be related to the fact that Cyperaceae species are generically considered as weeds and, thus, of little interest for pharmacological and chemical research. It is also clear that there are some gaps about the parts of the plants used for medicinal purposes, methods of preparation, and routes of administration of the phytomedicines. We hope this information stimulates further ethnopharmacological studies.

From a chemical point of view, several chemical compounds have already been isolated and some of them, such as flavonoids and sesquiterpenes, stand out in tests as candidates for natural anti-inflammatory drugs. Besides anti-inflammatory action, the products evaluated showed negligible toxicity in pre-clinical tests, which is very important when contrasted with commercial drugs used for inflammation. The carrageenan-induced paw edema model, a well-defined model of acute inflammation that involves a variety of inflammatory mediators, has widely been used to evaluate the anti-edematous effect of Cyperaceae products. The inhibition of the NF-κB signaling pathway and of some chemical mediators of inflammation has been shown to be one of the mechanisms involved in the anti-inflammatory activity of some representatives of Cypereceae with anti-inflammatory potential.

Finally, *Cyperus rotundus* stood out with the largest number of studies on anti-inflammatory potential. However, it is still important to highlight that other species traditionally indicated for the treatment of inflammation (e.g., *Cyperus alopecuroides*, *Cyperus articulatus*, *Cyperus distans*, *Cyperus glomeratus*, *Cyperus papyrus*, *Scirpoides. holoschoenus*, and *Scleria*

gaertneri) also deserve to be investigated to validate or refute the medicinal indications popularly suggested.

Declaration of Competing Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Funding

This study was financed in part by the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES) - Finance Code 001.

Acknowledgements

The first author is grateful to the National Council for Scientific and Technological Development (CNPq – Brazil) for granting PhD scholarships. The last author is also grateful to the CNPq for the award of a Research Fellowship (Process 310811/2019-8).

References

Agarwal, H., Nakara, A., Shanmugam, V.K., 2019. Anti-inflammatory mechanism of various metal and metal oxide nanoparticles synthesized using plant extracts: A review. Biomed. Pharmacother. 109, 2561-2572. https://doi.org/10.1016/j.biopha.2018.11.116

Ahmad, S., Alam, K., Wariss, H.M., Anjum, S., Mukhtar, M., 2014a. Ethnobotanical studies of plant resources of Cholistan desert, Pakistan. Int. J. Sci. Res. 3, 1782-1788.

Ahmad, M., Rookh, M., Rehman, A.B., Muhammad, N., Younus, M., Wazir, A., 2014b. Assessment of anti-inflammatory, anti-ulcer and neuropharmacological activities of *Cyperus rotundus* Linn. Pak. J. Pharm. Sci. 27, 2241-2246.

Ajaib, M., Khan, Z., Zikrea, A., 2014. Ethnobotanical survey of some important herbaceous plants of District Kotli, Azad Jammu & Kashmir. Biologia (Pakistan). 601, 11-22.

Alam, M.A., Jahan, R., Rahman, S., Das, A.K., Rahmatullah, M., 2011. Antinociceptive and anti-hyperglycemic activity of methanol leaf extract of *Cyperus scariosus*. Pak. J. Pharm. Sci. 24, 53-56.

Ali, M.A.B., Ahmed, H.A.A.M., 2020. Ethnobotanical Studies of flora of Jebel Aulia district, Khartoum state with emphasis to toxicity of the common medicinal plants. J. Agric. Environ. Vet. Sci. 4, 67-85. https://doi.org/10.26389/AJSRP.L180620

Amjad, M.S., Arshad, M., Saboor, A., Page, S., Chaudhari, S.K., 2017. Ethnobotanical profiling of the medicinal flora of Kotli, Azad Jammu and Kashmir, Pakistan: Empirical reflections on multinomial logit specifications. Asian Pac. J. Trop. Med. 10, 503-514. https://doi.org/10.1016/j.apjtm.2017.05.008

Azimi, A., Ghaffari, S.M., Riazi, G.H., Arab, S.S., Tavakol, M.M., Pooyan, S., 2016. *α*-Cyperone of *Cyperus rotundus* is an effective candidate for reduction of inflammation by destabilization of microtubule fibers in brain. J. Ethnopharmacol. 194, 219-227. https://doi.org/10.1016/j.jep.2016.06.058

Badgujar, S.B., Bandivdekar, A.H., 2015. Evaluation of a lactogenic activity of an aqueous extract of *Cyperus rotundus* Linn. J. Ethnopharmacol. 163, 39-42. https://doi.org/10.1016/j.jep.2015.01.019

Bersan, S.M., Galvão, L.C., Goes, V.F., Sartoratto, A., Figueira, G.M., Rehder, V.L., et al., 2014. Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms. BMC Complement. Altern. Med. 14, 451. https://doi.org/10.1186/1472-6882-14-451

Bezerra, J.J.L., Oliveira, J.R.S., Lima, V.L.M., Silva, M.V., Araújo, D.R.C., Oliveira, A.F.M., 2022. Evaluation of the anti-inflammatory, antipyretic and antinociceptive activities of the hydroalcoholic extract of *Rhynchospora nervosa* (Vahl) Boeckeler (Cyperaceae). J. Ethnopharmacol. 284. http://doi:10.1016/j.jep.2021.114811

Biradar, S., Kangralkar, V.A., Mandavkar, Y., Thakur, M., Chougule, N., 2010. Antiinflammatory, antiarthritic, analgesic and anticonvulsant activity of *Cyperus* essential oils. Int. J. Pharm. Pharm. Sci. 2, 112-115.

Borges, K.N., Bautista, H., 2010. Etnobotânica de plantas medicinais na comunidade de Cordoaria, litoral norte do estado da Bahia, Brasil. Plurais – Rev. Multidisciplinar. 1, 153-174. https://doi.org/10.29378/plurais.2447-9373.2010.v1.n2.%p

Brune, K., Patrignani, P., 2015. New insights into the use of currently available non-steroidal anti-inflammatory drugs. J Pain Res. 8, 105-118. https://doi.org/10.2147/JPR.S75160

Bussa, N.F., Belayneh, A., 2019. Traditional medicinal plants used to treat cancer, tumors and inflammatory ailments in Harari Region, Eastern Ethiopia. S. Afr. J. Bot. 122, 360-368. https://doi.org/10.1016/j.sajb.2019.03.025

Cao, Q.Y., Guo, X.Y., Duan, J.A., Liang, Q.L., 2020. The active fraction from the tuber of *Bolboschoenus yagara* inhibits melanoma B16 cells metastasis LPS-induced in vitro and *in vivo*. Nat. Prod. Res. 34, 3378-3381. https://doi.org/10.1080/14786419.2019.1566722

Chaulya, N.C., Haldar, P.K., Mukherjee, A., 2011. Antidiabetic activity of methanol extract of rhizomes of *Cyperus tegetum* Roxb. (Cyperaceae). Acta Pol. Pharm. 68, 989-992.

Chaulya, N.C., Haldar, P.K., Mukherjee, A., 2012. Anti-inflammatory and Analgesic Activity of Methanol Extracts of *Cyperus tegetum* Roxb. Rhizome. J. PharmaSciTech. 1, 27-29.

Chukwuma, E.R., Obioma, N., Christopher, O.I., 2010 The phytochemical composition and some biochemical effects of Nigerian tigernut (*Cyperus esculentus* L.) tuber. Pak. J. Nutr. 9, 709-715. https://doi.org/10.3923/pjn.2010.709.715

Chung, E.Y., Kim, B.H., Lee, M.K., Yun, Y.P., Lee, S.H., Min, K.R., Kim, Y., 2003. Anti-inflammatory effect of the oligomeric stilbene α-viniferin and its mode of the action through inhibition of cyclooxygenase-2 and inducible nitric oxide synthase. Planta Med. 69, 710-714. https://doi.org/10.1055/s-2003-42787

Clifford, H.T., Harborne, J.B., 1969. Flavonoid pigmentation in the sedges (Cyperaceae). Phytochemistry. 8, 123-126. https://doi.org/10.1016/S0031-9422(00)85804-5

Dang, G.K., Parekar, R.R., Kamat, S.K., Scindia, A.M., Rege, N.N., 2011. Antiinflammatory activity of *Phyllanthus emblica, Plumbago zeylanica* and *Cyperus rotundus* in acute models of inflammation. Phytother. Res. 25, 904-908. https://doi.org/10.1002/ptr.3345

Dhar, P., Dhar, D. G., Rawat, A. K. S., Srivastava, S., 2017. Medicinal chemistry and biological potential of *Cyperus rotundus* Linn.: An overview to discover elite chemotype (s) for industrial use. Ind. Crops Prod. 108, 232-247. https://doi.org/10.1016/j.indcrop.2017.05.053

Dong, S.H., Zhang, J.F., Tang, Y.M., Li, J., Xiang, Y.R., Liang, Q.L., 2016. Chemical constituents from the tubers of *Scirpus yagara* and their anti-inflammatory activities. J. Asian Nat. Prod. Res. 18, 791-797. http://dx.doi.org/10.1080/10286020.2016.1158166

Duarte, M.C.T., Leme, E.E., Delarmelina, C., Soares, A.A., Figueira, G.M., Sartoratto, A., 2007. Activity of essential oils from Brazilian medicinal plants on *Escherichia coli*. J. Ethnopharmacol. 111, 197-201. https://doi.org/10.1016/j.jep.2006.11.034

Elshamy, A.I., El-Shazly, M., Yassine, Y.M., El-Bana, M.A., Farrag, A.R., Nassar, M.I., et al., 2017. Phenolic constituents, anti-inflammatory and antidiabetic activities of *Cyperus laevigatus* L. Pharmacogn. J. 9, 828-833. https://doi.org/10.5530/pj.2017.6.129

Fatima, I., Munawar, M., Iqbal, S., Sadaf, Z., 2019. Ethno-medicinal uses of wild herbs and shrubs of Tehsil Yazman, Punjab, Pakistan. Pak. J. Agri. Sci. 56, 735-741. https://doi.org/10.21162/PAKJAS/19.6930

Francisco, V., Costa, G., Figueirinha, A., Marques, C., Pereira, P., Miguel Neves, B., Celeste Lopes, M., García-Rodríguez, C., Teresa Cruz, M., Batista, M.T., 2013. Anti-inflammatory activity of *Cymbopogon citratus* leaves infusion via proteasome and nuclear factor-κB pathway inhibition: contribution of chlorogenic acid. J. Ethnopharmacol. 148, 126–134. https://doi.org/10.1016/j.jep.2013.03.077

Gao, P., Ding, N., Lv, J., Ramzan, M. N., & Wen, Q., 2021. α-Cyperone inhibitory effects on tumor-derived DNA trigger microglia by STING pathway. J. Ethnopharmacol. 264, 113246. https://doi.org/10.1016/j.jep.2020.113246

Ghulam Y., Manik, S.R., Shravagi, N., Nathar, V.N., Saudagar, S.A.A.G., Aabid, M., Mohd, J., 2015. Ethnobotanical study of common medicinal plants used by the people of village Fubgaon, District Amravati Maharashtra, India. Int. J. Int. J. Cur. Tr. Res. 4, 29-34.

Gomez, M., Rocha, E.A., Gomberg, E., 2016. Análise das publicações etnobotânicas sobre plantas medicinais da Mata Atlântica na Região Sul do Estado da Bahia, Brasil. Rev. Fitos. 10, 115-140. https://doi.org/10.5935/2446-4775.20160010

Gupta, M., Singh, N., Gulati, M., Gupta, R., Sudhakar, K., Kapoor, B. 2021. Herbal bioactives in treatment of inflammation: An overview. S. Afr. J. Bot. 143, 205-225. https://doi.org/10.1016/j.sajb.2021.07.027

Harborne, J.B., Williams, C.A., Wilson, K.L., 1982. Flavonoids in leaves and inflorescences of Australian *Cyperus* species. Phytochemistry. 21, 2491-2507. https://doi.org/10.1016/0031-9422(82)85246-1

Ikram, S., Bhatti, K.H., Parvaiz, M., 2014. Ethnobotanical studies of aquatic plants of district Sialkot, Punjab (Pakistan). J. Med. Plants Stud. 2, 58-63.

Imam, M.Z., Sumi, C.D., 2014. Evaluation of antinociceptive activity of hydromethanol extract of *Cyperus rotundus* in mice. BMC Complement. Altern. Med. 14, 83. https://doi.org/10.1186/1472-6882-14-83

Jung, S.H., Kim, S.J., Jun, B.G., Lee, K.T., Hong, S.P., Oh, M.S., Jang, D.S., Choi, J.H., 2013. α-Cyperone, isolated from the rhizomes of *Cyperus rotundus*, inhibits LPS-induced COX-2 expression and PGE2 production through the negative regulation of NFκB signalling in RAW 264.7 cells. J. Ethnopharmacol. 147, 208-214. https://doi.org/10.1016/j.jep.2013.02.034

Juthani, V.V., Clearfield, E., Chuck, R.S., 2017. Non-steroidal anti-inflammatory drugs versus corticosteroids for controlling inflammation after uncomplicated cataract surgery. Cochrane Database Syst. Rev. 7, 1-158. https://doi.org/10.1002/14651858.CD010516.pub2

Kakarla, L., Mathi, P., Allu, P.R., Rama, C., Botlagunta, M., 2014. Identification of human cyclooxegenase-2 inhibitors from *Cyperus scariosus* (R. Br) rhizomes. Bioinformation. 10, 637-646. https://doi.org/10.6026/97320630010637

Kakarla, L., Katragadda, S.B., Tiwari, A.K., Kotamraju, K.S., Madhusudana, K., Kumar, D.A., Botlagunta, M., 2016. Free radical scavenging, α-glucosidase inhibitory and anti-inflammatory constituents from Indian sedges, *Cyperus scariosus* R. Br and *Cyperus rotundus* L. Pharmacogn. Mag. 12, 488-496. https://doi.org/10.4103/0973-1296.191467

Kazemi, S., Shirzad, H., Rafieian-Kopaei, M., 2018. Recent findings in molecular basis of inflammation and anti-inflammatory plants. Curr. Pharm. Des. 24, 1551-1562. https://doi.org/10.2174/1381612824666180403122003

Khalid, S., Siddiqui, S.U., 2014. Weeds of Pakistan: Cyperaceae. Pak. J. Weed Sci. Res. 20, 233-263.

Khan, S., Choi, R.J., Lee, D.U., Kim, Y.S., 2011. Sesquiterpene derivatives isolated from *Cyperus rotundus* L. inhibit inflammatory signaling mediated by NF-kB. Nat. Prod. Sci. 17, 250-255.

Khumalo, G.P., Van Wyk, B.E., Feng, Y., Cock, I.E., 2021. A review of the traditional use of southern African medicinal plants for the treatment of inflammation and inflammatory pain. J. Ethnopharmacol. 114436. https://doi.org/10.1016/j.jep.2021.114436

Kim, S.J., Ryu, B., Kim, H.Y., Yang, Y.I., Ham, J., Choi, J.H., Jang, D.S., 2013. Sesquiterpenes from the rhizomes of *Cyperus rotundus* and their potential to inhibit LPS-induced nitric oxide production. Bull. Korean Chem. Soc. 34, 2207-2210. http://dx.doi.org/10.5012/bkcs.2013.34.7.2207

Kim, K.H., Bae, E.Y., Lim, H.G., Kim, M.H., Oh, T.S., Lee, S.W., 2020. *Eleocharis kuroguwai* Ohwi Ameliorates LPS-mediated Inflammation by Suppressing MAPKs Signaling. J. Life Sci. 30, 476-482. https://doi.org/10.5352/JLS.2020.30.5.476

Kumar, S., Tiwari, R., Alam, N., 2012. Anti-inflammatory activity of methanolic extract of *Cyperus rotundus* rhizome on carrageenan induced paw edema in rats. Int. J. Pharm. Sci. Res. 3, 5097-5100. http://dx.doi.org/10.13040/IJPSR.0975-8232.3(12).5097-00

Kumar, K., Sharma, Y.P., Manhas, R.K., Bhatia, H., 2015. Ethnomedicinal plants of Shankaracharya Hill, Srinagar, J&K, India. J. Ethnopharmacol. 170, 255-274. https://doi.org/10.1016/j.jep.2015.05.021

Kumari, R., Kumar, A., Kumar, B., 2019. Ethnobotanical Investigation of Medicinal Plants used by Rural Communities of District Chatra, Jharkhand, India. IOSR J. Biotechnol. Biochem. 5, 34-49. https://doi.org/10.9790/264X-0506013449

Lee, S.H., Shin, N.H., Kang, S.H., Park, J.S., Chung, S.R., Min, K.R., Kim, Y., 1998. α-Viniferin: a prostaglandin H2 synthase inhibitor from root of *Carex humilis*. Planta Med. 64, 204-207. https://doi.org/10.1055/s-2006-957409

Li, P., Liang, Q.L., Cui, X.D., Li, J., Zou, N.S., Wu, Q.N., Duan, J.A., 2014. Protective effects of the active fraction from the tuber of *Scirpus yagara* in mouse endotoxin shock model. J. Ethnopharmacol. 158, 331-337. https://doi.org/10.1016/j.jep.2014.10.032

Lin, H.C., Lin, T.H., Wu, M.Y., Chiu, Y.C., Tang, C.H., Hour, M.J., et al., 2014. 5-Lipoxygenase inhibitors attenuate TNF-α-induced inflammation in human synovial fibroblasts. PLoS One, 9, e107890. https://doi.org/10.1371/journal.pone.0107890

Maione, F., Russo, R., Khan, H., Mascolo, N., 2015. Medicinal plants with anti-inflammatory activities. Nat. Prod. Res. 30, 1343-1352. https://doi.org/10.1080/14786419.2015.1062761

Maitreya, B.B., 2015. Ethnomedicinal values of some weed plant species of Bhavnagar, Gujarat, India. Int. J. Emerg. Trends Sci. Technol. 2, 2675-2681.

Masferrer, J. L., Zweifel, B. S., Hardy, M., Anderson, G. D., Dufield, D., Cortes-Burgos, L., et al. 2010. Pharmacology of PF-4191834, a novel, selective non-redox 5-lipoxygenase inhibitor effective in inflammation and pain. J. Pharmacol. Exp. Ther. 334, 294-301. https://doi.org/10.1124/jpet.110.166967

Metuge, J.A., Nyongbela, K.D., Mbah, J.A., Samje, M., Fotso, G., Babiaka, S.B., Cho-Ngwa, F., 2014. Anti-Onchocerca activity and phytochemical analysis of an essential oil from *Cyperus articulatus* L. BMC Complement. Altern. Med. 14, 223. https://doi.org/10.1186/1472-6882-14-223

Mhlongo, L.S., Wyk, B.E.V., 2019. Zulu medicinal ethnobotany: New records from the Amandawe area of KwaZulu-Natal, South Africa. S. Afr. J. Bot. 122, 266-290. https://doi.org/10.1016/j.sajb.2019.02.012

Mir, T.A., Jan, M., Dhyani, S., 2018. A Comprehensive account of ethno-medicinal uses of monocot flora (reported from February–June) of Karwapani forest Doon valley-Uttarakhand. SERBD-Int. J. Multidiscip. Sci. 1, 22-27.

Mohamed-Ibrahim, S.R. Mohamed, G.A., Khayat, M.T.A., Zayed, M.F., El-Kholy, A.A.E.S., 2018a. Anti-inflammatory terpenoids from *Cyperus rotundus* rhizomes. Pak. J. Pharm. Sci. 31, 1449-1456.

Mohamed-Ibrahim, S.R., Mohamed, G.A., Alshali, K.Z., Haidari, R.A.A., El-Kholy, A.A., Zayed, M.F., 2018b. Lipoxygenase inhibitors flavonoids from *Cyperus rotundus* aerial parts. Rev. Bras. Farmacogn. 28, 320-324. https://doi.org/10.1016/j.bjp.2018.04.002

Mohammed, M.S., Ahmed, W.J., Khalid, H.S., Mahmoud, A.M., Garelnabi, E.A., 2014. Di-(2'-ethylhexyl) phthalate and stigmasterol with antiinflammatory effect from *Cyperus rotundus* L. Int. J. Pharm. Chem. Biol. Sci. 4, 453- 459.

Moreira, R.D.C.T., Costa, L.C.D.B., Costa, R.C.S., Rocha, E.A., 2002. Abordagem etnobotânica acerca do uso de plantas medicinais na Vila Cachoeira, Ilhéus, Bahia, Brasil. Acta Farm. Bonaerense. 21, 205-211.

Namsa, N.D., Tag, H., Mandal, M., Kalita, P., Das, A.K., 2009. An ethnobotanical study of traditional anti-inflammatory plants used by the Lohit community of Arunachal Pradesh, India. J. Ethnopharmacol. 125, 234-245. https://doi.org/10.1016/j.jep.2009.07.004

Napagoda, M.T., Sundarapperuma, T., Fonseka, D., Amarasiri, S., Gunaratna, P., 2018. An ethnobotanical study of the medicinal plants used as anti-inflammatory remedies in Gampaha District, Western Province, Sri Lanka. Scientifica. 2018, 9395052. https://doi.org/10.1155/2018/9395052

Nwangwa, J.N., Udefa, A.L., Amama, E.A., Inah, I.O., Ibrahim, H.J., Iheduru, S.C., et al., 2020. *Cyperus esculentus* L. (tigernut) mitigates high salt diet-associated testicular toxicity in Wistar rats by targeting testicular steroidogenesis, oxidative stress and inflammation. Andrologia. 52, e13780. https://doi.org/10.1111/and.13780

Okwu, G.N., Abanobi, S.E., Nnadi, U.V., Ujowundu, C.O., Ene, A.C., 2015. Hypolipidemic properties of ethanol extract of *Cyperus rotundus* rhizome. Int. J. Biochem. Res. Rev. 7, 132-138. https://doi.org/10.9734/IJBCRR/2015/17158

Oliveira, G.L., Rodrigues, C.J., Santos, P.O., Silva, L.R.C., Santos, A.L., Belasco, I.C., 2019. Plantas medicinais utilizadas nas práticas integrativas e complementares de saúde no Espaço Crescer, Alcobaça, Bahia. Rev. Integrat. Inov. Tecnol. Ciênc. Saúde. 5, 195-218.

Oguntibeju, O.O., 2018. Medicinal plants with anti-inflammatory activities from selected countries and regions of Africa. J. Inflamm. Res. 11, 307-317. https://doi.org/10.2147/JIR.S167789

Owoyele, B.V., Abioye, A.I.R., Oyewole, A.L., Ameen, M.O., Owemidu, I.O., Adewusi M.O., 2015. Effects of the ethanolic extract of *Bulbostylis coleotricha* (Hochst. Exa. Rich.) on inflammation in adult wistar rats. Niger. J. Nat. Prod. Med. 19, 101-105. https://doi.org/10.4314/njnpm.v19i0.11

Padmavathy, A., Anbarashan, M., 2011. Phytomedicinal study of coastal sand dune floras in Puducherry. J. Med. Plant Res. 5, 2566-2571. https://doi.org/10.5897/JMPR.9001015

Parada, M., Carrió, E., Bonet, M. À., Vallès, J., 2009. Ethnobotany of the Alt Emporda region (Catalonia, Iberian Peninsula): plants used in human traditional medicine. J. Ethnopharmacol. 124, 609-618. https://doi.org/10.1016/j.jep.2009.04.050

Parul, B.D.V., 2015. An Ethnobotanical study of plains of Yamuna Nagar District, Haryana, India. Int. J. Innov. Res. Sci. Eng. Technol. 4, 18600-18607. https://doi.org/10.15680/IJIRSET.2015.0401033

Peerzada, A.M., Ali, H.H., Naeem, M., Latif, M., Bukhari, A.H., Tanveer, A., 2015. *Cyperus rotundus* L.: Traditional uses, phytochemistry, and pharmacological activities. J. Ethnopharmacol. 174, 540-560. https://doi.org/10.1016/j.jep.2015.08.012

Penchala, P.G., Husain, M.K., Sudarsanam, G., Alam, M., Khair, S., Kazmi, M.H., 2018. Ethnomedicinal plants used by tribes of chittoor district of Andhra Pradesh to cure muscular pain and inflammation. Int. J. Ayurveda Pharma Res. 6, 8-16.

Pompermaier, L., Marzocco, S., Adesso, S., Monizi, M., Schwaiger, S., Neinhuis, C., Stuppner, H., Lautenschläger, T., 2018. Medicinal plants of northern Angola and their anti-inflammatory properties. J. Ethnopharmacol. 216, 26-36. https://doi.org/10.1016/j.jep.2018.01.019

Qasim, M., Abideen, Z., Adnan, M.Y., Ansari, R., Gul, B., Khan, M.A., 2014. Traditional ethnobotanical uses of medicinal plants from coastal areas. J. Coast. Life Med. 2, 22-30. https://doi.org/10.12980/JCLM.2.2014C1177

Qureshi, S.J., Khan, M.A., Ahmad, M., 2008. A survey of useful medicinal plants of Abbottabad in northern Pakistan. Trakia J. Sci. 6, 39-51.

Rabelo, A.S., Oliveira, I.D., Guimarães, A.G., Quintans, J.S.S., Prata, A.P.N., Gelain, D.P., et al., 2013. Antinociceptive, anti-inflammatory and antioxidant activities of aqueous extract from *Remirea maritima* (Cyperaceae). J. Ethnopharmacol. 145, 11-17. https://doi.org/10.1016/j.jep.2012.10.020

Rabelo, A.S., Serafini, M.R., Rabelo, T.K., Melo, M.G.D., Prado, D.S., Gelain, D.P., et al., 2014. Chemical composition, antinociceptive, anti-inflammatory and redox properties *in vitro* of the essential oil from *Remirea maritima* Aubl. (Cyperaceae). BMC Complement. Altern. Med. 14, 514. https://doi.org/10.1186/1472-6882-14-514

Rajamanickam, M., Rajamanickam, A., 2016. Analgesic and anti-inflammatory activity of the extracts from *Cyperus rotundus* Linn rhizomes. J. Appl. Pharm. Sci. 6, 197-203. https://doi.org/10.7324/JAPS.2016.60929

Ramesh, S., Mahesh, V., Prabhaker, T., 2012. Pharmacological study of anti-depressant like activity of *Cyperus scariosus* oil in mice. Int. Res. J. Pharm. Applied Sci. 2, 139-142.

Recio, M.C., Andujar, I., Rios, J.L., 2012. Anti-inflammatory agents from plants: progress and potential. Curr. Med. Chem. 19, 2088-2103. https://doi.org/10.2174/092986712800229069

Rehman, A., Hussain, K., Nawaz, K., Arshad, N., Iqbal, I., Ali, S.S., et al., 2020. Indigenous knowledge and medicinal significance of seasonal weeds of district Gujrat, Punjab, Pakistan. Ethnobot. Res. Appl. 20, 1-19. http://dx.doi.org/10.32859/era.20.12.1-19

Ribeiro, R.V., Bieski, I.G.C., Balogun, S.O., Martins, D.T.O., 2017. Ethnobotanical study of medicinal plants used by Ribeirinhos in the North Araguaia microregion, Mato Grosso, Brazil. J. Ethnopharmacol. 205, 69-102. https://doi.org/10.1016/j.jep.2017.04.023

Rocha, F.G., Brandenburg, M.M., Pawloski, P.L., Soley, B.S., Costa, S.C.A., Meinerz, C.C., et al., 2020. Preclinical study of the topical anti-inflammatory activity of *Cyperus rotundus* L. extract (Cyperaceae) in models of skin inflammation. J. Ethnopharmacol. 254, 112709. https://doi.org/10.1016/j.jep.2020.112709

Ren, J., Su, D., Li, L., Cai, H., Zhang, M., Zhai, J., Li, M., Wu, H., Hu, K., 2020. Anti-inflammatory effects of aureusidin in LPS-stimulated RAW264.7 macrophages via suppressing NF-κB and activating ROS- and MAPKs-dependent Nrf2/HO-1 signaling pathways. Toxicol. Appl. Pharmacol. 387. http://10.1016/j.taap.2019.114846

Salaritabar, A., Darvishi, B., Hadjiakhoondi, F., Manayi, A., Sureda, A., Nabavi, S. F., Fitzpatrick, L.R., Nabavi, S.M., Bishayee, A., 2017. Therapeutic potential of flavonoids in inflammatory bowel disease: A comprehensive review. World J. Gastroenterol. 23, 5097. https://doi.org/10.3748/wjg.v23.i28.5097

Santana, B.F., Voeks, R.A., Funch, L.S., 2016. Ethnomedicinal survey of a maroon community in Brazil's Atlantic tropical forest. J. Ethnopharmacol. 181, 37-49. https://doi.org/10.1016/j.jep.2016.01.014

Seo, W.G., Pae, H.O., Oh, G.S., Chai, K.Y., Kwon, T.O., Yun, Y.G., et al., 2001. Inhibitory effects of methanol extract of *Cyperus rotundus* rhizomes on nitric oxide and superoxide productions by murine macrophage cell line, RAW 264.7 cells. J. Ethnopharmacol. 76, 59-64. https://doi.org/10.1016/s0378-8741(01)00221-5

Seo, Y.J., Jeong, M., Lee, K.T., Jang, D.S., Choi, J.H., 2016. Isocyperol, isolated from the rhizomes of *Cyperus rotundus*, inhibits LPS-induced inflammatory responses via suppression of the NF-κB and STAT3 pathways and ROS stress in LPS-stimulated RAW 264.7 cells. Int. Immunopharmacol. 38, 61-69. https://doi.org/10.1016/j.intimp.2016.05.017

Shakerin, Z., Esfandiari, E., Razavi, S., Alaei, H., Ghanadian, M., Dashti, G., 2020. Effects of *Cyperus rotundus* extract on spatial memory impairment and neuronal differentiation in rat model of Alzheimer's disease. Adv. Biomed. Res. 9, 17. https://doi.org/10.4103/abr.abr_173_19

Shin, J.S., Hong, Y., Lee, H.H., Ryu, B., Cho, Y.W., Kim, N.J., Jang, D.S., Lee, K.T., 2015. Fulgidic acid isolated from the rhizomes of *Cyperus rotundus* suppresses LPS-induced iNOS, COX-2, TNF-α, and IL-6 expression by AP-1 inactivation in RAW264. 7 macrophages. Biol. Pharm. Bull. 38, 1081-1086. https://doi.org/10.1248/bpb.b15-00186

Siani, A.C., Silva, A.M., Nakamura, M.J., Carvalho, M.V., Henriques, M.G., Ramos, M.F., Kaiser, C.R., 2001. Chemical composition and anti-inflammatory activity of the hydrodistillate from *Mariscus pedunculatus*. J. Braz. Chem. Soc. 12, 354-359. https://doi.org/10.1590/S0103-50532001000300006

Silva, N.C.D., Goncalves, S.F., Araújo, L.S.D., Kasper, A.A.M., Fonseca, A.L.D., Sartoratto, A., et al., 2019. *In vitro* and *in vivo* antimalarial activity of the volatile oil of *Cyperus articulatus* (Cyperaceae). Acta Amaz. 49, 334-342. https://doi.org/10.1590/1809-4392201804331

Singh, P.K., Kumar, V., Tiwari, R.K., Sharma, A., Rao, C.V., Singh, R.H., 2010. Medico-ethnobotany of ‘chatara’block of district sonebhadra, Uttar Pradesh, India. Adv. Biol. Res. 4, 65-80.

Singh, P., Khosa, R.L., Mishra, G., Jha, K.K., 2015. Antidiabetic activity of ethanolic extract of *Cyperus rotundus* rhizomes in streptozotocin-induced diabetic mice. J. Pharm. Bioallied Sci. 7, 289–292. https://doi.org/10.4103/0975-7406.168028

Soumaya, K.J., Dhekra, M., Fadwa, C., Zied, G., Ilef, L., Kamel, G., Leila, C.G., 2013. Pharmacological, antioxidant, genotoxic studies and modulation of rat splenocyte functions by *Cyperus rotundus* extracts. BMC Complement. Altern. Med. 13, 28. https://doi.org/10.1186/1472-6882-13-28

Sukjamnong, S., Santiyanont, R., 2015. Effect of *Fimbristylis ovata* on receptor for advanced glycation end-products, proinflammatory cytokines, and cell adhesion molecule level and gene expression in U937 and bEnd. 3 cell lines. Genet. Mol. Res. 14, 3984-3994. https://doi.org/10.4238/2015.April.27.13

Takeuchi, O., Akira, S., 2010. Pattern recognition receptors and inflammation. Cell. 140, 805-820. https://doi.org/10.1016/j.cell.2010.01.022

Talhouk, R.S., Karam, C., Fostok, S., El-Jouni, W., Barbour, E.K., 2007. Anti-inflammatory bioactivities in plant extracts. J. Med. Food. 10, 1-10. https://doi.org/10.1089/jmf.2005.055

Tasneem, S., Liu, B., Li, B., Choudhary, M.I., Wang, W., 2019. Molecular pharmacology of inflammation: Medicinal plants as anti-inflammatory agents. Pharmacol. Res. 139, 126-140. https://doi.org/10.1016/j.phrs.2018.11.001

Tsoyi, K., Jang, H.J., Lee, Y.S., Kim, Y.M., Kim, H.J., Seo, H.G., et al., 2011. (+)-Nootkatone and (+)-valencene from rhizomes of *Cyperus rotundus* increase survival rates in septic mice due to heme oxygenase-1 induction. J. Ethnopharmacol. 137, 1311-1317. https://doi.org/10.1016/j.jep.2011.07.062

Tufail, M., Hussain, K., Nawaz, K., Bhatti, K.H., Yasin, G., Ali, S.S., 2020. Ethnobotanical Survey of Important Wild Medicinal Plants of Tehsil Gojra, District Toba Tek Singh, Punjab, Pakistan. Ethnobot. Res. Appl. 20, 1-14. http://dx.doi.org/10.32859/era.20.23.1-14

Udefa, A.L., Amama, E.A., Archibong, E.A., Nwangwa, J.N., Adama, S., Inyang, V.U., et al., 2020. Antioxidant, anti-inflammatory and anti-apoptotic effects of hydro-ethanolic extract of *Cyperus esculentus* L. (tigernut) on lead acetate-induced testicular dysfunction in Wistar rats. Biomed. Pharmacother. 129, 110491. https://doi.org/10.1016/j.biopha.2020.110491

Upadhyay, A., Jain, S., 2017. Nephro protective, diuretic and anti-inflammatory evaluation of monocot grass *Kyllinga triceps* Rottb. IOSR J. Pharm. 7, 1-4.

Vanapatla, S.R., Mohan, G.K., Kumar, B.R., 2011. Effect of root extract fractions of *Kyllinga triceps* Rottb on streptozotocin induced diabetic rats. S. J. Pharm. Sci. 4, 25-30. https://doi.org/10.3329/sjps.v4i1.8863

Vijayashalini, P., Jayanthi, G., Abirami, P., 2017. Survey of the traditional medicinal plants at Vanavasi hill of Salem district. J. Med. Plants. 5, 331-335.

Zhang, H., Li, S., Lu, J., Jin, J., Zhu, G., Wang, L., et al., 2021. *α*-Cyperone (CYP) down-regulates NF-κB and MAPKs signaling, attenuating inflammation and extracellular matrix degradation in chondrocytes, to ameliorate osteoarthritis in mice. Aging. 13, 17690-17706. https://doi.org/10.18632/aging.203259

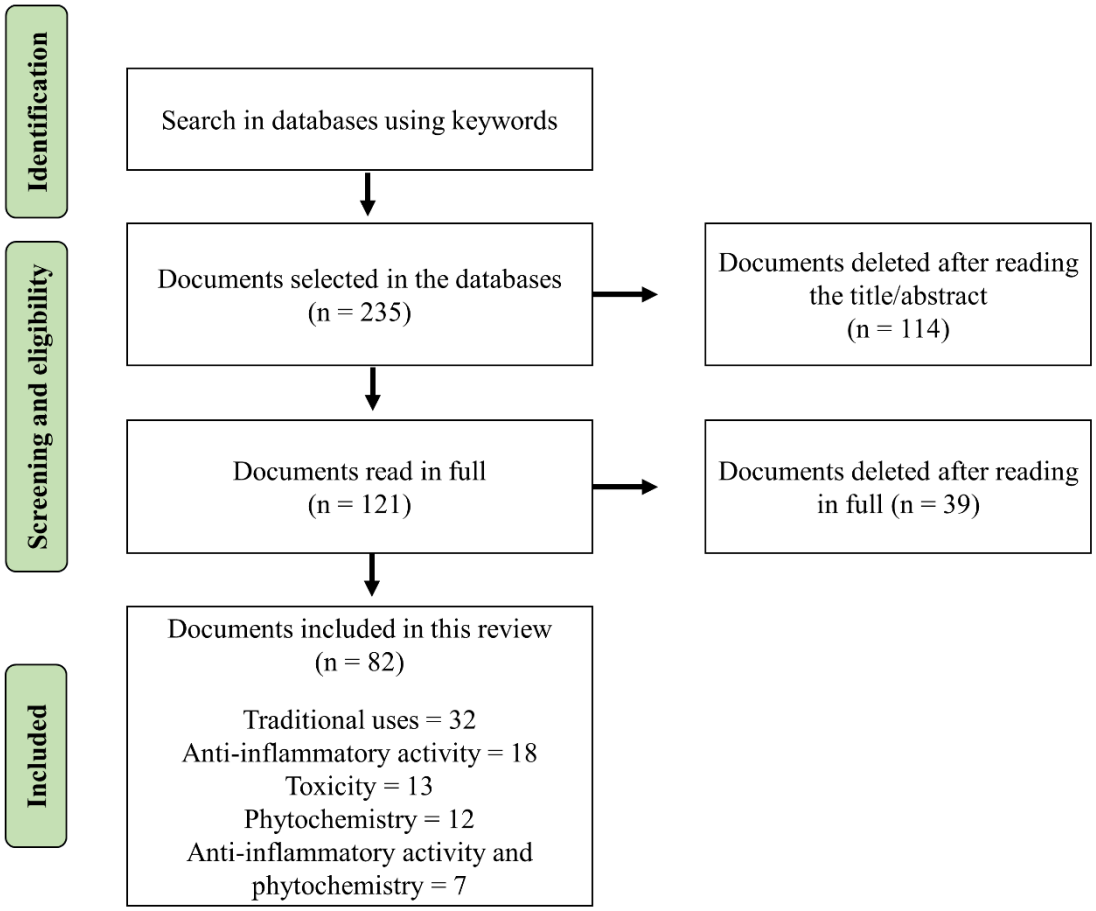


Fig. 1. Flowchart of selection of scientific documents for the systematic review.

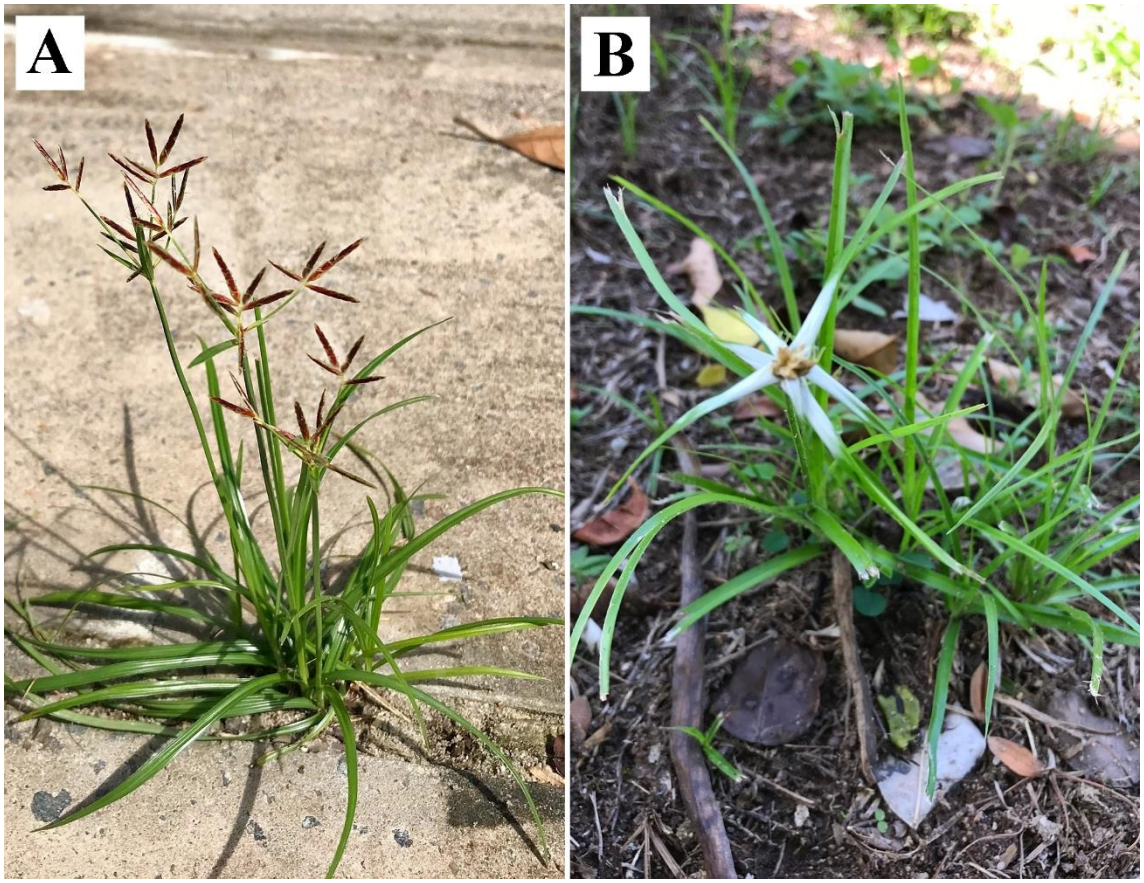


Fig. 2. Cyperaceae species used for the treatment of inflammation. A) *Cyperus rotundus* L.; B) *Rhynchospora nervosa* Boeckeler.

Fig. 3. Geographic location of scientific documents with information on the traditional use of Cyperaceae species for the treatment of inflammation. Based on Wikipedia Commons (Wikimedia Foundation, Inc., San Francisco, California, USA).

Table 1. Cyperaceae species used in traditional medicine for the treatment of inflammation.

Species[1]	**Part used**	**Preparation mode**	**Administration mode**	**Country**	**References**
Cyperus alopecuroides Rottb.	Corms	Decoction	Oral use	Sudan	Ali and Ahmed (2020)
Cyperus articulatus L.	Roots	Decoction	External use	Brazil	Duarte et al. (2007)
	Bulbs	-	-	Brazil	Bersan et al. (2014)
	Roots	-	-	Angola	Pompermaier et al. (2018)
	Roots	Essential oil	-	Brazil	Oliveira et al. (2019)
Cyperus distans L.f	Whole plant	-	-	India	Mir et al. (2018)
Cyperus glomeratus L.	Whole plant	-	-	Pakistan	Ikram et al. (2014)
Cyperus papyrus L.	-	-	-	South Africa	Mhlongo and Wyk (2019)
Cyperus rotundus L.	Whole plant	Infusion	-	Sri Lanka	Napagoda et al. (2018)
	Whole plant, tubers	-	-	Pakistan	Qureshi et al. (2008)
	Stems	Decoction	-	Brazil	Borges and Bautista (2010)
	Roots	Powder	External use	Pakistan	Qasim et al. (2014)
	Whole plant	-	-	Pakistan	Ajaib et al. (2014)
	Root, tubers	Decoction, infusion	-	Pakistan	Ahmad et al. (2014a)

	Rhizomes	Powder	Oral	Pakistan	Tufail et al. (2020)
	Whole plant	-	-	India	Ghulam et al. (2015)
	-	Extract	-	Pakistan	Amjad et al. (2017)
	-	-	-	India	Singh et al. (2010)
	Tubers, roots	Paste	External use	India	Penchala et al. (2018)
	Roots	-	-	India	Parul (2015)
	Rhizomes	-	-	India	Maitreya (2015)
	Rhizomes	-	Oral use	Pakistan	Rehman et al. (2020)
	Whole plant	-	-	Pakistan	Fatima et al. (2019)
	Bulbs	-	-	India	Vijayashalini et al. (2017)
	Rhizomes	Paste	External use	India	Kumar et al. (2015)
	-	-	-	India	Padmavathy and Anbarashan (2011)
Cyperus scariosus R.Br.	Leaves	Decoction	-	India	Kumari et al. (2019)
Rhynchospora nervosa Boeckeler	-	-	-	Brazil	Santana et al. (2016)
	Whole plant	Tea	-	Brazil	Gomez et al. (2016)
	Whole plant	Tea	-	Brazil	Moreira et al. (2002)

Scirpoides holoschoenus (L.) Soják	Stems	Infusion	Internal use	Spain	Parada et al. (2009)
Scleria gaertneri Raddi	Whole plant	Decoction, maceration	-	Brazil	Ribeiro et al. (2017)

[1] The scientific names of the species are according to the World Flora Online World Flora Online (http://www.worldfloraonline.org/); - not mentioned.

Table 2. *In vivo* and *in vitro* anti-inflammatory activity reported for Cyperaceae species.

Species[1]	**Plant organ**	**Essential oil, extracts and fractions**	**Dose or concentration**	**Anti-inflammatory model**	**Main results**	**Reference**
Bolboschoenus yagara (Ohwi) Y.C.Yang & M.Zhan	Tubers	ActF	0, 10, 50 and 100 µg/mL	LPS-induced inflammation (*in vivo*)	ActF protected mice against LPS-induced lethality and inhibited the production of multiple cytokines and organ dysfunction.	Li et al. (2014)
	Tubers	EAF, BF	10 and 50 µg/mL (EAF), 20 and 100 µg/mL (BF)	LPS-induced inflammation (*in vitro*)	EAF and BF can interrupt B16 cells migration and invasion.	Cao et al. (2020)
Bulbostylis coleotricha C.B.Clarke	Whole plant	EE	25, 50 and 100 mg/kg	Carrageenan-induced paw edema (*in vivo*)	100 mg/kg of EE reduced paw edema from 7.0 mm to 2.4 mm.	Owoyele et al. (2015)
Cyperus dubius Rottb.	Rhizomes	EE	100 and 200 mg/kg	Carrageenan-induced paw edema (*in vivo*)	200 mg/kg of EE reduced 44.01% of the paw edema volume.	Upadhyay and Jain (2017)

Cyperus esculentus L.	Tubers	HAE	500 mg/kg	Pb-induced inflammation (*in vitro* and *in vivo*)	HAE decreased C-reactive protein, TNF-α and IL-6 levels in a dose-dependent manner.	Udefa et al. (2020)
	-	EO	200 and 400 mg/kg	Carrageenan-induced paw edema (*in vivo*)	EO showed a dose-dependent effect.	Biradar et al. (2010)
Cyperus laevigatus L.	Aerial parts	EE, MF, EAF	12.5, 25, 50 and 100 µg/mL	LPS-induced inflammation (*in vitro*)	EE, MF and EAF decreased NO accumulation between 84 and 66%.	Elshamy et al. (2017)
Cyperus pangorei Rottb.	Rhizomes	ME	250 and 500 mg/kg	Carrageenan-induced paw edema (*in vivo*)	The percentage reduction of paw edema in animals treated with ME was 49.57 and 86.40% at doses of 250 and 500 mg/kg, respectively.	Chaulya et al. (2012)

Cyperus pedunculatus (R.Br.) J.Kern	Rhizomes, roots	CH	100 and 200 mg/kg	LPS-induced inflammation (*in vitro*)	CH inhibited the accumulation of neutrophils and eosinophils in the pleural cavity of the animals in a dose-dependent manner.	Siani et al. (2001)
Cyperus rotundus L.	Roots	AE	270 mg/kg	Carrageenan-induced paw edema (*in vivo*)	AE showed only 9.31% reduction of paw edema.	Dang et al. (2011)
	Rhizomes	ME	5, 10, 25 and 50 μg/mL	LPS-induced inflammation (*in vitro*)	ME increased HO-1 expression in a concentration-dependent manner, which was correlated with significant inhibition of iNOS/NO production.	Tsoyi et al. (2011)
	Rhizomes	EE	300 and 500 mg/kg	Carrageenan-induced paw edema (*in vivo*)	The maximum percent reduction of paw edema	Ahmad et al. (2014b)

				(36%) was observed at the dose of 500 mg/kg.	
Rhizomes	CE, EAE, ME	250 and 500 mg/kg	Carrageenan-induced paw edema (*in vivo*)	500 mg/kg of EAE reduced the volume of paw edema in 2.20 mL 4 h after administration.	Rajamanickam and Rajamanickam (2016)
Rhizomes	ME	500 and 1000 mg/kg	Carrageenan-induced paw edema (*in vivo*)	1000 mg/kg of ME showed maximum reduction of paw edema (57.5%).	Kumar et al. (2012)
Rhizomes	EE	0.1, 0.3 and 1.0 mg/ear	AA/TPA-induced skin inflammation (*in vivo*)	Topical application of EE was able of significantly reduce ear edema up to the ninth day of treatment (68.4%).	Rocha et al. (2020)
Leaves, rhizomes	ME	2000 mg/kg	Carrageenan-induced paw edema (*in vivo*)	ME showed a reduction of 73.5% of paw edema.	Mohammed et al. (2014)

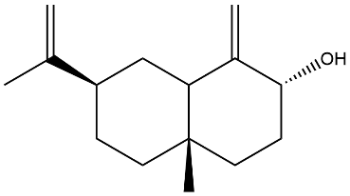
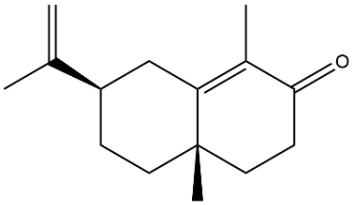
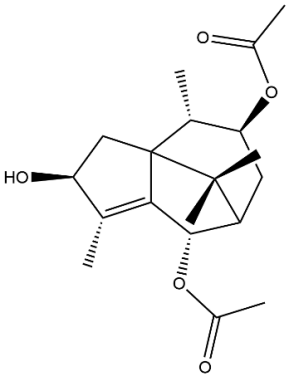
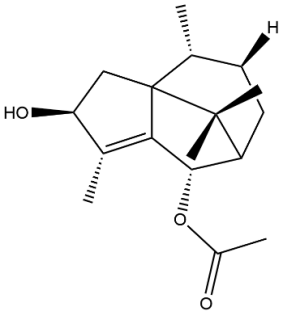
-	EO	250 and 500 mg/kg	Carrageenan-induced paw edema (*in vivo*)	EO showed a dose-dependent effect.	Biradar et al. (2010)
Aerial parts	TOF, AE, EAE, ME	50, 150 and 300 mg/kg	Xylene-induced ear edema (*in vivo*)	The percentages of reduction in ear edema of the LA, EAE, ME and TOF at the dose of 300 mg/kg were 74.38%, 62.73%, 44.6% and 77.25%, respectively.	Soumaya et al. (2013)
Rhizomes	EE, HF	25, 50 and 100 μg/mL (EE), 12.5, 25 and 50 μg/mL (HF)	LPS-induced inflammation (*in vitro*)	EE and HF inhibited the production of NO and PGE2 in RAW 264.7 cells.	Jung et al. (2013)
Rhizomes	ME	5, 10, 25, 50 and 100 μg/mL	LPS/IFN-γ-induced inflammation (*in vitro*)	Isocyperol isolated from ME significantly inhibited the production of NO, PGE2	Seo et al. (2001)

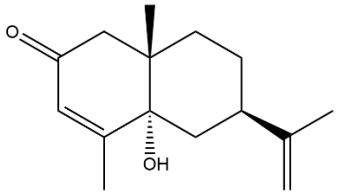
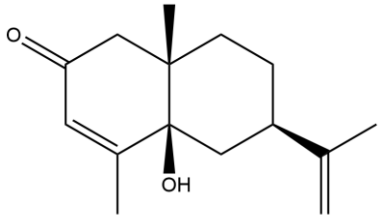
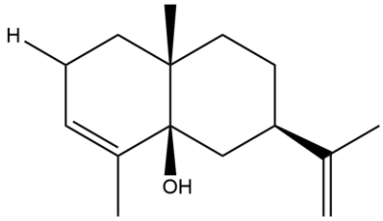
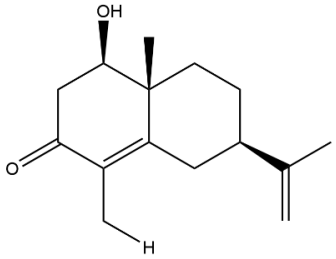
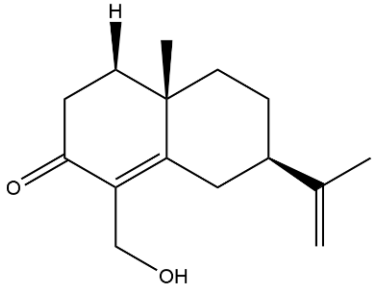
					and suppressed the expression of iNOS and COX-2 in RAW 264.7 cells.	
Cyperus scariosus R.Br.	Rhizomes	ME	40-5000 µg/mL	BSA assay (*in vitro*)	40-5000 µg/mL of ME inhibited BSA denaturation in a concentration-dependent manner.	Kakarla et al. (2014)
Eleocharis kuroguwai Ohwi	Aerial parts	EE, sub-fractions	10, 30 and 60 µg/mL	LPS-induced inflammation (*in vitro*)	The 80% subfraction significantly inhibited the expression of iNOS and the mRNA of the pro-inflammatory mediators IL-6, TNF-α and IL-1β.	Kim et al. (2020)
Fimbristylis ovata (Burm.f.) J.Kern	Stems, flower	AE, EE, ME	12.5, 25, 50 and 100 µg/mL	LPS-induced inflammation (*in vitro*)	AE, EE and ME can inhibit IL-6 level and gene expression through of RAGE signaling pathway.	Sukjamnong and Santiyanont (2015)

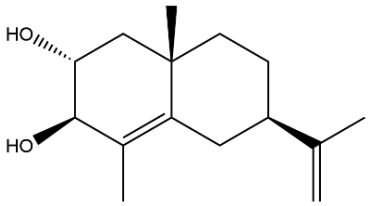
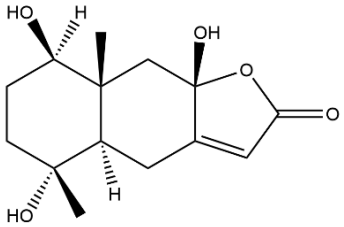
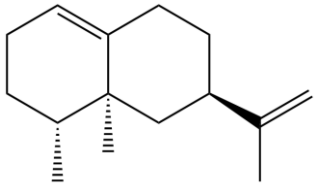
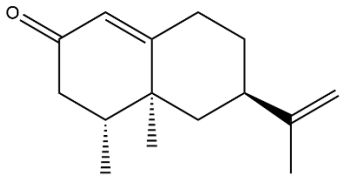
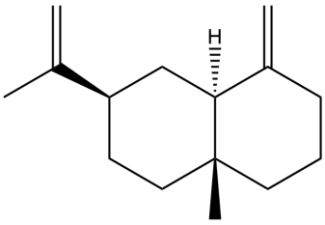
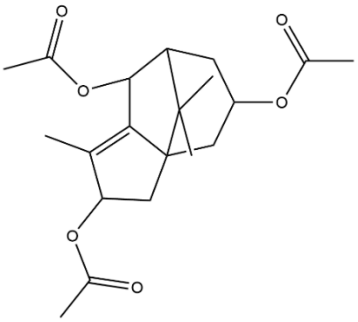
Remirea maritima Aubl.	Rhizomes, roots	EO	50, 100, and 200 mg/kg	Carrageenan-induced paw edema (*in vivo*)	EO caused a significant reduction of paw edema, suggesting inhibition of 5-LOX and/or COX, both enzymes involved in the formation of prostaglandins and leukotrienes.	Rabelo et al. (2014)
	Whole plant	AE	100, 200 and 400 mg/kg	Carrageenan-induced peritonitis (*in vivo*)	AE significantly reduced leukocyte migration at all concentrations evaluated.	Rabelo et al. (2013)
Rhynchospora nervosa Boeckeler	Aerial parts	HAE	100, 200 and 400 mg/kg	Carrageenan-induced paw edema and carrageenan-induced peritonitis (*in vivo*)	HAE significantly reduced paw edema (96.37%), NO levels, and number of white cells in the peritoneal fluid.	Bezerra et al. (2022)

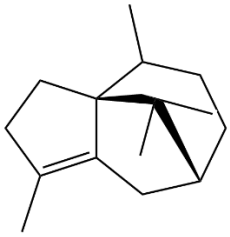
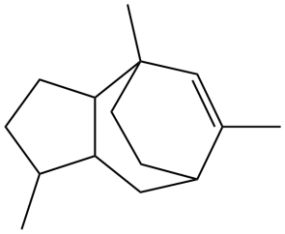
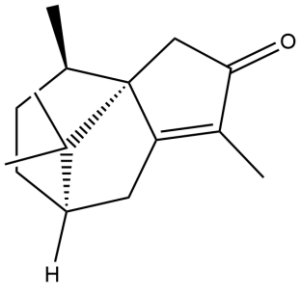
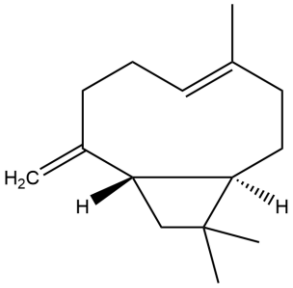
[1] The scientific names of the species are according to the World Flora Online (http://www.worldfloraonline.org/). AA: Arachidonic acid; ActF: Active fraction; AE: Aqueous extract; BF: *n*-butanol fraction; BSA: Bovine serum albumin; CE: Chloroform extract; CH: Crude hydrodistillate; COX: Cyclooxygenase; COX-2: Cyclooxygenase-2; EAE: Ethyl acetate extract; EAF: Ethyl acetate fraction; EE: Ethanol extract; EO: Essential oil; HAE: Hydroalcoholic extract; HF: *n*-hexane fraction; HO-1: Heme oxygenase-1; IL-6: Interleukin-6; IL-1*β*: Interleukin-1*β*; iNOS: Inducible nitric oxide synthase; IFN-γ: Interferon-γ; LPS: Lipopolysaccharide; 5-LOX, 5-Lipoxygenase; ME: Methanol extract; MF: Methanol fraction; NO: Nitric oxide; Pb: Lead acetate; PGE2: Prostaglandin E2; RAGE: Receptor for advanced glycation end-products; TNF-*α*: Tumor necrosis factor-*α*; TOF: Extract enriched with Total Oligomer Flavonoids; TPA: 12-O-tetradecanoylphorbol-13-acetate.

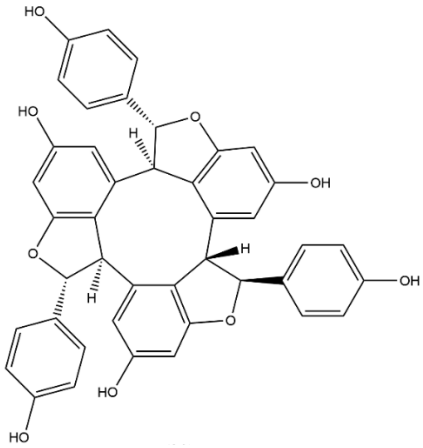
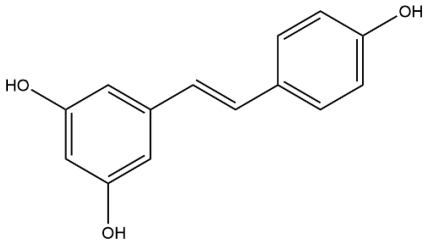
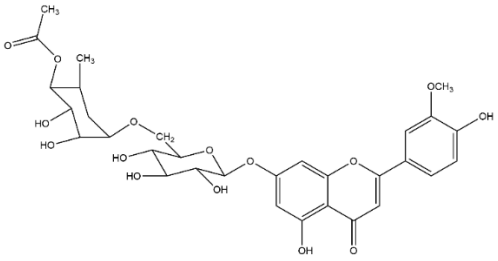
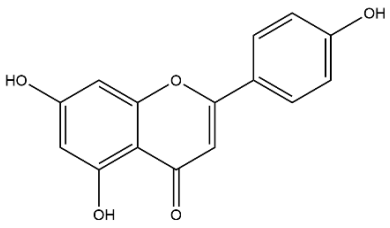
Table 3. Chemical compounds isolated from Cyperaceae species with anti-inflammatory potential.

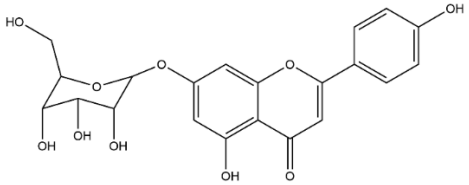
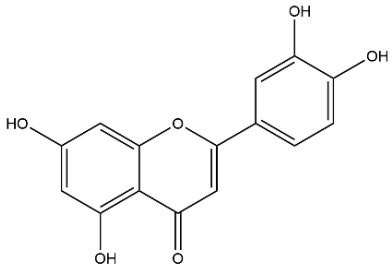
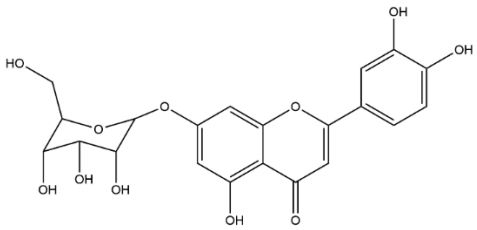
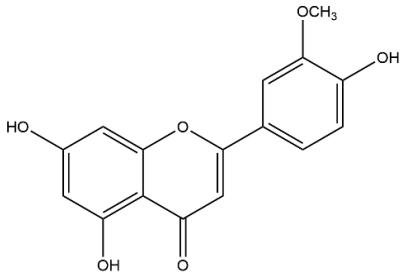
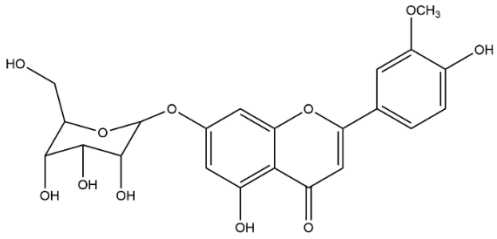
Class/Compound	Species	Plant organ	Reference
Sesquiterpenes			
1) Isocyperol 	*Cyperus rotundus*	Rhizomes	Seo et al. (2016)
2) *α*-Cyperone 	*Cyperus rotundus*	Rhizomes	Khan et al. (2011); Jung et al. (2013); Azimi et al. (2016); Zhang et al. (2021)
3) Sugetriol 6,9-diacetate 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)
4) Sugebiol 6-acetate 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)

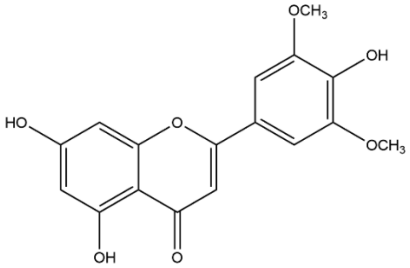
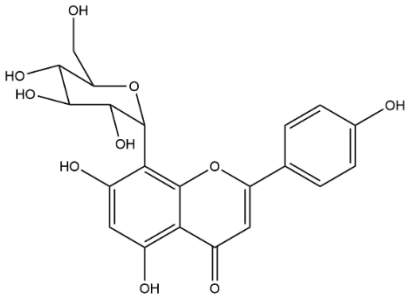
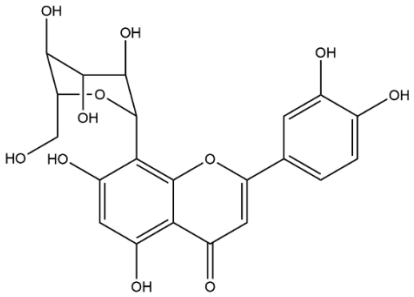
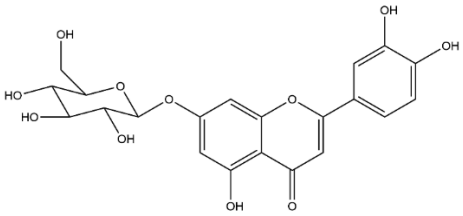
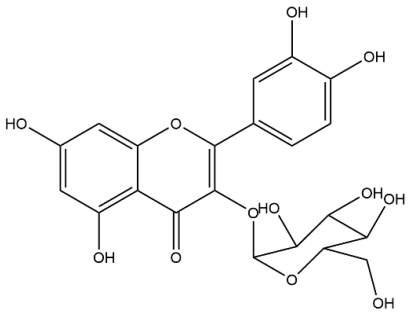
5) *α*-Rotunol 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)
6) *β*-Rotunol 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)
7) (−)-Eudesma-3,11-diene-5-ol 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)
8) Ligucyperonol 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)
9) 14-Hydroxy-*α*-cyperone 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)

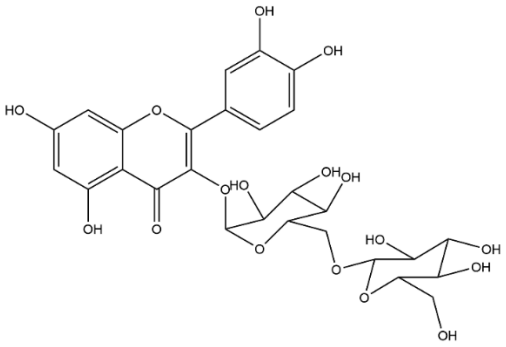
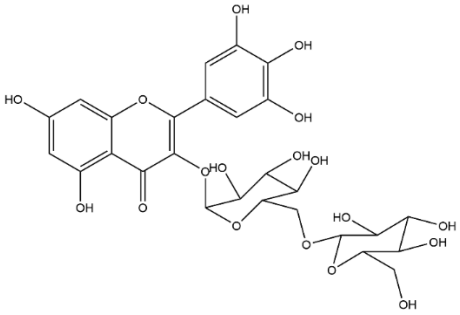
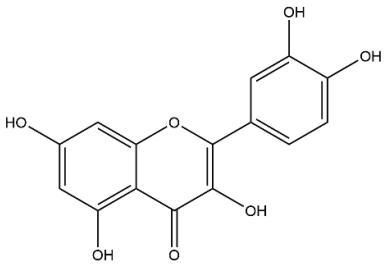
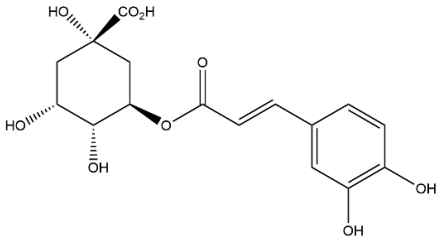
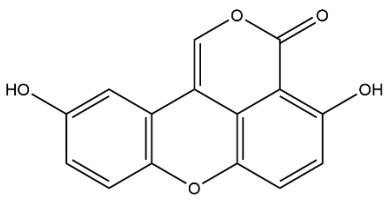
10) Britanlin E 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)
11) 1*β*,4*β*-Dihydroxyeudesma-11-ene 	*Cyperus rotundus*	Rhizomes	Kim et al. (2013)
12) Valencene 	*Cyperus rotundus*	Rhizomes	Khan et al. (2011)
13) Nootkatone 	*Cyperus rotundus*	Rhizomes	Khan et al. (2011)
14) *β*-*S*elinene 	*Cyperus rotundus*	Rhizomes	Khan et al. (2011)
15) Sugetriol triacetate 	*Cyperus rotundus*	Rhizomes	Mohamed-Ibrahim et al. (2018a)

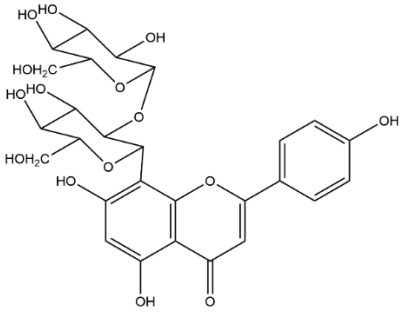
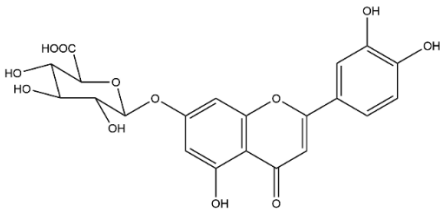
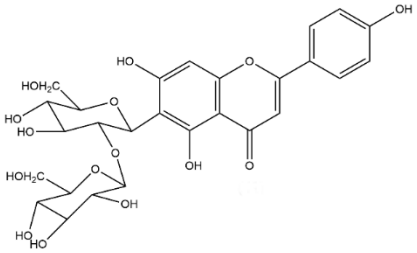
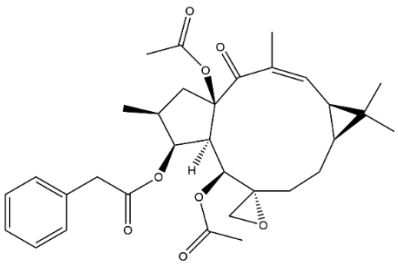
16) Cyperene 	*Remirea maritima*	Roots, rhizomes	Rabelo et al. (2014)
17) Rotundene 	*Remirea maritima*	Roots, rhizomes	Rabelo et al. (2014)
18) Cyperotundone 	*Remirea maritima*	Roots, rhizomes	Rabelo et al. (2014)
19) Caryophyllene oxide 	*Remirea marítima*	Roots, rhizomes	Rabelo et al. (2014)

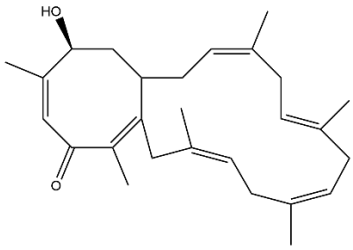
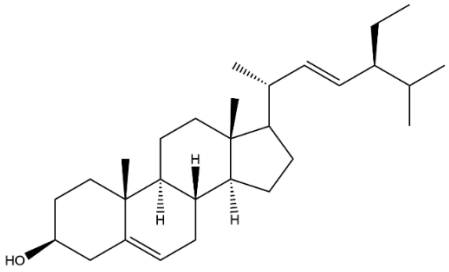
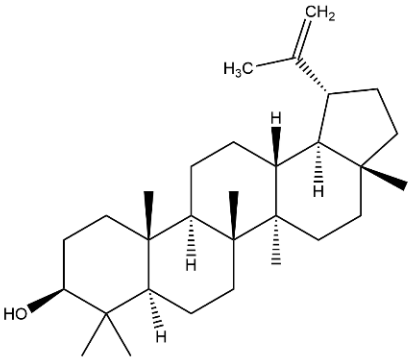
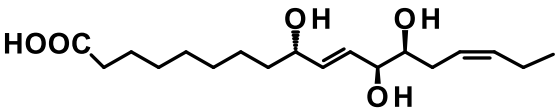
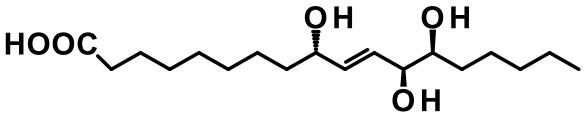
Phenolic compounds			
20) *α*-Viniferin 	*Carex humilis*	Root	Lee et al. (1998); Chung et al. (2003)
21) Resveratrol 	*Carex humilis*	Root	Lee et al. (1998)
22) Chrysoeriol 7-*O*-*β*-(6‴-*O*-acetyl-*β*-D-glucopyranosyl)-(1→4) glucopyranoside 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)
23) Apigenin 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)

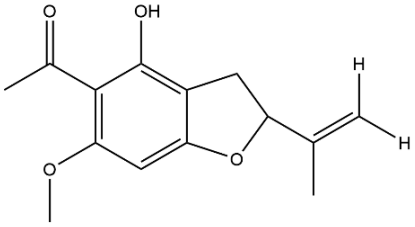
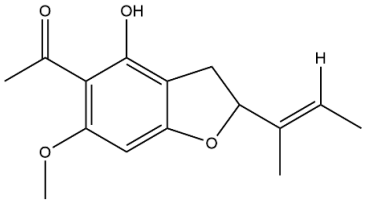
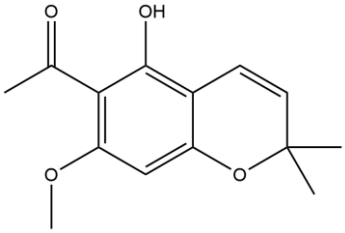
24) Apigenin 7-*O*-*β*-glucopyranoside 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)
25) Luteolin 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)
26) Luteolin 7-*O*-*β*-glucopyranoside 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)
27) Chrysoeriol 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)
28) Chrysoeriol 7-*O*-*β*-glucopyranoside 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)

29) Tricin 	*Cyperus laevigatus*	Aerial parts	Elshamy et al. (2017)
30) Vitexin 	*Cyperus roundus*	Aerial parts	Mohamed-Ibrahim et al. (2018b)
31) Orientin 	*Cyperus rotundus*	Aerial parts	Mohamed-Ibrahim et al. (2018b)
32) Cinaroside 	*Cyperus rotundus*	Aerial parts	Mohamed-Ibrahim et al. (2018b)
33) Quercetin 3-*O*-*β*-D-glucopyranoside 	*Cyperus rotundus*	Aerial parts	Mohamed-Ibrahim et al. (2018b)

34) Myrcetin 3-*O*-*β*-D -glucopyranoside 	*Cyperus rotundus*	Aerial parts	Mohamed-Ibrahim et al. (2018b)
35) Cyperaflavoside 	*Cyperus rotundus*	Aerial parts	Mohamed-Ibrahim et al. (2018b)
36) Quercetin 	*Cyperus rotundus*	Rhizomes	Rocha et al. (2020)
37) Chlorogenic acid 	*Cyperus rotundus*	Rhizomes	Rocha et al. (2020)
38) Sparstolonin B 	*Bolboschoenus yagara*	Tubers	Dong et al. (2016)

39) Vitexin-2″-*O*-*β*-D-glucopyranoside 	*Remirea maritima*	Whole plant	Rabelo et al. (2013)
40) Luteolin-7-*O*-glucuronide 	*Remirea maritima*	Whole plant	Rabelo et al. (2013)
41) Isovitexin-2″-*O*-*β*-D-glucopyranoside 	*Remirea maritima*	Whole plant	Rabelo et al. (2013)
Diterpenoids			
42) Euphorbia factor L1 	*Bolboschoenus yagara*	Tubers	Dong et al. (2016)

Norterpenoids			
43) Cyperalin A 	*Cyperus rotundus*	Rhizomes	Ibrahim et al. (2018a)
Phytosterols			
44) Stigmasterol 	*Cyperus rotundus*	Whole plant	Mohammed et al. (2014)
Triterpenes			
45) Lupeol 	*Cyperus scariosus, Cyperus rotundus*	Rhizomes	Kakarla et al. (2016)
Unsaturated fatty acids			
46) Fulgidic acid 	*Cyperus rotundus*	Rhizomes	Shin et al. (2015)
47) Pinellic acid 	*Cyperus rotundus*	Rhizomes	Shin et al. (2015)

Benzenoids			
48) Remirol 	*Remirea maritima*	Roots, rhizomes	Rabelo et al. (2014)
49) Dihydroremirol 	*Remirea maritima*	Rhizomes	Siani et al. (2001)
50) Iso-evodionol 	*Remirea maritima*	Rhizomes	Siani et al. (2001)

Supplementary material

Table S1 Characterization of the articles selected in the databases and included in the review (n = 82).

Traditional uses (n = 32)		
Database	**Title**	**Author/Year**
Google Scholar	Ethnobotanical Studies of flora of Jebel Aulia district, Khartoum state with emphasis to toxicity of the common medicinal plants.	Ali and Ahmed (2020)
	Plantas medicinais utilizadas nas práticas integrativas e complementares de saúde no Espaço Crescer, Alcobaça, Bahia.	Oliveira et al. (2019)
	A Comprehensive account of ethno-medicinal uses of monocot flora (reported from February–June) of Karwapani forest Doon valley-Uttarakhand.	Mir et al. (2018)
	Ethnobotanical studies of aquatic plants of district Sialkot, Punjab (Pakistan).	Ikram et al. (2014)
	A survey of useful medicinal plants of Abbottabad in northern Pakistan.	Qureshi et al. (2008)
	Etnobotânica de plantas medicinais na comunidade de Cordoaria, litoral norte do estado da Bahia, Brasil.	Borges and Bautista (2010)
	Traditional ethnobotanical uses of medicinal plants from coastal areas.	Qasim et al. (2014)
	Ethnobotanical survey of some important herbaceous plants of District Kotli, Azad Jammu & Kashmir.	Ajaib et al. (2014)
	Ethnobotanical studies of plant resources of Cholistan desert, Pakistan.	Ahmad et al. (2014a)

Ethnobotanical Survey of Important Wild Medicinal Plants of Tehsil Gojra, District Toba Tek Singh, Punjab, Pakistan.	Tufail et al. (2020)
Ethnobotanical study of common medicinal plants used by the people of village Fubgaon, District Amravati Maharashtra, India.	Ghulam et al. (2015)
Medico-ethnobotany of ‘chatara’block of district sonebhadra, Uttar Pradesh, India.	Singh et al. (2010)
Ethnomedicinal plants used by tribes of chittoor district of Andhra Pradesh to cure muscular pain and inflammation.	Penchala et al. (2018)
An Ethnobotanical study of plains of Yamuna Nagar District, Haryana, India.	Parul (2015)
Ethnomedicinal values of some weed plant species of Bhavnagar, Gujarat, India.	Maitreya (2015)
Indigenous knowledge and medicinal significance of seasonal weeds of district Gujrat, Punjab, Pakistan.	Rehman et al. (2020)
Ethno-medicinal uses of wild herbs and shrubs of Tehsil Yazman, Punjab, Pakistan.	Fatima et al. (2019)
Survey of the traditional medicinal plants at Vanavasi hill of Salem district.	Vijayashalini et al. (2017)
Phytomedicinal study of coastal sand dune floras in Puducherry.	Padmavathy and Anbarashan (2011)

	Ethnobotanical Investigation of Medicinal Plants used by Rural Communities of District Chatra, Jharkhand, India.	Kumari et al. (2019)
	Análise das publicações etnobotânicas sobre plantas medicinais da Mata Atlântica na Região Sul do Estado da Bahia, Brasil.	Gomez et al. (2016)
	Abordagem etnobotânica acerca do uso de plantas medicinais na Vila Cachoeira, Ilhéus, Bahia, Brasil.	Moreira et al. (2002)
Scopus	Activity of essential oils from Brazilian medicinal plants on *Escherichia coli*.	Duarte et al. (2007)
	Medicinal plants of northern Angola and their anti-inflammatory properties.	Pompermaier et al. (2018)
	Zulu medicinal ethnobotany: New records from the Amandawe area of KwaZulu-Natal, South Africa.	Mhlongo and Wyk (2019)
	Ethnobotanical profiling of the medicinal flora of Kotli, Azad Jammu and Kashmir, Pakistan: Empirical reflections on multinomial logit specifications.	Amjad et al. (2017)
	Ethnomedicinal plants of Shankaracharya Hill, Srinagar, J&K, India.	Kumar et al. (2015)
	Ethnomedicinal survey of a maroon community in Brazil's Atlantic tropical forest.	Santana et al. (2016)
	Ethnobotany of the Alt Emporda region (Catalonia, Iberian Peninsula): plants used in human traditional medicine.	Parada et al. (2009)

	Ethnobotanical study of medicinal plants used by Ribeirinhos in the North Araguaia microregion, Mato Grosso, Brazil.	Ribeiro et al. (2017)
PubMed	Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms.	Bersan et al. (2014)
	An ethnobotanical study of the medicinal plants used as anti-inflammatory remedies in Gampaha District, Western Province, Sri Lanka.	Napagoda et al. (2018)

Anti-inflammatory activity (n = 18)		
Database	**Title**	**Author/Year**
Google Scholar	Effects of the ethanolic extract of *Bulbostylis coleotricha* (Hochst. Exa. Rich.) on inflammation in adult wistar rats.	Owoyele et al. (2015)
	Antiinflammatory, antiarthritic, analgesic and anticonvulsant activity of *Cyperus* essential oils.	Biradar et al. (2010)
	Analgesic and anti-inflammatory activity of the extracts from *Cyperus rotundus* Linn rhizomes.	Rajamanickam and Rajamanickam (2016)
	Anti-inflammatory activity of methanolic extract of *Cyperus rotundus* rhizome on carrageenan induced paw edema in rats.	Kumar et al. (2012)
	Anti-inflammatory and analgesic activity of methanol extracts of *Cyperus tegetum* Roxb. rhizome.	Chaulya et al. (2012)
	Eleocharis kuroguwai Ohwi Ameliorates LPS-mediated Inflammation by Suppressing MAPKs Signaling.	Kim et al. (2020)

	Nephro protective, diuretic and anti-inflammatory evaluation of monocot grass *Kyllinga triceps* Rottb.	Upadhyay and Jain (2017)
Scopus	Antioxidant, anti-inflammatory and anti-apoptotic effects of hydro-ethanolic extract of *Cyperus esculentus* L. (tigernut) on lead acetate-induced testicular dysfunction in Wistar rats.	Udefa et al. (2020)
	(+)-Nootkatone and (+)-valencene from rhizomes of *Cyperus rotundus* increase survival rates in septic mice due to heme oxygenase-1 induction	Tsoyi et al. (2011)
	Inhibitory effects of methanol extract of *Cyperus rotundus* rhizomes on nitric oxide and superoxide productions by murine macrophage cell line, RAW 264.7 cells.	Seo et al. (2001)
	Protective effects of the active fraction from the tuber of *Scirpus yagara* in mouse endotoxin shock model.	Li et al. (2014)
	Evaluation of the anti-inflammatory, antipyretic and antinociceptive activities of the hydroalcoholic extract of *Rhynchospora nervosa* (Vahl) Boeckeler (Cyperaceae).	Bezerra et al. (2022)
PubMed	The active fraction from the tuber of *Bolboschoenus yagara* inhibits melanoma B16 cells metastasis LPS-induced *in vitro* and *in vivo*.	Cao et al. (2020)
	Antiinflammatory activity of *Phyllanthus emblica, Plumbago zeylanica* and *Cyperus rotundus* in acute models of inflammation.	Dang et al. (2011)

	Assessment of anti-inflammatory, anti-ulcer and neuropharmacological activities of *Cyperus rotundus* Linn.	Ahmad et al. (2014b)
	Pharmacological, antioxidant, genotoxic studies and modulation of rat splenocyte functions by *Cyperus rotundus* extracts	Soumaya et al. (2013)
	Identification of human cyclooxegenase-2 inhibitors from *Cyperus scariosus* (R. Br) rhizomes.	Kakarla et al. (2014)
	Effect of *Fimbristylis ovata* on receptor for advanced glycation end-products, proinflammatory cytokines, and cell adhesion molecule level and gene expression in U937 and bEnd. 3 cell lines.	Sukjamnong and Santiyanont (2015)
Phytochemistry (n = 12)		
Database	**Title**	**Author/Year**
Google Scholar	Sesquiterpenes from the rhizomes of *Cyperus rotundus* and their potential to inhibit LPS-induced nitric oxide production.	Kim et al. (2013)
	Sesquiterpene derivatives isolated from *Cyperus rotundus* L. inhibit inflammatory signaling mediated by NF-kB	Khan et al. (2011)
Scopus	Isocyperol, isolated from the rhizomes of *Cyperus rotundus*, inhibits LPS-induced inflammatory responses via suppression of the NF-κB and STAT3 pathways and ROS stress in LPS-stimulated RAW 264.7 cells.	Seo et al. (2016)
	α-Cyperone of *Cyperus rotundus* is an effective candidate for reduction of inflammation by destabilization of microtubule fibers in brain.	Azimi et al. (2016)

	Lipoxygenase inhibitors flavonoids from *Cyperus rotundus* aerial parts.	Ibrahim et al. (2018b)
PubMed	Anti-inflammatory terpenoids from *Cyperus rotundus* rhizomes.	Ibrahim et al. (2018a)
	α-Viniferin: a prostaglandin H2 synthase inhibitor from root of *Carex humilis.*	Lee et al. (1998)
	Anti-inflammatory effect of the oligomeric stilbene *α*-viniferin and its mode of the action through inhibition of cyclooxygenase-2 and inducible nitric oxide synthase.	Chung et al. (2003)
	Chemical constituents from the tubers of *Scirpus yagara* and their anti-inflammatory activities.	Dong et al. (2016)
	Free radical scavenging, α-glucosidase inhibitory and anti-inflammatory constituents from Indian sedges, *Cyperus scariosus* R. Br and *Cyperus rotundus* L.	Kakarla et al. (2016)
	Fulgidic acid isolated from the rhizomes of *Cyperus rotundus* suppresses LPS-induced iNOS, COX-2, TNF-*α*, and IL-6 expression by AP-1 inactivation in RAW264. 7 macrophages.	Shin et al. (2015)
	α-Cyperone (CYP) down-regulates NF-κB and MAPKs signaling, attenuating inflammation and extracellular matrix degradation in chondrocytes, to ameliorate osteoarthritis in mice.	Zhang et al. (2021)

Anti-inflammatory activity and phytochemistry (n = 7)

Database	**Title**	**Author/Year**
Google Scholar	Phenolic constituents, anti-inflammatory and antidiabetic activities of *Cyperus laevigatus* L.	Elshamy et al. (2017)

	Di-(2'-ethylhexyl) phthalate and stigmasterol with antiinflammatory effect from *Cyperus rotundus* L.	Mohammed et al. (2014)
Scopus	*α*-Cyperone, isolated from the rhizomes of *Cyperus rotundus*, inhibits LPS-induced COX-2 expression and PGE2 production through the negative regulation of NFκB signalling in RAW 264.7 cells.	Jung et al. (2013)
	Antinociceptive, anti-inflammatory and antioxidant activities of aqueous extract from *Remirea maritima* (Cyperaceae).	Rabelo et al. (2013)
	Chemical composition, antinociceptive, anti-inflammatory and redox properties *in vitro* of the essential oil from *Remirea maritima* Aubl.	Rabelo et al. (2014)
	Preclinical study of the topical anti-inflammatory activity of *Cyperus rotundus* L. extract (Cyperaceae) in models of skin inflammation.	Rocha et al. (2020)
SciELO	Chemical composition and anti-inflammatory activity of the hydrodistillate from *Mariscus pedunculatus.*	Siani et al. (2001)

Toxicity (n = 13)

Database	**Title**	**Author/Year**
Google Scholar	Hypolipidemic properties of ethanol extract of *Cyperus rotundus* rhizome.	Okwu et al. (2015)
	Pharmacological study of anti-depressant like activity of *Cyperus scariosus* oil in mice.	Ramesh et al. (2012)
	The phytochemical composition and some biochemical effects of Nigerian tigernut (*Cyperus esculentus* L.) tuber.	Chukwuma et al. (2010)

	Effect of root extract fractions of *Kyllinga triceps* Rottb on streptozotocin induced diabetic rats	Vanapatla et al. (2011)
Scopus	Evaluation of a lactogenic activity of an aqueous extract of *Cyperus rotundus* Linn.	Badgujar and Bandivdekar (2015)
PubMed	Evaluation of antinociceptive activity of hydromethanol extract of *Cyperus rotundus* in mice.	Imam and Sumi (2014)
	Antidiabetic activity of ethanolic extract of *Cyperus rotundus* rhizomes in streptozotocin-induced diabetic mice.	Singh et al. (2015)
	Antinociceptive and anti-hyperglycemic activity of methanol leaf extract of *Cyperus scariosus.*	Alam et al. (2011)
	Antidiabetic activity of methanol extract of rhizomes of *Cyperus tegetum* Roxb. (Cyperaceae)	Chaulya et al. (2011)
	Cyperus esculentus L. (tigernut) mitigates high salt diet-associated testicular toxicity in Wistar rats by targeting testicular steroidogenesis, oxidative stress and inflammation.	Nwangwa et al. (2020)
	Effects of *Cyperus rotundus* extract on spatial memory impairment and neuronal differentiation in rat model of Alzheimer's disease.	Shakerin et al. (2020)
	Anti-Onchocerca activity and phytochemical analysis of an essential oil from *Cyperus articulatus* L.	Metuge et al. (2014)
SciELO	*In vitro* and *in vivo* antimalarial activity of the volatile oil of *Cyperus articulatus* (Cyperaceae).	Silva et al. (2019)

5 ARTIGO 3

Evaluation of the anti-inflammatory, antipyretic and antinociceptive activities of the hydroalcoholic extract of *Rhynchospora nervosa* (Vahl) Boeckeler (Cyperaceae)

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Abstract

Ethnopharmacological relevance: Rhynchospora nervosa (Vahl) Boeckeler (Cyperaceae), popularly known as "capim-estrela", is a native species widely distributed in Brazil. The whole plant has been used in local traditional medicine in the form of teas or syrups to treat inflammation, flu, nasal congestion, fever, swelling, and venereal disease. This is the first study to investigate the pharmacological properties of this species. *Aim of the study:* The present study aimed to evaluate the *in vivo* anti-inflammatory, antipyretic and antinociceptive potential of the lyophilized hydroalcoholic extract of *R. nervosa* in heterogenic Swiss mice. In addition to pharmacological studies, the total phenol and flavonoid contents of the extract were determined. *Material and methods:* The anti-inflammatory effect was evaluated through carrageenan-induced paw edema and peritonitis models. For the antinociceptive assay, the number of acetic acid-induced writhing responses in the animals was counted. Antipyretic activity was tested by yeast-induced pyrexia in mice and evaluated for 4 h. Nitric oxide (NO) concentration and leukocyte migration in the peritoneal fluid were quantified. The acute toxicity of the extract

was also calculated. Quantitative analyses of total phenols and flavonoids in the extract were performed by spectrophotometric methods.

Results: In short, the lyophilized hydroalcoholic extract of *R. nervosa* showed low acute toxicity in the preclinical tests (LD_{50} = 3807 mg/kg). A significant anti-inflammatory effect was observed, with an average reduction of carrageenan-induced paw edema of 96.37%. Comparatively, indomethacin inhibited the development of the carrageenin paw edema by 97.52%. In the peritonitis test, a significant reduction in NO levels was recorded. A reduction in the number of white cells, notably monocytes, was also observed, confirming the anti-inflammatory effect. Writhing was reduced by 86.53%, which indicates antinociceptive activity. As for antipyretic activity, no positive effects of the extract were observed. The lyophilized hydroalcoholic extract of *R. nervosa* presented a high content of phenolic compounds (322.47 μg GAE/mg) and total flavonoids (440.50 μg QE/mg).

Conclusion: The lyophilized hydroalcoholic extract of *R. nervosa* showed significant *in vivo* anti-inflammatory and antinociceptive activity in mice. These preliminary findings support the indication of the use of this species in folk medicine in Brazil for the treatment of inflammation.

Keywords: Analgesic; Anti-inflammatory activity; Ethnopharmacology; *In vivo* bioactivity; Medicinal plants; Phenolic compounds.

Abbreviations

$AlCl_3$: Aluminium chloride, ANOVA: Analysis of variance, CEUA: Animal Care and Use Committee, EDTA: Ethylenediaminetetraacetic acid, GAE: Gallic acid equivalents, IPA: Agronomic Institute of Pernambuco, iNOS: Inducible nitric oxide synthase, LD50: Lethal dose required to kill 50% of a group of animals, LHERn: Lyophilized hydroalcoholic extract of *Rhynchospora nervosa*, LIKA: Keizo Asami Immunopathology Laboratory, LPS: Lipopolysaccharides, Na_2CO_3: Sodium carbonate, NO: Nitric oxide, PBS: Phosphate buffer solution, QE: Quercetin equivalents, RAW 264.7: Cells lines, SD: Standard deviation, SH-SY5Y: Cells lines, SisGen: National System of Management of Genetic Heritage and Associated Traditional Knowledge, UFPE: Federal University of Pernambuco.

1. Introduction

The family Cyperaceae has species distributed in all regions of Brazil and the genera *Cyperus* L., *Eleocharis* R. Br., *Rhynchospora* Vahl, and *Scleria* P. J. Bergius are the most

representative (Alves et al., 2009a). Several biological activities have been reported for members of this family, namely, antioxidant (Luo et al., 2014; Popescu et al., 2016), antimicrobial (Nassar et al., 2015; Pagning et al., 2016; Erdem et al., 2018), anti-inflammatory (Owoyele et al., 2015; Dong et al., 2016), anticancer (Nidugala et al., 2016; Pham et al., 2017), anthelmintic (Kasala et al., 2016), antinociceptive (Roy et al., 2019), antidiabetic (Njoku-Oji et al., 2019), antidiarrheal (Shorinwa and Dambani, 2020), and neuroprotective (Shakerin et al., 2020) activities, among others.

From a chemical perspective, sesquiterpenes (Tsoyi et al., 2011; Xu et al., 2015; Sultana et al., 2017; Park et al., 2019), iridoid glycosides (Zhou and Zhang, 2013; Zhou et al., 2013), phenolic compounds (Ito et al., 2012; Zhou and Yin, 2012; Vega-Morales et al., 2019), and triterpenes (Pagning et al., 2016) have already been isolated from different species of Cyperaceae. The sesquiterpenes (+)-nootkatone and (+)-valencene, for example, have been frequently isolated from the rhizomes and tubers of *Cyperus rotundus* L., one of the best-studied species of the family (Tsoyi et al., 2011; Jaiswal et al., 2014; Nam et al., 2016; Nuryana et al., 2019). Mustakone, another sesquiterpene, was isolated from the rhizomes of *Cyperus articulatus* L. and presented antiparasitic and anticonvulsant activity (Metuge et al., 2014; Brillatz et al., 2020). According to some authors, the flavone glycosides vitexin-2″*–O-β*-D-glucopyranoside, isovitexin-2″*–O-β*-D-glucopyranoside and luteolin-7-*O*-glucuronide, identified in extracts of *Remirea maritima* Aubl., demonstrated anti-inflammatory, antinociceptive, antioxidant, and antitumor activities (Rabelo et al., 2013; Dória et al., 2016).

Rhynchospora nervosa (Vahl) Boeckeler, a native species endemic to Brazil, is popularly known as “capim-estrela” and is found in all regions of the country (Thomas et al., 2020). From a medicinal point of view, the whole plant is used in the form of tea or syrup to treat flu, inflammation, fever, venereal disease, nasal congestion, and swelling (Moreira et al., 2002; Costa et al., 2006; Rodrigues et al., 2006; Gomez et al., 2016; Santana et al., 2016; Lisboa et al., 2017; Ramírez and Blair, 2017). As for the chemical composition, catechin and apigenin were identified from the aerial parts of *R. nervosa* (Bezerra et al., 2019). Some studies unrelated to *R. nervosa* have demonstrated the anti-inflammatory activity of these phenolics (Nakanishi et al., 2010; Wang et al., 2014; Patil et al., 2016).

To date, no scientific studies exist in the literature demonstrating the anti-inflammatory activity of *R. nervosa*. Thus, information from popular knowledge motivated the realization of the present study, whose objective was to evaluate the use of *R. nervosa* as a therapeutic alternative to treat inflammation and other clinical signs associated with the inflammatory

process, such as pain and fever, in mice. Total phenolic compounds and flavonoids were also quantified.

2. Material and methods

2.1. Plant material

Individuals of *R. nervosa* were collected at the campus of the Federal University of Pernambuco (UFPE) (8°03'01.2" S 34°56'55.5" W) and an exsiccate was deposited at the Dárdano de Andrade Lima Herbarium (Agronomic Institute of Pernambuco – IPA) under registration number 93709. The species was registered in the National System of Management of Genetic Heritage and Associated Traditional Knowledge (SisGen - Brazil) under number A2279F9.

2.2. Plant extract

The aerial part of the plant was naturally dehydrated at a temperature of 28 ºC for a period of five days, pulverized using knife mills and stored until extract preparation. The dried and pulverized aerial part of *R. nervosa* (500 g) and 7 L of 70% ethanol solution were used for the extraction. The extractive process was carried out at 28 ºC by the maceration method for 72 h. After extraction, the alcohol was evaporated in a rotary evaporator under reduced pressure and the resulting aqueous phase was subjected to lyophilization, providing 21.8 g of dry extract. The lyophilized hydroalcoholic extract of *R. nervosa* (LHERn) was placed in an amber flask and kept at -10 °C until chemical and pharmacological analyses.

2.3. Total phenols

The Folin-Ciocalteu method, following Waterman and Mole (1994) with some adaptations, was used for determination of total phenolics. Briefly, 1 mg/mL of LHERn was added into a 10-mL volumetric flask and mixed with 0.25 mL of Folin-Ciocalteu reagent and 3 mL of distilled water. After stirring for 30 seconds, 1 mL of 15% sodium carbonate (Na_2CO_3) was added. A control (blank) solution was also prepared containing only water and reagents. After 2 h, at room temperature and protected from light, a spectrophotometric reading at 760 nm was taken (SmartSpec Plus, Bio Rad, USA) and compared with the standard curve of gallic acid at five different concentrations (200, 400, 600, 800, and 1000 μg/mL), resulting in the following equation: $y = 0.0017x - 0.0355$, where y is the absorbance and x is the concentration. The coefficient of determination obtained was $R^2 = 0.9885$. The total phenolic content was

expressed as μg of gallic acid equivalents per mg of LHERn (GAE/mg). The total phenol content of the doses of LHERn adopted in the pharmacological tests was estimated by simple proportion calculation based on the content measured for 1 mg of LHERn.

2.4. Total flavonoids

The method of Woisky and Salatino (1998) with modifications was used to determine the total flavonoid content. Briefly, LHERn was diluted in distilled water to a concentration of 1 mg/mL and then 3 mL of methanol and 1 mL of aluminium chloride (5% $AlCl_3$) were added. After incubation for 30 min, absorbance was measured at 425 nm in a spectrophotometer (SmartSpec Plus, Bio Rad, USA) against a blank composed only of methanol.

The total flavonoid content was determined using a standard curve of quercetin (Sigma-Aldrich®) with five concentration points (200, 400, 600, 800, and 1000 μg/mL), resulting in the following equation: $y = 0.0674x - 0.0459$, where y is the absorbance and x is the concentration. The coefficient of determination obtained was $R^2 = 0.9937$. The total flavonoid content was expressed as μg of quercetin equivalents per mg of *R. nervosa* extract (QE/mg). The total flavonoid content for the doses of LHERn adopted in the pharmacological tests was also estimated by simple proportion calculation based on the content measured for 1 mg of LHERn.

2.5. Animals

Heterogenic Swiss mice (males and females, 25-30 g, 8-12 weeks old) from the animal house of the Keizo Asami Immunopathology Laboratory (LIKA) of the Federal University of Pernambuco (UFPE) were used for evaluation of anti-inflammatory, antinociceptive and antipyretic activities and acute toxicity. The animals were kept under a 12-h light-dark cycle at a temperature of 22 ± 2 ºC, with free access to feed and water. Animal experiments were approved by the Animal Care and Use Committee (CEUA-UFPE) under number 127/2019. The assays were carried out at the Experimental Animal Laboratory at the Department of Biochemistry of the UFPE.

2.6. Acute toxicity

Acute toxicity was evaluated by the assessment of median lethal dose (LD_{50}) according to the methodology described by Lorke (1983). Initially, 12 female Swiss mice were divided into three groups of three animals. The animals in each group received different doses of LHERn (10, 100 and 1000 mg/kg), previously solubilized in distilled water. After gavage administration

of the extract, the mice were kept under observation for 24 h for monitoring of behavior and evaluation of mortality. In the second phase of the experiment, three mice received higher doses of the extract (1600, 2900 and 5000 mg/kg) and then observed for 24 h for monitoring of behavior and evaluation of mortality. The LD_{50} was calculated using the following formula:

$$LD_{50} = \sqrt{(D_0 \text{ x } D_{100}}$$

Where: LD_{50} = Lethal dose required to kill 50% of a group of animals; D_0 = Highest dose without mortality; and D_{100} = Lowest dose that produced mortality.

2.7. Determination of doses for evaluation of biological activities

The doses of 100, 200 and 400 mg/kg of LHERn adopted for evaluation of anti-inflammatory, antinociceptive and antipyretic activities were determined according to the doses established by Rabelo et al. (2013) and Roy et al. (2019) for Cyperaceae species. Importantly, these doses of LHERn are below the LD_{50} obtained through the acute toxicity test.

2.8. Anti-inflammatory activity in vivo

2.8.1. Carrageenan-induced paw edema test

Thirty male mice were randomly selected for the carrageenan-induced paw edema test. The positive control group (n = 6) was treated with 50 mg/kg of indomethacin (Aspen Pharma, South Africa) while the negative control group (n = 6) was treated with saline solution (0.9% NaCl). The groups treated with LHERn received doses of 100, 200 and 400 mg/kg orally. After 1 h of treatment, paw edema was induced by carrageenan (1% in saline, w/v), injected in a volume of 50 µL in the subplantar region of the right paw, while the left paw received 50 µL of 0.9% saline solution. Paw thickness was measured using a caliper (SR44, MTX, Brazil) at time intervals of 0, 1, 2, 3, 4, and 5 h after induction. The edema was measured based on the difference between the thickness of right and the left paw and expressed as variation over time in centimeter (Amdekar et al., 2012). The animals were anesthetized and euthanized with an overdose of Ketamine (MSD, Kenilworth, NJ, USA) at 100 mg/kg + Xylazine (Syntec, Brazil) at 10 mg/kg, administered intraperitoneally.

2.8.2. Carrageenan-induced peritonitis

For the carrageenan-induced peritonitis test, groups of six animals were assigned to each treatment, including positive and negative controls. The positive control group received indomethacin at a dose of 50 mg/kg orally; the negative control group received vehicle (0.9% NaCl); and the test groups received LHERn at doses of 100, 200, and 400 mg/kg orally. After

1 h of the administration, inflammation was induced by intraperitoneal administration of 50 µL of carrageenan (1% in saline, w/v). Four hours after induction of inflammation, the animals were euthanized in a CO_2 chamber and 2 mL of phosphate buffer solution (PBS) containing ethylenediaminetetraacetic acid (EDTA) (3 µM) was injected into the peritoneal cavity, followed by 50 light abdominal compressions and then collection of peritoneal fluid. The peritoneal lavage fluid was stored in eppendorfs for further analysis of inflammatory mediators (Prasad and Gupta, 2005). The concentration of nitric oxide (NO) in the peritoneal fluid was analyzed by reaction with Griess' reagent and leukocyte migration was quantified in peritoneal fluid samples stained with Turk's solution and observed in a Neubauer chamber (Bright-Light, HBG, Germany) with the aid of a Coleman – N107 binocular microscope (Coleman Laboratory Equipment Trade and Import Ltda., Brazil) (Daniel et al., 2009).

2.9. Antinociceptive activity

Antinociceptive activity was evaluated according to the method described by Collier et al. (1968) with modifications. The mice were divided into five groups of six animals. Nociception was induced by acetic acid (Vetec, Rio de Janeiro, Brazil) administered intraperitoneally in a volume of 0.1 mL/10 g. The animals were treated with LHERn at 100, 200 and 400 mg/kg, vehicle (0.9% NaCl) (negative control), and indomethacin at 50 mg/kg (positive control), administered orally 1 h before the nociceptive agent. The number of abdominal writhes was recorded between 5-15 min after injection of acetic acid (Queiroz et al., 2010).

2.10. Antipyretic activity

After measurement of rectal temperature, 30 animals were treated with brewer's yeast (*Saccharomyces cerevisiae*, 15% in saline) subcutaneously. After 18 h, animals with temperature above 38 °C were selected and randomly distributed into five groups and then treated orally with vehicle (0.9% NaCl) (negative control), dipyrone (EMS, Brazil) at 100 mg/kg (positive control), or LHERn at 100, 200 and 400 mg/kg. After 30 min of fever induction, the temperature was taken every 1 h for 4 h (Winter et al., 1962).

2.11. Statistical analysis

Phytochemical tests were carried out in triplicates (n = 3), while pharmacological tests were carried out in sextuplicates (n = 6). Statistical analyses were performed using the GraphPad Prism software version 5.0 (GraphPad Software Inc., San Diego, CA, USA). Data are

represented as mean ± SD. Statistically significant differences between treatments were tested by ANOVA and Tukey's test ($P < 0.05$).

3. Results and discussion

3.1. Total phenolic compounds and flavonoids

Information about the chemical constitution of *R. nervosa* is scarce in the literature. Thus, the present study is fundamental for the phytochemical knowledge of this species and of the genus *Rhynchospora*, which is also chemically little known. The total phenol and flavonoid contents were quantified in our study, and values of 322.47 ± 0.013 μg GAE/mg and 440.50 ± 0.003 μg QE/mg, respectively, were found. The total content of phenols and flavonoids present at the doses of 100, 200 and 400 mg/kg of LHERn were estimated to be 32.2, 64.4 and 128.8 mg/kg of LHERn and 44, 88 and 176 mg/kg of LHERn, respectively.

The total phenol and flavonoid contents of other species of Cyperaceae, especially of *C. rotundus*, are reported in the literature (Kilani-Jaziri et al., 2011; Kilani-Jaziri et al., 2014; Kumar et al., 2014; Kamala et al., 2018). Kilani-Jaziri et al. (2011), for example, found 260 to 440 μg GAE/mg and between 200 to 320 μg QE/mg of phenols and flavonoids, respectively, in extracts obtained from the aerial parts of *C. rotundus*. These values are similar to those found here for *R. nervosa*. Kumar et al. (2014), on the other hand, found that the 70% ethanolic extract from the roots of *C. rotundus* contained 254.5 μg GAE/mg of total phenols and 164.34 μg QE/mg of flavonoids. Although these values are lower than ours, these authors only analyzed the extract from roots and not from whole plants as in our study.

According to some authors, phenolic compounds, especially flavonoids, have remarkable anti-inflammatory activity and are able to intervene at various stages of the immune response (Talhouk et al., 2007; Salaritabar et al., 2017; Gupta et al., 2021). The *in vitro* anti-inflammatory activity exhibited by *α*-viniferin, for example, isolated from the roots of *Carex humilis* Kunth may be related to the inhibitory effects on the activities of cyclooxygenase and protein kinase C (Lee et al., 1998). According to Dong et al. (2016), sparstolonin B isolated from *Bolboschoenus yagara* (Ohwi) Y. C. Yang & M. Zhan showed significant anti-inflammatory activity on tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) levels in Lipopolysaccharide (LPS)- or Pam3csk4-stimulated macrophages. The flavonoids orientin, quercetin 3-O-*β*-D-glucopyranoside, cyperaflavoside, and myrcetin 3-O-*β*-D-glucopyranoside isolated from the aerial parts of *C. rotundus* exhibited 5-lipoxygenase (5-LOX) inhibition activity, showing their anti-inflammatory potential (Ibrahim et al., 2018). Topical anti-

inflammatory activity in irritant dermatitis and skin hyperproliferation models in mice was found for the ethanol extract of the rhizomes of *C. rotundus* (Rocha et al., 2020). Quercetin and chlorogenic acid were identified by these authors as the main constituents of the extract. These findings, added to others reported in other families, may indicate that the anti-inflammatory activity of some species may in fact be due to the occurrence of flavonoids identified in the extracts. It is noteworthy, however, that although phenolic compounds stand out for their anti-inflammatory activity, non-phenolic compounds may also have the same potential (Talhouk et al., 2007; Gupta et al., 2021).

3.3. Acute toxicity

After gavage administration of LHERn in female mice, it was observed that the animal that received the dose of 5,000 mg/kg experienced sudden death within 5 minutes. The other animals that received different doses of LHERn (10, 100, 1000, 1600, and 2900 mg/kg) and were monitored for a period of 24 h did not show any clinical changes. The LD_{50} of LHERn was 3807 mg/kg. Therefore, LHERn can be categorized as having a low degree of toxicity.

Non-significant levels of toxicity of other polar extracts obtained from species of *Cyperus* in animal models have been documented in the literature. The ethanolic extract of *Cyperus alternifolius* L., for example, did not induce behavioral changes or mortality in mice at doses up to 5000 mg/kg (Awaad et al., 2012). In the acute toxicity test of the ethanolic extract of *C. rotundus* rhizomes (5000 mg/kg), no behavioral changes or mortality were seen in Wistar rats during 72 h of observation (Okwu et al., 2015). In another study, the ethanolic extract of *Cyperus conglomertus* Rottb. was characterized as safe, presenting a low degree of toxicity, with LD_{50} greater than 5000 mg/kg (Al-Hazmi et al., 2018). These studies demonstrate that extracts obtained from different species of Cyperaceae have a low degree of toxicity, as in the case of LHERn, thus reinforcing the importance of pharmacological research on representatives of this family.

3.4. Anti-inflammatory activity

3.4.1. Carrageenan-induced paw edema

The results regarding the anti-inflammatory activity of LHERn are shown in Table 1 and are presented in terms of paw thickness variation expressed in centimeters (cm) and percentage of inhibition. The different concentrations of LHERn showed promising anti-inflammatory activity from the first until the fifth hour of observation (Table 1). The tested doses inhibited on average 96.37% of the carrageenan-induced paw edema in mice. The results did not differ

significantly from positive control indomethacin (50 mg/kg), a standard anti-inflammatory drug, which caused an average inhibition of 97.52%.

Table 1

Effect of the lyophilized hydroalcoholic extract of *Rhynchospora nervosa* (LHERn) on carrageenan-induced paw edema in mice.

Paw thickness (cm)* (% Inhibition**)					
			LHERn (mg/kg)		
Time (h)	0.9% NaCl	Indomethacin 50 mg/kg	100	200	400
1	0.950 ± 0.19[a]	0.016 ± 0.04[b] (98.3%)	0.166 ± 0.13[b] (82.5%)	0.083 ± 0.09[b] (91.2%)	0.000 ± 0.00[b] (100%)
2	1.050 ± 0.28[a]	0.033 ± 0.05[b] (96.8%)	0.133 ± 0.12[b] (87.3%)	0.033 ± 0.05[b] (96.8%)	0.016 ± 0.04[b] (98.4%)
3	1.216 ± 0.26[a]	0.033 ± 0.08[b] (97.2%)	0.050 ± 0.05[b] (97.2%)	0.000 ± 0.00[b] (100%)	0.000 ± 0.00[b] (100%)
4	1.016 ± 0.11[a]	0.016 ± 0.04[b] (98.4%)	0.000 ± 0.00[b] (100%)	0.016 ± 0.04[b] (98.4%)	0.000 ± 0.00[b] (100%)
5	1.066 ± 0.18[a]	0.033 ± 0.08[b] (96.9%)	0.050 ± 0.08[b] (95.3%)	0.016 ± 0.04[b] (98.4%)	0.000 ± 0.00[b] (100%)

* Edema was measured based on the difference between the thickness of right and the left paw and expressed as variation over time. ** Inhibition is reported as a percentage compared to NaCl. Values are expressed as mean ± SD (n = 6). Different superscript letters in the same line indicate differences between treatments by one-way ANOVA and Tukey's test ($P < 0.05$).

The anti-inflammatory activity of Cyperaceae species has been evaluated by the carrageenan-induced paw edema method by different authors (Kumar et al., 2012; Chaulya et al., 2012; Rabelo et al., 2013), but none included species of *Rhynchospora*. In a study carried out by Kumar et al. (2012), for example, it was seen that the methanolic extract of *C. rotundus*

rhizomes at a dose of 1000 mg/kg exhibited anti-inflammatory activity, with 57.5% of inhibition of edema as compared to the control. In another study, the methanolic extract of *Cyperus tegetum* Roxb. caused a reduction of 49.57% to 86.40% in paw edema in Wistar rats when compared to the control group (Chaulya et al., 2012). LHERn was more effective in reducing carrageenan-induced paw edema when compared to other Cyperaceae species. Although more studies are needed, we believe that LHERn can be preliminarily considered as a promising alternative in the treatment of inflammation.

Catechin and apigenin have already been identified in the hydroalcoholic extract of aerial parts of *R. nervosa* (Bezerra et al., 2019). There are reports that these compounds showed anti-inflammatory activity when individually tested in *in vivo* and *in vitro* assays (El-Aziz et al., 2012; Wang et al., 2014; Patil et al., 2016; Cheng et al., 2019). Although the profile of phenolic compounds was not described in the present study, it is possible that the observed anti-inflammatory effect is associated with compounds of this nature in view of the high concentration of phenols and flavonoids in LHERn.

3.4.2. Carrageenan-induced peritonitis

The mean total count of leukocytes in the peritoneal fluid showed a significant difference between treatments (Table 2). The dose of 200 mg/kg of LHERn, for example, showed anti-inflammatory activity similar to indomethacin. The anti-inflammatory activity of the extract was even more pronounced at 400 mg/kg, reducing all types of white cells evaluated, especially monocytes (0.66 x 10^6).

Table 2

Total white blood cell count in the peritoneal fluid of mice from control groups and treated with the lyophilized hydroalcoholic extract of *Rhynchospora nervosa* (LHERn) submitted to carrageenan-induced peritonitis test.

	White blood cells (x10^6)/Treatment				
			LHERn (mg/kg)		
White cells	0.9% NaCl	Indomethacin50 mg/kg	100	200	400

Leukocytes	14.45 ± 1.57[a]	7.20 ± 0.82[c]	10.20 ± 0.59[b]	7.10 ± 0.43[c]	4.58 ± 0.45[d]
Lymphocytes	8.89 ± 0.64[a]	4.71 ± 0.53[c]	7.06 ± 0.26[b]	4.17 ± 0.19[c]	3.21 ± 0.22[d]
Neutrophils	3.02 ± 0.68[a]	1.58 ± 0.68[b]	1.87 ±0.56[b]	1.97 ± 0.53[b]	0.70 ± 0.36[d]
Monocytes	2.53 ± 0.57[a]	0.89 ± 0.14[b]	1.26 ± 0.13[b]	0.96 ± 0.07[b]	0.66 ± 0.07[d]

Values are expressed as mean ± SD (n = 6). Different superscript letters in the same line indicate differences between treatments by one-way ANOVA and Tukey's test ($P < 0.05$).

To our knowledge, the reduction of white blood cells or inhibition of their migration by Cyperaceae species-based extracts was reported in only two studies (Siani et al., 2001; Rabelo et al., 2013). Siani et al. (2001) reported that pre-treatment of mice with the hydrodistillate from rhizomes and roots of *Mariscus pedunculatus* (R.Br.) T.Koyama (= *Remirea maritima* Aubl.) significantly inhibited the LPS-induced neutrophil and eosinophil accumulation at a dose of 200 mg/kg. According to these authors, the phenolic compounds remirol (4-hydroxy-6-methoxytremetone) and the hydrogenated derivative dihydroremirol demonstrated anti-inflammatory activity. In the study by Rabelo et al. (2013), the aqueous extract of *R. maritima* inhibited carrageenan-induced leukocyte migration in mice, possibly due to inhibition of the synthesis of inflammatory mediators involved in cell migration. According to these authors, three flavone glycosides may have accounted for the analgesic and anti-inflammatory activities observed. According to the above reports as well as those of other authors and ours, polar extracts from different species of Cyperaceae have marked anti-inflammatory activity (Kakarla et al., 2014; Sukjamnong and Santiyanont, 2015; Rocha et al., 2020).

LHERn also caused a reduction in NO levels. At all doses, there was a significant reduction in NO levels when compared to the group receiving the vehicle only (Fig. 1). Although the doses of 200 and 400 mg/kg of LHERn did not differ statistically from the positive control (indomethacin 50 mg/kg), they proved to be efficient in reducing NO levels.

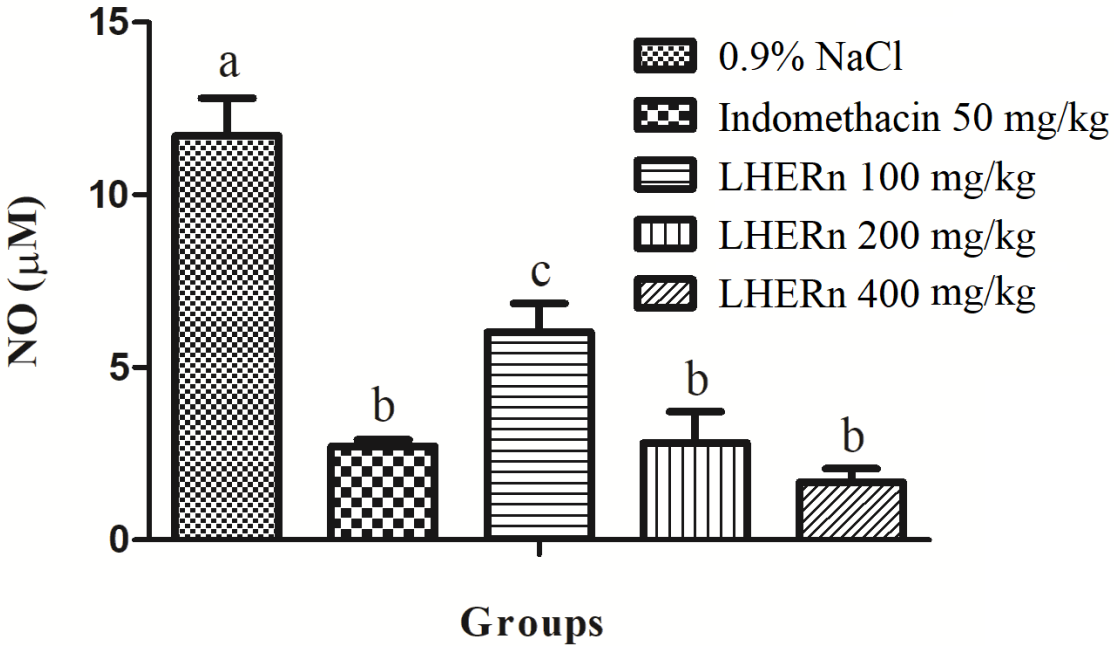

Fig. 1. Effect of the lyophilized hydroalcoholic extract of *Rhynchospora nervosa* (LHERn) on the nitric oxide (NO) concentration in the peritoneal fluid of animals submitted to the carrageenan-induced peritonitis test. Values are expressed as mean ± SD (n = 6). Different letters indicate differences between treatments by one-way ANOVA and Tukey's test ($P < 0.0001$).

In addition to *in vivo* experiments, there are reports in the literature on the influence of Cyperaceae extracts on NO production *in vitro*, but all focused on a single species. According to Seo et al. (2001), the methanolic extract of *C. rotundus* significantly reduced NO production in RAW 264.7 cells. Kandikattu et al. (2013) found that the ethanolic extract of *C. rotundus* rhizomes regulated inducible nitric oxide synthase (iNOS) expression, restoring the mitochondrial membrane potential in SH-SY5Y human neuroblastoma cell lines. These findings add to ours to further demonstrate the potential of Cyperaceae species to reduce NO both in *in vitro* and *in vivo* models.

According to Nahrevanian (2009), in normal physiological states, NO acts in vital processes in the body, however, in conditions of high production, NO can contribute to some types of cell damage. Furthermore, many of the effects of cytokines that are released during the inflammatory process are mediated by NO (Alves et al., 2009b). Thus, extracts that act to reduce the high levels of NO in organisms, as it was the case of LHERn and extracts from other Cyperaceae species, are of great pharmacological relevance.

3.5. Antinociceptive activity

The dose of 400 mg/kg of LHERn reduced by 86.53% the abdominal writhes in the animals, differing statistically from the other treatments evaluated ($P < 0.05$). At the two lower concentrations (100 and 200 mg/kg), LHERn reduced writhing by 67.35% and 61.23%, respectively, values similar to those observed in animals receiving indomethacin (Fig. 2). When compared to other species of Cyperaceae, LHERn showed better analgesic activity at all doses tested (Alam et al., 2011; Rabelo et al., 2013; Roy et al., 2019).

According to Rajamanickam and Rajamanickam (2016), acetic acid-induced pain is indirectly caused by endogenous mediators such as prostaglandin, which stimulate peripheral nociceptive neurons. In another study, the antinociceptive effect observed in mice was associated with the flavonoids isovitexin-2″–*O*-*β*-D-glucopyranoside, vitexin-2″–*O*-*β*-D-glucopyranoside, and luteolin-7-*O*-glucuronide present in the aqueous extract of *R. maritima* (Rabelo et al., 2013). Thus, the results presented here may indicate that the phenolic compounds present in LHERn could act on prostaglandin pathways, thus reducing the number of writhes in mice, and, consequently, be directly associated with the observed analgesic effect.

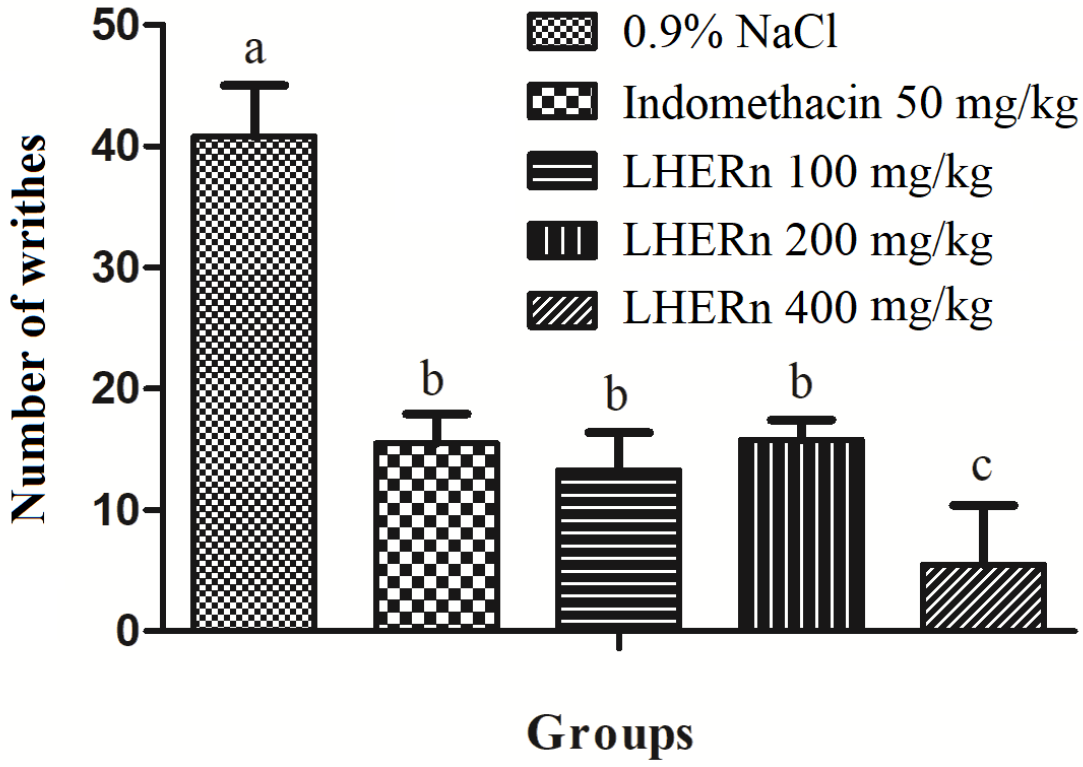

Fig. 2. Effect of the lyophilized hydroalcoholic extract of *Rhynchospora nervosa* (LHERn) on 0.8% acetic acid-induced writhing in mice. Values are expressed as mean ± SD (n = 6). Different letters indicate differences between treatments by one-way ANOVA and Tukey's test ($P < 0.0001$).

3.6. Antipyretic activity

Despite the promising results presented by LHERn in terms of anti-inflammatory and antinociceptive activities, no antipyretic effect was found at any dose. After treatment and 4 h of monitoring, the mice remained in a state of pyrexia with rectal temperatures varying between 38.1 ºC and 38.4 ºC, depending on the dose. On the other hand, the positive control based on dipyrone (100 mg/kg) significantly reduced the rectal temperature up to 36.0 ºC in the same time interval (Table 3). Despite our findings, extracts from other species of Cyperaceae have shown significant antipyretic activity (Gupta et al., 1980; Subedi et al., 2016; Roy et al., 2019). The occurrence of phenolics was not investigated in such cases, but the *β*-sitosterol isolated from *C. rotundus* reduced the temperature of albino rats from 38.9 ºC to 36 ºC after 2 h of the experiment (Gupta et al., 1980). The occurrence of *β*-sitosterol in LHERn was not evaluated, but due to its hydrophobic characteristic, its presence in the tested extract can be minimized.

Table 3

Effect of the lyophilized hydroalcoholic extract of *Rhynchospora nervosa* (LHERn) on pyrexia induced by yeast (*Saccharomyces cerevisae*) in mice.

	Body Temperature (ºC)/Treatment				
			LHERn (mg/kg)		
Time (h)	0.9% NaCl	Dipyrone	100	200	400
0	38.18 ± 0.19^{a}	38.15 ± 0.15^{a}	38.23 ± 0.19^{a}	38.81 ± 0.43^{a}	38.38 ± 0.41^{a}
1	38.33 ± 0.24^{a}	36.05 ± 0.21^{b}	38.25 ± 0.15^{a}	38.21 ± 0.66^{a}	38.10 ± 0.45^{a}
2	38.38 ± 0.13^{a}	35.93 ± 0.30^{b}	38.25 ± 0.55^{a}	38.78 ± 0.24^{a}	38.50 ± 0.54^{a}
3	38.46 ± 0.13^{a}	36.03 ± 0.35^{b}	38.15 ± 0.76^{a}	38.63 ± 0.45^{a}	38.48 ± 0.48^{a}
4	38.36 ± 0.17^{a}	36.05 ± 0.30^{b}	38.45 ± 0.56^{a}	38.18 ± 0.25^{a}	38.31 ± 0.29^{a}

Values are expressed as mean ± SD (n = 6). Different superscript letters in the same line indicate differences between treatments by ANOVA one-way and Tukey's test **(**$P < 0.05$).

4. Conclusion

The lyophilized hydroalcoholic extract of *R. nervosa* showed significant anti-inflammatory and antinociceptive activity *in vivo* using heterogenic Swiss mice. These preliminary findings

indicate that the use of this species in Brazilian traditional medicine for the treatment of inflammation is supported by the presence of substances with anti-inflammatory potential. The high content of phenols and flavonoids in LHERn may indicate that compounds of this nature may be responsible for the pharmacological activities found. Additional chemical and pharmacological studies of LHERn are needed to elucidate the active molecules and their mechanisms of action against pro-inflammatory mediators in *in vivo* systems.

CRediT authorship contribution statement

J.J.L.B. designed the study and wrote the manuscript. J.J.L.B. and J.R.S.O. performed the experiments, analyzed and collected the data. V.L.M.L., M.V.S. and D.R.C.A. provided technical support. A.F.M.O. supervised the work, and performed a critical and substantial review of the manuscript. All authors have read and approved the final manuscript.

Declaration of competing interest

The authors declared no potential conflicts of interest.

Acknowledgments

The authors are thankful to the National Institute of Semi-arid. (INSA), Campina Grande, Paraíba state, Brazil and Dárdano de Andrade Lima Herbarium (Agronomic Research Institute - IPA), Recife, Pernambuco state, Brazil for collaboration and support.

Funding

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES) - Finance Code 001. The first author is grateful to the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq - Brazil) for the provision of a PhD scholarship. The last author is grateful to the CNPq for the provision of a research grant (310811/2019-8).

References

Alam, M.A., Jahan, R., Rahman, S., Das, A.K., Rahmatullah, M., 2011. Antinociceptive and anti-hyperglycemic activity of methanol leaf extract of *Cyperus scariosus*. Pak. J. Pharm. Sci. 24, 53-56.

Alves, M., Araújo, A.C., Prata, A.P., Vitta, F., Hefler, S., Trevisan, R., Gil, A.S.B., Martins, S., Thomas, W., 2009a. Diversity of Cyperaceae in Brazil. Rodriguésia. 60, 771-782. https://doi.org/10.1590/2175-7860200960405

Alves, C.F., Alves, V.B., Assis, I.P., Clemente-Napimoga, J.T., Uber-Bucek, E., Dal-Secco, D., et al., 2009b. Anti-inflammatory activity and possible mechanism of extract from *Mikania laevigata* in carrageenan induced peritonitis. J. Pharm. Pharmacol. 61, 1097-1104. https://doi.org/10.1211/jpp/61.08.0014

Al-Hazmi, G.H., Awaad, A.S., Alothman, M.R., Alqasoumi, S.I., 2018. Anticandidal activity of the extract and compounds isolated from *Cyperus conglomertus* Rottb. Saudi Pharm. J. 26, 891-895. https://doi.org/10.1016/j.jsps.2018.03.007

Amdekar S., Roy, P., Singh, V., Kumar, A., Singh, R., Sharma, P., 2021. Anti-inflammatory activity of lactobacillus on carrageenan-induced paw edema in male wistar rats. Int. J. Inflam. 2012. https://doi.org/10.1155/2012/752015

Awaad, A.S., Soliman, G.A., El-Sayed, D.F., El-Gindi, O.D., Alqasoumi, S.I., 2012. Hepatoprotective activity of *Cyperus alternifolius* on carbon tetrachloride–induced hepatotoxicity in rats. Pharm. Biol. 50, 155-161. https://doi.org/10.3109/13880209.2011.580351

Bezerra, J.J.L., Nascimento, T.G., Kamiya, R.U., Prata, A.P.N., Medeiros, P.M., Silva, S.A.S., Mendonça, C.N., 2019. Phytochemical screening, chromatographic profile and evaluation of antimicrobial and antioxidant activities of three species of the Cyperaceae Juss. Family. J. Med. Plants Res. 13, 312-320. https://doi.org/10.5897/JMPR2019.6796

Brillatz, T., Jacmin, M., Queiroz, E. F., Marcourt, L., Slacanin, I., Petit, C., et al., 2020. Zebrafish bioassay-guided isolation of antiseizure compounds from the Cameroonian medicinal plant *Cyperus articulatus* L. Phytomedicine. 70, 153175. https://doi.org/10.1016/j.phymed.2020.153175

Chaulya, N.C., Haldar, P.K., Mukherjee, A., 2012. Anti-inflammatory and Analgesic Activity of Methanol Extracts of *Cyperus tegetum* Roxb. Rhizome. J. PharmaSciTech. 1, 27-29.

Cheng, A.W., Tan, X., Sun, J.Y., Gu, C.M., Liu, C., Guo, X., 2019. Catechin attenuates TNF-α induced inflammatory response via AMPK-SIRT1 pathway in 3T3-L1 adipocytes. PLoS One. 14, e0217090. https://doi.org/10.1371/journal.pone.0217090

Collier, H.O., Dinneen, L.C., Johnson, C.A., Schneider, C., 1968. The abdominal constriction response and its suppression by analgesic drugs in the mouse. Br. J. Pharmacol. Chemother. 32, 295-310. https://doi.org/10.1111/j.1476-5381.1968.tb00973.x

Costa, L.C.B., Rocha, E.A., Silva, L.A.M., Jardim, J.G., Silva, D.C., Gaião, L.O., Moreira, R.D.C.T., 2006. Levantamento preliminar das espécies vegetais com potencial econômico no Parque Municipal da Boa Esperança, Ilhéus, Bahia, Brasil. Acta Farm. Bonaer. 25, 184-191.

Daniel, A.N., Sartoretto, S.M., Schmidt, G., Caparroz-Assef, S.M., Bersani-Amado, C.A., Cuman, R.K.N., 2009. Anti-inflammatory and antinociceptive activities A of eugenol essential oil in experimental animal models. Rev. Bras. Farmacogn. 19, 212-217. https://doi.org/10.1590/S0102-695X2009000200006

Dong, S.H., Zhang, J.F., Tang, Y.M., Li, J., Xiang, Y.R., Liang, Q.L., 2016. Chemical constituents from the tubers of *Scirpus yagara* and their anti-inflammatory activities. J. Asian Nat. Prod. Res. 18, 791-797. https://doi.org/10.1080/10286020.2016.1158166

Dória, G.A.A., Menezes, P.P., Lima, B.S., Vasconcelos, B.S., Silva, F.A., Henriques, R.M., et al., 2016. *In vivo* antitumor effect, induction of apoptosis and safety of *Remirea maritima* Aubl. (Cyperaceae) extracts. Phytomedicine 23, 914-922. https://doi.org/10.1016/j.phymed.2016.05.001

El-Aziz, T.A.A., Mohamed, R.H., Pasha, H.F., Abdel-Aziz, H.R., 2012. Catechin protects against oxidative stress and inflammatory-mediated cardiotoxicity in adriamycin-treated rats. Clin. Exp. Med. 12, 233-240. https://doi.org/10.1007/s10238-011-0165-2

Erdem, B., Bagci, E., Dogan, G., Aktoklu, E., Dayangac, A., 2018. Chemical composition and antimicrobial activities of essential oil and ethanol extract of *Cyperus fuscus* L burs from Turkey. Trop. J. Pharm. Res. 17, 1637-1643. https://doi.org/10.4314/tjpr.v17i8.24

Gomez, M., Rocha, E.A., Gomberg, E., 2016. Análise das publicações etnobotânicas sobre plantas medicinais da Mata Atlântica na Região Sul do Estado da Bahia, Brasil. Rev. Fitos. 10, 115-140. https://doi.org/10.5935/2446-4775.20160010

Gupta, M.B., Nath, R., Srivastava, N., Shanker, K., Kishor, K., Bhargava, K.P., 1980. Anti-inflammatory and antipyretic activities of β-sitosterol. Planta Med. 39, 157-163. https://doi.org/10.1055/s-2008-1074919

Gupta, M., Singh, N., Gulati, M., Gupta, R., Sudhakar, K., Kapoor, B., 2021. Herbal bioactives in treatment of inflammation: An overview. S. Afr. J. Bot. 143, 205-225. https://doi:10.1016/j.sajb.2021.07.027

Ibrahim, S.R., Mohamed, G.A., Alshali, K.Z., Haidari, R.A.A., El-Kholy, A.A., Zayed, M.F., 2018. Lipoxygenase inhibitors flavonoids from *Cyperus rotundus* aerial parts. Rev. Bras. Farmacogn. 28, 320-324. https://doi.org/10.1016/j.bjp.2018.04.002

Ito, T., Endo, H., Shinohara, H., Oyama, M., Akao, Y., Iinuma, M., 2012. Occurrence of stilbene oligomers in *Cyperus* rhizomes. Fitoterapia. 83, 1420-1429. https://doi.org/10.1016/j.fitote.2012.08.005

Jaiswal, Y., Liang, Z., Guo, P., Ho, H. M., Chen, H., Zhao, Z., 2014. Tissue-specific metabolite profiling of *Cyperus rotundus* L. rhizomes and (+)-nootkatone quantitation by laser microdissection, ultra-high-performance liquid chromatography–quadrupole time-of-flight mass spectrometry, and gas chromatography–mass spectrometry techniques. J. Agric. Food Chem. 62, 7302-7316. https://doi.org/10.1021/jf502494z

Kakarla, L., Mathi, P., Allu, P. R., Rama, C., Botlagunta, M., 2014. Identification of human cyclooxegenase-2 inhibitors from *Cyperus scariosus* (R. Br) rhizomes. Bioinformation. 10, 637-646. https://doi.org/10.6026/97320630010637

Kamala, A., Middha, S.K., Gopinath, C., Sindhura, H.S., Karigar, C.S., 2018. *In vitro* antioxidant potentials of *Cyperus rotundus* L. Rhizome extracts and their phytochemical analysis. Pharmacogn. Mag. 14, 261–267. https://doi.org/10.4103/pm.pm_228_17

Kandikattu, H.K., Tamatam, A., Pal, A., Khanum, F., 2013. Neuroprotective effects of *Cyperus rotundus* on SIN-1 induced nitric oxide generation and protein nitration: ameliorative effect against apoptosis mediated neuronal cell damage. Neurotoxicology. 34, 150-159. https://doi.org/10.1016/j.neuro.2012.11.002

Kasala, S., Ramanjaneyulu, K., Himabindhu, J., Alluri, R., Babu, R.R., 2016. Preliminary phytochemical screening and *in vitro* anthelmintic activity of *Cyperus rotundus* (L). J. Pharmacogn. Phytochem. 5, 407-409.

Kilani-Jaziri, S., Bhouri, W., Skandrani, I., Limem, I., Chekir-Ghedira, L., Ghedira, K., 2011. Phytochemical, antimicrobial, antioxidant and antigenotoxic potentials of *Cyperus rotundus* extracts. S. Afr. J. Bot. 77, 767-776. https://doi.org/10.1016/j.sajb.2011.03.015

Kilani-Jaziri, S., Ghedira, Z., Nasr, N., Krifa, M., Ghedira, K., Franca, G.M.D., Ghedira, L.C., 2014. Evaluation of *in vitro* antioxidant and apoptotic activities of *Cyperus rotundus*. Asian Pac. J. Trop. Med. 7, 105-112. https://doi.org/10.1016/S1995-7645(14)60004-3

Kumar, S., Tiwari, R., Alam, N., 2012. Anti-inflammatory activity of methanolic extract of *Cyperus rotundus* rhizome on carrageenan induced paw edema in rats. Int. J. Pharm. Sci. Res. 3, 5097-5100.

Kumar, K.H., Razack, S., Nallamuthu, I., Khanum, F., 2014. Phytochemical analysis and biological properties of *Cyperus rotundus* L. Ind. Crops Prod. 52, 815-826. https://doi.org/10.1016/j.indcrop.2013.11.040

Lee, S.H., Shin, N.H., Kang, S.H., Park, J.S., Chung, S.R., Min, K.R., Kim, Y., 1998. α-Viniferin: a prostaglandin H2 synthase inhibitor from root of *Carex humilis*. Planta Med. 64, 204-207. https://doi.org/10.1055/s-2006-957409

Lisboa, M.S., Pinto, A.S., Barreto, P.A., Ramos, Y.J., Silva, M.Q.O.R., Caputo, M.C., Almeida, M.Z., 2017. Estudo Etnobotânico em Comunidade Quilombola Salamina/Putumujú em Maragogipe, Bahia. Rev. Fitos. 11, 48-61. https://doi.org/10.5935/2446-4775.20170006

Lorke, D., 1983. A new approach to practical acute toxicity testing. Arch. Toxicol. 54, 275-287. https://doi.org/10.1007/BF01234480

Luo, Y., Li, X., He, J., Su, J., Peng, L., Wu, X., Du, R., Zhao, Q., 2014. Isolation, characterisation, and antioxidant activities of flavonoids from chufa (*Eleocharis tuberosa*) peels. Food Chem. 164, 30-35. https://doi.org/10.1016/j.foodchem.2014.04.103

Metuge, J.A., Babiaka, S.B., Mbah, J.A., Ntie-Kang, F., Ayimele, G.A., Cho-Ngwa, F., 2014. Anti-onchocerca metabolites from *Cyperus articulatus*: Isolation, *in vitro* activity and i*n silico* 'drug-likeness'. Nat. Prod. Bioprospect. 4, 243-249. https://doi.org/10.1007/s13659-014-0023-5

Moreira, R.D.C.T., Costa, L.C.D.B., Costa, R.C.S., Rocha, E.A., 2002. Abordagem etnobotânica acerca do uso de plantas medicinais na Vila Cachoeira, Ilhéus, Bahia, Brasil. Acta Farm. Bonaer. 21, 205-211.

Nahrevanian, H., 2009. Involvement of nitric oxide and its up/down stream molecules in the immunity against parasitic infections. Brazilian Braz. J. Infect. Dis. 13, 440-448. https://doi.org/10.1590/S1413-86702009000600010

Nakanishi, T., Mukai, K., Yumoto, H., Hirao, K., Hosokawa, Y., Matsuo, T., 2010. Anti-inflammatory effect of catechin on cultured human dental pulp cells affected by bacteria-derived factors. Eur. J. Oral Sci. 118, 145-150. https://doi.org/10.1111/j.1600-0722.2010.00714.x

Nam, J.H., Nam, D.Y., Lee, D.U., 2016. Valencene from the rhizomes of *Cyperus rotundus* inhibits skin photoaging-related ion channels and UV-induced melanogenesis in B16F10 melanoma cells. J. Nat. Prod. 79, 1091-1096. https://doi.org/10.1021/acs.jnatprod.5b01127

Nassar, M.I., Yassine, Y.M., Elshamy, A.I., El-Beih, A.A., El-Shazly, M., Singab, A.N. B., 2015. Essential oil and antimicrobial activity of aerial parts of *Cyperus leavigatus* L. (Family: Cyperaceae). J. Essent. Oil Bear. Pl. 18, 416-422. https://doi.org/10.1080/0972060X.2014.971073

Nidugala, H., Avadhani, R., Prabhu, A., Basavaiah, R., 2016. *In vitro* cytotoxic activity of rhizome extracts of *Cyperus rotundus* (L.) against colon carcinoma and Ehrlich ascites carcinoma. J. Appl. Pharm. Sci. 6, 172-175. https://doi.org/10.7324/JAPS.2016.601127

Njoku-Oji, N.N., Ifegwu, N.O., Umahi, G.O., Sobanke, A.O., Uchefuna, R.C., 2019. Beneficial effects of ethanolic seed extract of *Cyperus esculentus* on blood glucose and sperm quality in alloxan-induced diabetic rats. IOSR J. Pharm. Biol. Sci. 14, 84-90. https://doi.org/10.9790/3008-1401018490

Nuryana, F.I., Chozin, M.A., Guntoro, D., 2019. High-performance liquid chromatography analysis for α-cyperone and nootkatone from the tuber of nutsedge (*Cyperus rotundus* L.) in the tropics. Rasayan J. Chem. 12, 360-365. http://dx.doi.org/10.31788/RJC.2019.1215024

Okwu, G.N., Abanobi, S.E., Nnadi, U.V., Ujowundu, C.O., Ene, A.C., 2015. Hypolipidemic Properties of Ethanol Extract of *Cyperus rotundus* Rhizome. Int. J. Biochem. Res. Rev. 7, 132-138. https://doi.org/10.9734/IJBcRR/2015/17158

Owoyele, B.V., Abioye, A.I.R., Oyewole, A.L., Ameen, M.O., Owemidu, I.O., Adewusi M.O., 2015. Effects of the Ethanolic Extract of *Bulbostylis coleotricha* (Hochst. Exa. Rich.) on Inflammation in Adult Wistar Rats. Nig. J. Nat. Prod. Med. 19, 101-105. http://dx.doi.org/10.4314/njnpm.v19i1.11

Pagning, A.L.N., Lateef, M., Tapondjou, L.A., Kuiate, J.R., Ngnokam, D., Ali, M.S., 2016. New triterpene and new flavone glucoside from *Rhynchospora corymbosa* (Cyperaceae)

with their antimicrobial, tyrosinase and butyrylcholinesterase inhibitory activities. Phytochem. Lett. 16, 121-128. https://doi.org/10.1016/j.phytol.2016.03.011

Park, Y.J., Zheng, H., Kwak, J.H., Chung, K.H., 2019. Sesquiterpenes from *Cyperus rotundus* and 4α, 5α-oxidoeudesm-11-en-3-one as a potential selective estrogen receptor modulator. Biomed. Pharmacother. 109, 1313-1318. https://doi.org/10.1016/j.biopha.2018.10.186

Patil, R.H., Babu, R.L., Kumar, M.N., Kumar, K.K., Hegde, S.M., Nagesh, R., et al., 2016. Anti-inflammatory effect of apigenin on LPS-induced pro-inflammatory mediators and AP-1 factors in human lung epithelial cells. Inflammation. 39, 138-147. https://doi.org/10.1007/s10753-015-0232-z

Pham, H.H.T., Seong, Y.A., Ngabire, D., Oh, C.W., Kim, G.D., 2017. *Cyperus amuricus* induces G1 arrest and apoptosis through endoplasmic reticulum stress and mitochondrial signaling in human hepatocellular carcinoma Hep3B cells. J. Ethnopharmacol. 208, 157-164. https://doi.org/10.1016/j.jep.2017.07.002

Popescu, A., Pavalache, G., Pirjol, T.N., Istudor, V., 2016. Antioxidant comparative activity and total phenolic content of *Scirpus holoschoenus* L. (*Holoschoenus vulgaris* Link) depending on extraction condition and the solvent used. Rev. Chim. 67, 255-259.

Prasad, N., Gupta, A., 2005. Fungal peritonitis in peritoneal dialysis patients. Perit. Dial. Int. 25, 207–222. https://doi.org/10.1177/089686080502500302

Queiroz, A.C., Lira, D.P., Dias, T.L.M.F., Souza, E.T., Matta, C.B.B., Aquino, A.B. et al., 2010. The antinociceptive and anti-inflammatory activities of *Piptadenia stipulacea* Benth. (Fabaceae). J. Ethnopharmacol. 128, 377-383. https://doi.org/10.1016/j.jep.2010.01.041

Rabelo, A.S., Oliveira, I.D., Guimarães, A.G., Quintans, J.S.S., Prata, A.P.N., Gelain, D.P., et al., 2013. Antinociceptive, anti-inflammatory and antioxidant activities of aqueous extract from *Remirea maritima* (Cyperaceae). J. Ethnopharmacol. 145, 11-17. https://doi.org/10.1016/j.jep.2012.10.020

Rajamanickam, M., Rajamanickam, A., 2016. Analgesic and anti-inflammatory activity of the extracts from *Cyperus rotundus* Linn rhizomes. J. Appl. Pharm. Sci. 6, 197-203. https://doi.org/10.7324/JAPS.2016.60929

Ramírez, O., Blair, S., 2017. Ethnobotany of medicinal plants used to treat malaria by traditional healers from ten indigenous Colombian communities located in Waupes Medio. Biodiversity Int. J. 1, 151-167. https://doi.org/10.15406/bij.2017.01.00022

Rocha, F.G., Brandenburg, M.M., Pawloski, P.L., Soley, B.S., Costa, S.C.A., Meinerz, C.C., et al., 2020. Preclinical study of the topical anti-inflammatory activity of *Cyperus rotundus* L. extract (Cyperaceae) in models of skin inflammation. J. Ethnopharmacol. 254, 112709, 2020. https://doi.org/10.1016/j.jep.2020.112709

Rodrigues, E., Mendes, F.R., Negri, G., 2006. Plants indicated by Brazilian Indians for disturbances of the central nervous system: a bibliographical survey. Cent. Nerv. Syst. Agents Med Chem. 6, 211-244. https://doi.org/10.2174/187152406778226725

Roy, R., Daula, A.S.U., Akter, A., Sultana, S., Barek, M.A., Liya, I.J., Basher, M.A., 2019. Antipyretic and anti-nociceptive effects of methanol extract of leaves of *Fimbristylis miliacea* in mice model. J. Ethnopharmacol. 243, 112080. https://doi.org/10.1016/j.jep.2019.112080

Salaritabar, A., Darvishi, B., Hadjiakhoondi, F., Manayi, A., Sureda, A., Nabavi, S. F., Fitzpatrick, L.R., Nabavi, S.M., Bishayee, A., 2017. Therapeutic potential of flavonoids in inflammatory bowel disease: A comprehensive review. World J. Gastroenterol. 23, 5097. https://doi.org/10.3748/wjg.v23.i28.5097

Santana, B.F., Voeks, R.A., Funch, L.S., 2016. Ethnomedicinal survey of a maroon community in Brazil's Atlantic tropical forest. J. Ethnopharmacol. 181, 37-49. https://doi.org/10.1016/j.jep.2016.01.014

Seo, W. G., Pae, H. O., Oh, G. S., Chai, K. Y., Kwon, T. O., Yun, Y. G., et al., 2001. Inhibitory effects of methanol extract of *Cyperus rotundus* rhizomes on nitric oxide and superoxide productions by murine macrophage cell line, RAW 264.7 cells. J. Ethnopharmacol. 76, 59-64. https://doi.org/10.1016/S0378-8741(01)00221-5

Shakerin, Z., Esfandiari, E., Razavi, S., Alaei, H., Ghanadian, M., Dashti, G., 2020. Effects of *Cyperus rotundus* extract on spatial memory impairment and neuronal differentiation in rat model of Alzheimer's disease. Adv. Biomed. Res. 9, 17. https://doi.org/10.4103/abr.abr_173_19

Shorinwa, O.A., Dambani, D.T., 2020. Antidiarrheal activity of aqueous ethanol extract of *Cyperus esculentus* tuber in albino rats. J. Appl. Biol. Biotechnol. 8, 47-50. https://doi.org/10.7324/JABB.2020.80309

Siani, A.C., Silva, A.M., Nakamura, M.J., Carvalho, M.V., Henriques, M.G., Ramos, M.F., Kaiser, C.R., 2001. Chemical composition and anti-inflammatory activity of the hydrodistillate from *Mariscus pedunculatus*. J. Braz. Chem. Soc. 12, 354-359. http://dx.doi.org/10.1590/S0103-50532001000300006

Subedi, N.K., Rahman, S.M., Akbar, M.A., 2016. Analgesic and antipyretic activities of methanol extract and its fraction from the root of *Schoenoplectus grossus*. Evid. Based Complement. Alternat. Med. 2016, 1-8. https://doi.org/10.1155/2016/3820704

Sukjamnong, S., Santiyanont, R., 2015. Effect of *Fimbristylis ovata* on receptor for advanced glycation end-products, proinflammatory cytokines, and cell adhesion molecule level and gene expression in U937 and bEnd. 3 cell lines. Genet. Mol. Res. 14, 3984-3994. https://doi.org/10.4238/2015.April.27.13

Sultana, S., Ali, M., Mir, S.R., 2017. Chemical Constituents from the rhizomes of *Cyperus rotundus* L. Open Plant. Sci. J. 10, 82-91. https://doi.org/10.2174/1874294701710010082

Talhouk, R.S., Karam, C., Fostok, S., El-Jouni, W., Barbour, E.K., 2007. Anti-inflammatory bioactivities in plant extracts. J. Med. Food. 10, 1-10. https://doi.org/10.1089/jmf.2005.055

Thomas, W.W., Weber, P., Silva Filho, P.J.S., 2020. *Rhynchospora* in Flora do Brasil 2020. Jardim Botânico do Rio de Janeiro. Available in: <http://floradobrasil.jbrj.gov.br/reflora/floradobrasil/FB7276>. Access in: October 28, 2021.

Tsoyi, K., Jang, H.J., Lee, Y.S., Kim, Y.M., Kim, H.J., Seo, H.G., et al., 2011. (+)-Nootkatone and (+)-valencene from rhizomes of *Cyperus rotundus* increase survival rates in septic mice due to heme oxygenase-1 induction. J. Ethnopharmacol. 137, 1311-1317. https://doi.org/10.1016/j.jep.2011.07.062

Vega-Morales, T., Mateos-Díaz, C., Pérez-Machín, R., Wiebe, J., Gericke, N.P., Alarcón, C., López-Romero, J.M., 2019. Chemical composition of industrially and laboratory processed *Cyperus esculentus* rhizomes. Food Chem. 297, 124896. https://doi.org/10.1016/j.foodchem.2019.05.170

Wang, J., Liu, Y.T., Xiao, L., Zhu, L., Wang, Q., Yan, T., 2014. Anti-inflammatory effects of apigenin in lipopolysaccharide-induced inflammatory in acute lung injury by suppressing COX-2 and NF-kB pathway. Inflammation. 37, 2085-2090. https://doi.org/10.1007/s10753-014-9942-x

Waterman, P.G., Mole, S., 1994. Analysis of phenolic plant metabolites. Blackwell Scientific Publications. 38, 1064.

Winter, C.A., Risley, E.A., Nuss, G.W., 1962. Carrageenan-induced oedema in hind paw of rat as an assay for anti-inflammatory drugs. Proc. Soc. Exp. Biol. Med. 111, 544-547. https://doi.org/10.3181/00379727-111-27849

Woisky, R.G., Salatino, A., 1998. Analysis of propolis: some parameters and procedures for chemical quality control. J. Apic. Res. 37, 99-105. http://dx.doi.org/10.1080/00218839.1998.11100961

Xu, H.B., Ma, Y.B., Huang, X.Y., Geng, C.A., Wang, H., Zhao, Y., et al., 2015. Bioactivity-guided isolation of anti-hepatitis B virus active sesquiterpenoids from the traditional Chinese medicine: Rhizomes of *Cyperus rotundus*. J. Ethnopharmacol. 171, 131-140. https://doi.org/10.1016/j.jep.2015.05.040

Zhou, Z., Yin, W., 2012. Two novel phenolic compounds from the rhizomes of *Cyperus rotundus* L. Molecules. 17, 12636-12641. https://doi.org/10.3390/molecules171112636

Zhou, Z., Zhang, H., 2013. Phenolic and iridoid glycosides from the rhizomes of *Cyperus rotundus* L. Med. Chem. Res. 22, 4830-4835. https://doi.org/10.1007/s00044-013-0504-9

Zhou, Z., Yin, W., Zhang, H., Feng, Z., Xia, J., 2013. A new iridoid glycoside and potential MRB inhibitory activity of isolated compounds from the rhizomes of *Cyperus rotundus* L. Nat. Prod. Res. 27, 1732-1736. https://doi.org/10.1080/14786419.2012.750318

6 CONCLUSÃO GERAL

De forma geral, as espécies de Cyperaceae são tradicionalmente utilizadas como medicinais em diversos países do mundo, mas, vale ressaltar, que das 5.500 espécies até então conhecidas pela ciência, apenas 10 são utilizadas para o tratamento de inflamações e 13 tiveram sua atividade anti-inflamatória investigada em estudos *in vitro* e *in vivo*. Do ponto de vista químico, vários compostos já foram isolados e alguns deles, como os flavonoides e sesquiterpenos, se destacam em testes como candidatos a anti-inflamatórios naturais. Além da ação anti-inflamatória, os produtos avaliados apresentaram toxicidade insignificante em testes pré-clínicos, o que é muito importante.

Para o Brasil, vinte e sete espécies de Cyperaceae são utilizadas principalmente para o tratamento de inflamações. As raízes ou a planta inteira são as partes mais utilizadas, preparadas na forma de decocção ou infusão. Dentre estas espécies, apenas doze tiveram seus constituintes químicos e/ou atividades biológicas investigadas. Os sesquiterpenos foram a classe predominante de compostos identificados. *Cyperus rotundus* se destacou como a espécie com maior número de indicações medicinais, estudos farmacológicos e fitoquímicos. Embora as outras quinze espécies de Cyperaceae sejam relatadas como medicinais no Brasil, ainda são necessárias pesquisas científicas para confirmar ou refutar sua eficácia e segurança biológica.

Por fim, o extrato hidroalcoólico de *R. nervosa* (EHRn) apresentou significativa atividade anti-inflamatória e antinociceptiva *in vivo* em camundongos Swiss heterogênicos. Esses achados confirmam as indicações de uso desta espécie para o tratamento da inflamação na medicina popular no Brasil. O alto teor de fenóis e flavonoides no EHRn pode indicar que compostos dessa natureza podem ser os responsáveis pelas atividades farmacológicas encontradas. Estudos químicos e farmacológicos adicionais do EHRn são necessários para elucidar as moléculas ativas e seus mecanismos de ação contra mediadores pró-inflamatórios em sistemas *in vivo*.

REFERÊNCIAS

ADEONIPEKUN, P.A.; ADENIYI, T.A.; AMINU, S.O. Investigating the phytochemicals and antimicrobial activities of shoot and root of *Pycreus smithianus* (Ridl.) CB Clarke (Family Cyperaceae). **Journal of Botany**, v. 2014, p. 761613, 2014.

AHMED, S.A.; CHAKRAVARTHY, K. Simultaneous evaluation, estimation of hepatoprotective effects of *Kyllinga brevifolia* and antiepileptic activity of *Rorippa sarmentosa* extracts in rats. **Global Journal for Research Analysis**, v. 6, n. 6, p. 15-19, 2017.

AL-HAZMI, G.H.; AWAAD, A.S.; ALOTHMAN, M.R.; ALQASOUMI, S.I. Anticandidal activity of the extract and compounds isolated from *Cyperus conglomertus* Rottb. **Saudi Pharmaceutical Journal**, v. 26, n. 6, p. 891-895, 2018.

ARGUELHO, E.G.; MICHELAN, V.S.; NOGUEIRA, F.M.; SILVA, C.R.; RODRIGUEZ, C.; TREVISAN, R.; VANZELA, A.L. New chromosome counts in Brazilian species of *Rhynchospora* (Cyperaceae). **Caryologia**, v. 65, n. 2, p. 140-146, 2012.

BEZERRA, J.J.L.; NASCIMENTO, T.G.; KAMIYA, R.U.; PRATA, A.P.N.; MEDEIROS, P.M.; SILVA, S.A.S.; MENDONCA, C.N. Phytochemical screening, chromatographic profile and evaluation of antimicrobial and antioxidant activities of three species of the Cyperaceae Juss. Family. **Journal of Medicinal Plants Research**, v. 13, n. 14, p. 312-320, 2019.

BHUSHAN, B.; KUMAR, M. Ethnobotanically important medicinal plants of tehsil Billawar, District Kathua, J&K, India. **Journal of Pharmacognosy and Phytochemistry**, v. 2, n. 4, p. 14-21, 2013.

BIESKI, I.G.C.; SANTOS, F.R.; OLIVEIRA, R.M.; ESPINOSA, M.M.; MACEDO, M.; ALBUQUERQUE, U.P.; MARTINS, D.T.O. Ethnopharmacology of medicinal plants of the pantanal region (Mato Grosso, Brazil). **Evidence-Based Complementary and Alternative Medicine**, v. 2012, p. 1-36, 2012.

BRANDÃO, M.G.; PIGNAL, M.; ROMANIUC, S.; GRAEL, C.F.; FAGG, C.W. Useful Brazilian plants listed in the field books of the French naturalist Auguste de Saint-Hilaire (1779–1853). **Journal of Ethnopharmacology**, v. 143, n. 2, p. 488-500, 2012.

BRILLATZ, T.; JACMIN, M.; QUEIROZ, E.F.; MARCOURT, L.; SLACANIN, I.; PETIT, C.; et al. Zebrafish bioassay-guided isolation of antiseizure compounds from the Cameroonian medicinal plant *Cyperus articulatus* L. **Phytomedicine**, v. 70, p. 153175, 2020.

CAO, Q.Y.; GUO, X.Y.; DUAN, J.A.; LIANG, Q.L. The active fraction from the tuber of *Bolboschoenus yagara* inhibits melanoma B16 cells metastasis LPS-induced *in vitro* and *in vivo*. **Natural Product Research**, v. 34, n. 23, p. 3378-3381, 2020.

CASTRO, K.N.C.; WOLSCHICK, D.; LEITE, R.R.S.; ANDRADE, I.M.; MAGALHÃES, J.A.; MAYO, S.J. Ethnobotanical and ethnoveterinary study of medicinal plants used in the municipality of Bom Princpio do Piau, Piau, Brazil. **Journal of Medicinal Plants Research**, v. 10, n. 23, p. 318-330, 2016.

CHO, N.; VALENCIANO, A.L.; DU, Y.; CLEMENT, J.; CASSERA, M.B.; GOETZ, M.; KINGSTON, D.G. Antiplasmodial flavanones and a stilbene from *Carpha glomerata*. **Bioorganic & Medicinal Chemistry Letters**, v. 28, n. 20, p. 3368-3371, 2018.

COSTA, L.C.B.; ROCHA, E.A.; SILVA, L.A.M.; JARDIM, J.G.; SILVA, D.C.; GAIÃO, L.O.; MOREIRA, R.D.C.T. Levantamento preliminar das espécies vegetais com potencial econômico no Parque Municipal da Boa Esperança, Ilhéus, Bahia, Brasil. **Acta Farmacéutica Bonaerense**, v. 25, n. 2, p. 184-91, 2006.

DANG, G.K.; PAREKAR, R.R.; KAMAT, S.K.; SCINDIA, A.M.; REGE, N.N. Antiinflammatory activity of Phyllanthus emblica, Plumbago zeylanica and *Cyperus rotundus* in acute models of inflammation. **Phytotherapy Research**, v. 25, n. 6, p. 904-908, 2011.

DATTA, S.; DHAR, S.; NAYAK, S.S.; DINDA, S.C. Hepatoprotective activity of *Cyperus articulatus* Linn. against paracetamol induced hepatotoxicity in rats. **Journal of Chemical and Pharmaceutical Research**, v. 5, n. 1, p. 314-319, 2013.

DATTA, S.; SEAL, T.; SINHA, B.K.; BHATTACHARJEE, S. RP-HPLC based evidences of rich sources of phenolics and water-soluble vitamins in an annual sedge *Cyperus compressus.* **The Journal of Phytopharmacology**, v. 7, n. 3, p. 305-311, 2018.

DONG, S.H.; ZHANG, J.F.; TANG, Y.M.; LI, J.; XIANG, Y.R.; LIANG, Q.L. Chemical constituents from the tubers of *Scirpus yagara* and their anti-inflammatory activities. **Journal of Asian Natural Products Research**, v. 18, n. 8, p. 791-797, 2016.

DÓRIA, G.A.A.; MENEZES, P.P.; LIMA, B.S.; VASCONCELOS, B.S.; SILVA, F.A.; HENRIQUES, R.M.; et al. *In vivo* antitumor effect, induction of apoptosis and safety of *Remirea maritima* Aubl.(Cyperaceae) extracts. **Phytomedicine**, v. 23, n. 9, p. 914-922, 2016.

ELSHAMY, A.I.; EL-SHAZLY, M.; YASSINE, Y.M.; EL-BANA, M.A.; FARRAG, A.R.; NASSAR, M. I.; et al. Phenolic constituents, anti-inflammatory and antidiabetic activities of *Cyperus laevigatus* L. **Pharmacognosy Journal**, v. 9, n. 6, p. 828-833, 2017.

GANESAN, K.; XU, B. Ethnobotanical studies on folkloric medicinal plants in Nainamalai, Namakkal District, Tamil Nadu, India. **Trends in Phytochemical Research**, v. 1, n. 3, p. 153-168, 2017.

GHULAM Y.; MANIK, S.R.; SHRAVAGI, N.; NATHAR, V.N.; SAUDAGAR, S.A.A.G.; AABID, M.; MOHD, J. Ethnobotanical study of common medicinal plants used by the people of village Fubgaon, District Amravati Maharashtra, India. **International Journal of Current Research**, v. 4, p. 29-34, 2015.

GIRI, B.R.; BHARTI, R.R.; ROY, B. *In vivo* anthelmintic activity of *Carex baccans* and its active principle resveratrol against *Hymenolepis diminuta*. **Parasitology Research**, v. 114, n. 2, p. 785-788, 2015.

GOMEZ, M.; ROCHA, E.A.; GOMBERG, E. Análise das publicações etnobotânicas sobre plantas medicinais da Mata Atlântica na Região Sul do Estado da Bahia, Brasil. **Revista Fitos**, v. 10, n. 2, p. 115-140, 2016.

GOVAERTS, R.; SIMPSON, D.A.; GOETGHEBEUR, P.; WILSON, K.L.; EGOROVA T.; BRUHL J. **World checklist of Cyperaceae**. Kew: The Board of Trustees of the Royal Botanic Gardens, Kew. 2011.

GOVAERTS, R.; SIMPSON, D.A.; GOETGHEBEUR, P.; WILSON, K.L.; EGOROVA, T.; BRUHL, J.J. **World checklist of Cyperaceae**. Kew: The Board of Trustees of the Royal Botanic Gardens, Kew. 2018.

IBRAHIM, S.R.M.; MOHAMED, G.A.; KHAYAT, M.T.A.; ZAYED, M.F.; EL-KHOLY, A.A.E.S. Anti-inflammatory terpenoids from *Cyperus rotundus* rhizomes. **Pakistan Journal of Pharmaceutical Sciences**, v. 31, p. 1449-1456, 2018.

ITO, T.; ENDO, H.; SHINOHARA, H.; OYAMA, M.; AKAO, Y.; IINUMA, M. Occurrence of stilbene oligomers in *Cyperus rhizomes*. **Fitoterapia**, v. 83, n. 8, p. 1420-1429, 2012.

JARAMILLO-COLORADO, B.E.; MARTÍNEZ-CÁCERES, E.L.; DUARTE-RESTREPO, E. Volatile chemical composition and bioactivities from Colombian *Kyllinga pumila* Michx

(Cyperaceae) essential oil. **Acta Scientiarum. Biological Sciences**, v. 38, n. 3, p. 273-282, 2016.

KAKARLA, L.; KATRAGADDA, S.B.; TIWARI, A.K.; KOTAMRAJU, K.S.; MADHUSUDANA, K.; KUMAR, D.A.; BOTLAGUNTA, M. Free radical scavenging, α-glucosidase inhibitory and anti-inflammatory constituents from Indian sedges, *Cyperus scariosus* R. Br and *Cyperus rotundus* L. **Pharmacognosy Magazine**, v. 12, n. Suppl 4, p. S488-S496, 2016.

KARUNASREE, C.P.; PRASAD, P.; REDDY, V.J.; MADAKKA, M. Cardioprotective effect of *Scleria lithosperma* on doxorubicin-induced cardiotoxicity in Wistar albino rats. **Annual Research & Review in Biology**, v. 8, n. 6, 1-9, 2015.

LARRIDON, I.; REYNDERS, M.; HUYGH, W.; BAUTERS, K.; VRIJDAGHS, A.; LEROUX, O.; MUASYA, A.M.; SIMPSON, D.A.; GOETGHEBEUR, P. Taxonomic changes in C3 *Cyperus* (Cyperaceae) supported by molecular data, morphology, embryography, ontogeny and anatomy. **Plant Ecology and Evolution**, v. 144, n. 3, p. 327-356, 2011.

LARRIDON, I., BAUTERS, K., REYNDERS, M., HUYGH, W., MUASYA, A.M., SIMPSON, D.A., GOETGHEBEUR, P. Towards a new classification of the giant paraphyletic genus *Cyperus* (Cyperaceae): phylogenetic relationships and generic delimitation in C4 *Cyperus*. Botanical **Journal of the Linnean Society**, v. 172, n. 1, p. 106-126, 2013.

LISBOA, M.S.; PINTO, A.S.; BARRETO, P.A.; RAMOS, Y.J.; SILVA, M.Q.O.R.; CAPUTO, M.C.; ALMEIDA, M.Z. Estudo Etnobotânico em Comunidade Quilombola Salamina/Putumujú em Maragogipe, Bahia. **Revista Fitos**, v. 11, n. 1, p. 48-61, 2017.

MARTINS, M.L.L.; PACHECO, H.P.; PERINI, I.G.; LENZ, D.; ANDRADE, T.U.D.; ENDRINGER, D.C. *In vivo* hypotensive effect and *in vitro* inhibitory activity of some Cyperaceae species. **Brazilian Journal of Pharmaceutical Sciences**, v. 49, p. 803-809, 2013.

MARTINS, M.L.L.; PINTO, F.E.; ANDRADE, T.U.; LENZ, D.; PEREIRA, T.M.C.; ENDRINGER, D.C. Gastroprotective effect of *Lagenocarpus rigidus* (Kunth) Ness (tirica-do-nativo) leaf extract against indomethacin-induced gastric injury. **Revista Cubana de Plantas Medicinales**, v. 19, n. 2, p. 121-127, 2014.

MESSIAS, M.C.T.B.; MENEGATTO, M.F.; PRADO, A.C.C.; SANTOS, B.R.D.; GUIMARÃES, M.F.M. Uso popular de plantas medicinais e perfil socioeconômico dos

usuários: um estudo em área urbana em Ouro Preto, MG, Brasil. **Revista Brasileira de Plantas Medicinais**, v. 17, n. 1, p. 76-104, 2015.

MIA, S.; ROY, R.; AKTER, A.; BAREK, M.A.; BASHER, M.A. Hypoglycemic effect of leaf extract of *Fimbristylis miliacea* in mice model. **Clinical Phytoscience**, v. 5, n. 1, p. 26, 2019.

MOHAMMED, M.S.; AHMED, W.J.; KHALID, H.S.; MAHMOUD, A.M.; GARELNABI, E.A. Di-(2'-ethylhexyl) phthalate and stigmasterol with antiinflammatory effect from *Cyperus rotundus* L. **International Journal of Pharmaceutical, Chemical and Biological Sciences**, v. 4, p. 453- 459, 2014.

MOREIRA, R.D.C.T.; COSTA, L.C.D.B.; COSTA, R.C.S.; ROCHA, E.A. Abordagem etnobotânica acerca do uso de plantas medicinais na Vila Cachoeira, Ilhéus, Bahia, Brasil. **Acta Farmacêutica Bonaerense**, v. 21, n. 3, p. 205-2011, 2002.

MOTTA, A.O.; LIMA, D.C.S.; VALE, C.R. Levantamento do uso de Plantas Medicinais em um Centro de Educação Infantil em Goiânia–GO. **Revista da Universidade Vale do Rio Verde**, v. 14, n. 1, p. 629-646, 2016.

MUKTA, U.H.; ROY, R.; DAULA, A.S.U.; FERDOUS, M.; CHOWDHURY, A.; MIA, S.; et al. Phytochemical analysis, antioxidant and antidiarrhoeal activities of methanol extract of *Fimbristylis miliacea* (L.) Vahl. **Journal of Pharmacognosy and Phytotherapy**, v. 12, n. 1, p. 10-18, 2020.

NOGUEIRA, M.L.; LIMA, E.J.; ADRIÃO, A.A.; FONTES, S.S.; SILVA, V.R.; SANTOS, L.D.S.; et al. *Cyperus articulatus* L. (Cyperaceae) rhizome essential oil causes cell cycle arrest in the G2/M phase and cell death in HepG2 cells and inhibits the development of tumors in a xenograft model. **Molecules**, v. 25, n. 11, p. 2687, 2020.

OWOYELE, B.V.; ABIOYE, A.I.R.; OYEWOLE, A.L.; AMEEN, M.O.; OWEMIDU, I.O.; ADEWUSI, M.O. Effects of the ethanolic extract of *Bulbostylis coleotricha* (Hochst. Exa. Rich.) on inflammation in adult Wistar rats. **Nigerian Journal of Natural Products and Medicine**, v. 19, p. 101-105, 2015.

PAGNING, A.L.N.; LATEEF, M.; TAPONDJOU, L.A.; KUIATE, J.R.; NGNOKAM, D.; ALI, M.S. New triterpene and new flavone glucoside from *Rhynchospora corymbosa* (Cyperaceae) with their antimicrobial, tyrosinase and butyrylcholinesterase inhibitory activities. **Phytochemistry Letters**, v. 16, p. 121-128, 2016.

PENG, D.; LIN, X.; JIANG, L.; HUANG, J.; ZENG, G.; DENG, X.; ZHOU, Y. Five macrocyclic glycosides from *Schoenoplectus tabernaemontani*. **Natural Product Research**, v. 33, n. 3, p. 427-434, 2019.

PHAM, H.H.T.; SEONG, Y.A.; NGABIRE, D.; OH, C.W.; KIM, G.D. *Cyperus amuricus* induces G1 arrest and apoptosis through endoplasmic reticulum stress and mitochondrial signaling in human hepatocellular carcinoma Hep3B cells. **Journal of Ethnopharmacology**, v. 208, p. 157-164, 2017.

PINTO, J.S.; OLIVEIRA, A.K.M.; FERNANDES, V.; MATIAS, R. Ethnobotany and popular culture in the use of plants in settlements on the southern edge of southern Pantanal Mato Grosso. **Bioscience Journal**, v. 33, n. 1, p. 193-203, 2017.

POPESCU, A.; PAVALACHE, G.; PIRJOL, T.N.; ISTUDOR, V. Antioxidant comparative activity and total phenolic content of *Scirpus holoschoenus* L. (*Holoschoenus vulgaris* Link) depending on extraction condition and the solvent used. **Revista de Chimie,** v. 67, n. 2, p. 255-259, 2016.

RABELO, A.S.; SERAFINI, M.R.; RABELO, T.K.; MELO, M.G.D.; PRADO, D.S.; GELAIN, D.P.; et al. Chemical composition, antinociceptive, anti-inflammatory and redox properties *in vitro* of the essential oil from *Remirea maritima* Aubl.(Cyperaceae). **BMC Complementary and Alternative Medicine**, v. 14, n. 1, p. 1-9, 2014.

RAMANATHAN, R.; BHUVANESWARI, R.; INDHU, M.; SUBRAMANIAN, G.; DHANDAPANI, R. Survey of ethnobotanical observation on wild tuberous medicinal plants of Kollihills, Namakkal district, Tamilnadu. **Journal of Medicinal Plants Studies**, v. 2, n. 4, p. 50-58, 2014.

RAMÍREZ, O.; BLAIR, S. Ethnobotany of medicinal plants used to treat malaria by traditional healers from ten indigenous Colombian communities located in Waupes Medio. **Biodiversity International Journal**, v. 1, n. 4, p. 151-167, 2017.

RIBEIRO, A.R.O.; PRATA, A.P.N.; CAMACHO, R.G.V.; OLIVEIRA, O.F.; OLIVEIRA, R.C. Cyperaceae do rio Apodi-Mossoró, Estado do Rio Grande do Norte, Brasil. **Hoehnea,** v. 41, n. 2, p. 149-171, 2014.

RIBEIRO, R.V.; BIESKI, I.G.C.; BALOGUN, S.O.; MARTINS, D.T.O. Ethnobotanical study of medicinal plants used by Ribeirinhos in the North Araguaia microregion, Mato Grosso, Brazil. **Journal of Ethnopharmacology**, v. 205, p. 69-102, 2017.

RIVAS, L. Claves para identificar malezas asociadas con diversos cultivos en el Estado Monagas, Venezuela. **Revista UDO Agrícola**, v. 7, n. 1, p. 79-90, 2007.

RODRIGUES, E.; MENDES, F.R.; NEGRI, G. Plants indicated by Brazilian Indians for disturbances of the central nervous system: a bibliographical survey. **Central Nervous System Agents in Medicinal Chemistry**, v. 6, n. 3, p. 211-244, 2006.

ROMANUS, P.C.; MENDES, F.R.; CARLINI, E.A. Factors affecting the use of medicinal plants by migrants from rural areas of Brazilian Northeast after moving to a metropolitan region in Southeast of Brazil. **Journal of Ethnobiology and Ethnomedicine**, v. 14, n. 1, p. 1-25, 2018.

ROQUE, A.A.; ROCHA, R.M.; LOIOLA, M.I.B. Uso e diversidade de plantas medicinais da Caatinga na comunidade rural de Laginhas, município de Caicó, Rio Grande do Norte (nordeste do Brasil). **Revista Brasileira de Plantas Medicinais**, v. 12, p. 31-42, 2010.

ROSYIDAH, K.; ROHMAN, T.; FITRIANI, R. Aktivitas antioksidan ekstrak methanol daun purun tikus (*Eleocharis dulcis*). **Jurnal Kimia dan Pendidikan Kimia**, v. 3, n. 3, p. 135-140, 2018.

SANTANA, B.F.; VOEKS, R.A.; FUNCH, L.S. Ethnomedicinal survey of a maroon community in Brazil's Atlantic tropical forest. **Journal of Ethnopharmacology**, v. 181, p. 37-49, 2016.

SCHNEIDER, L.J.C.; BASTOS, M.N.C.; COSTA NETO, S.V.; GIL, A.S.B. Sinopse do gênero *Rhynchospora* (Cyperaceae) nas restingas do estado do Pará, Brasil. **Rodriguésia**, v. 68, n. 2, p. 653-670, 2017.

SCHNEIDER, L.J.C.; PEREIRA-SILVA, L.; THOMAS, W.W.; MATZENAUER, W.; HEFLER, S.M.; NUNES, C.S.; MACIEL-SILVA, J.F.; PRATA, A.P.N.; JIMÉNEZ-MEJÍAS, P.; WEBER, P.; SILVA FILHO, P.J.S.; COSTA, S.M.; SOARES NETO, R.L.; ALVES, K.N.L.; GIL, A.S.B.; TREVISAN, R.; LÓPEZ, M.G.; HALL, C.F.; FERNANDES-JÚNIOR, A.J.; VITTA, F.A.; ORSOLANO, G.N.; WANDERLEY, M.G.L. Cyperaceae in **Flora e Funga do Brasil**. 2020. Jardim Botânico do Rio de Janeiro.Disponível em: <https://floradobrasil.jbrj.gov.br/FB100>. Acesso em: 03 dez. 2022.

SEMMOURI, I.; BAUTERS, K.; LÉVEILLÉ-BOURRET, É.; STARR, J.R.; GOETGHEBEUR, P.; LARRIDON, I. Phylogeny and systematics of Cyperaceae, the evolution and importance of embryo morphology. **The Botanical Review**, v. 85, n. 1, p. 1-39, 2019.

SEO, E.J.; LEE, D.U.; KWAK, J.H.; LEE, S.M.; KIM, Y.S.; JUNG, Y.S. Antiplatelet effects of *Cyperus rotundus* and its component (+)-nootkatone. **Journal of Ethnopharmacology**, v. 135, n. 1, p. 48-54, 2011.

SHIN, J.S.; HONG, Y.; LEE, H.H.; RYU, B.; CHO, Y.W.; KIM, N.J.; et al. Fulgidic acid isolated from the rhizomes of *Cyperus rotundus* suppresses LPS-induced iNOS, COX-2, TNF-α, and IL-6 expression by AP-1 inactivation in RAW264.7 macrophages. **Biological and Pharmaceutical Bulletin**, v. 38, n. 7, p. 1081-1086, 2015.

STRONG, M.T. Taxonomy and distribution of *Rhynchospora* (Cyperaceae) in the Guianas, South America. **Contributions from the United States National Herbarium**, v. 53, p. 1-225, 2006.

SUBEDI, N.K.; RAHMAN, S.M.; AKBAR, M.A. Analgesic and antipyretic activities of methanol extract and its fraction from the root of *Schoenoplectus grossus*. **Evidence-Based Complementary and Alternative Medicine**, v. 2016, n. 3820704, p. 1-8, 2016.

THOMAS, W.W.; WEBER, P.; SILVA FILHO, P.J.S. *Rhynchospora* in **Flora e Funga do Brasil.** 2020. Jardim Botânico do Rio de Janeiro.Disponível em: <https://floradobrasil.jbrj.gov.br/FB7258>. Acesso em: 03 dez. 2022.

TSOYI, K.; JANG, H.J.; LEE, Y.S.; KIM, Y.M.; KIM, H.J.; SEO, H.G.; et al. (+)-Nootkatone and (+)-valencene from rhizomes of *Cyperus rotundus* increase survival rates in septic mice due to heme oxygenase-1 induction. **Journal of Ethnopharmacology**, v. 137, n. 3, p. 1311-1317, 2011.

VILHENA, K.S.; GUILHON, G.M.S.P.; ZOGHBI, M.D.G.B.; SANTOS, L.S.; SOUZA FILHO, A.P.S. Chemical investigation of *Cyperus distans* L. and inhibitory activity of scabequinone in seed germination and seedling growth bioassays. **Natural Product Research**, v. 28, n. 23, p. 2128-2133, 2014.

WANG, H.; WANG, P.; YANG, X.; CHENG, X.; DONG, M.; GUO, Y.; et al. Extraction, partial identification and bioactivities of total flavonoids from *Carex meyeriana* Kunth. **American Journal of Biochemistry and Biotechnology**, v. 15, n. 3, p. 125-137, 2019.

XU, H.B.; MA, Y.B.; HUANG, X.Y.; GENG, C.A.; WANG, H.; ZHAO, Y.; et al. Bioactivity-guided isolation of anti-hepatitis B virus active sesquiterpenoids from the traditional Chinese medicine: Rhizomes of *Cyperus rotundus*. **Journal of Ethnopharmacology**, v. 171, p. 131-140, 2015.

ZENI, A.L.B.; BOSIO, F. O uso de plantas medicinais em uma comunidade rural de Mata Atlântica-Nova Rússia, SC. **Neotropical Biology & Conservation**, v. 6, n. 1, 2011.

ZHOU, Z.; YIN, W.; ZHANG, H.; FENG, Z.; XIA, J. A new iridoid glycoside and potential MRB inhibitory activity of isolated compounds from the rhizomes of *Cyperus rotundus* L. **Natural Product Research**, v. 27, n. 19, p. 1732-1736, 2013.

ZHOU, Z.; ZHANG, H. Phenolic and iridoid glycosides from the rhizomes of *Cyperus rotundus* L. **Medicinal Chemistry Research**, v. 22, n. 10, p. 4830-4835, 2013.

ANEXO A

PRIMEIRA PÁGINA DO ARTIGO PUBLICADO NO SOUTH AFRICAN JOURNAL OF BOTANY (**ARTIGO 2**)

Disponível em: https://doi.org/10.1016/j.sajb.2022.09.020

South African Journal of Botany 150 (2022) 1138–1158

Contents lists available at ScienceDirect

South African Journal of Botany

journal homepage: www.elsevier.com/locate/sajb

Review

Cyperaceae species used for the treatment of inflammation: A review of ethnomedicinal, pharmacological, toxicological, and phytochemical evidence

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ARTICLE INFO

Article History:
Received 25 October 2021
Revised 17 August 2022
Accepted 9 September 2022
Available online xxx

Edited by: O.A. Aremu

Keywords:
Anti-inflammatory activity
Bioactive compounds
Ethnopharmacology
Medicinal plants
Phytoteraphy

ABSTRACT

Species of the family Cyperaceae are used in traditional medicine in several countries for the treatment of some illnesses. The indications of some representatives for the treatment of inflammation have been experimentally evaluated, suggesting that Cyperaceae has chemical compounds with anti-inflammatory activity. The present work aimed to carry out a systematic review of the traditional uses, anti-inflammatory potential, toxicity, and chemical compounds isolated from species of this family. Scientific articles were obtained through searches in the Google Scholar, PubMed®, SciELO, and Scopus® databases. Only works published in the last 31 years (1991–2022) were eligible. After application of the inclusion and exclusion criteria, a total of 82 articles were used in this review. Ten species of Cyperaceae are traditionally used to treat inflammation in different countries. *In vitro* and *in vivo* assays with the essential oil, extracts and its fractions exhibited potent anti-inflammatory action. Relevant preclinical toxicity was not found for different formulations. A total of 50 compounds belonging to the classes of sesquiterpenes, phenolic compounds, benzenoids, phytosterols, unsaturated fatty acids, diterpenoids, triterpenes, and norterpenoids presented anti-inflammatory potential. *Cyperus rotundus* stood out for the high amount of information on its traditional use, anti-inflammatory potential, and phytochemical studies. Bioprospecting other species indicated in traditional medicine for the treatment of inflammation is essential to validate or refute the suggested ethnopharmacological information.

1. Introduction

Inflammation is a highly dynamic process that can be characterized as the first protective response of the immune system (Tasneem et al., 2019). This clinical condition is triggered by factors such as injuries and infections (Agarwal et al., 2019) and is characterized by five main symptoms: redness, swelling, heat, pain and loss of tissue function (Takeuchi and Akira, 2010). Inflammatory lesions induce the release of a variety of systemic mediators that cause the resolution of the inflammatory response and restoration of the integrity of the affected tissue (Maione et al., 2015). The treatment of inflammation is done by administration of steroidal (corticosteroids) and non-steroidal anti-inflammatory drugs (Brune and Patrignani, 2015; Juthani et al., 2017; Oguntibeju, 2018), which, in most cases, cause side effects.

In several countries, some representatives of the family Cyperaceae have been used in traditional medicine for the treatment of inflammation. Medicinal plants are known for their therapeutic potential, including anti-inflammatory activity, with little or no side effects (Recio et al., 2012; Kazemi et al., 2018; Oguntibeju, 2018). Cyperaceae species such as *Cyperus rotundus* L. (Qureshi et al., 2008; Borges and Bautista, 2010; Napagoda et al., 2018; Penchala et al., 2018), *Scirpoides holoschoenus* (L.) Soják (Parada et al., 2009), *Cyperus*

Abbreviations: AA, Arachidonic acid; ActF, Active fraction; ADAMTS5, A disintegrin and metalloproteinase with thrombospondin motifs; AE, Aqueous extract; BF, *n*-butanol fraction; BSA, Bovine serum albumin; CE, Chloroform extract; CH, Crude hydrodistillate; COX, Cyclooxygenase; COX-2, Cyclooxygenase-2; EAE, Ethyl acetate extract; EAF, Ethyl acetate fraction; EE, Ethanol extract; EO, Essential oil; HAE, Hydroalcoholic extract; HF, *n*-hexane fraction; HO-1, Heme oxygenase-1; HPLC, High performance liquid chromatography; IC_{50}, Half the maximal inhibitory concentration; IFN-γ, Interferon-γ; IL-1β, Interleukin-1β; IL-6, Interleukin-6; iNOS, Inducible nitric oxide synthase; 5-LOX, 5-lipoxygenase; LPS, Lipopolysaccharide; LTC4, Leukotriene C4; LTD4, Leukotriene D4; LTE4, Leukotriene E4; MAPKs, Mitogen-activated protein kinase; ME, Methanol extract; MF, Methanol fraction; MMPs, Metalloproteinases; NF-κB, Factor nuclear kappa B; NO, Nitric oxide; Pb, Lead acetate; PGE2, Prostaglandin E2; RAGE, Receptor for advanced glycation end-products; RAW 264.7, Cell line; THP-1, Cell-line; TNF-α, Tumor necrosis factor-α; TOF, extract enriched with total oligomer flavonoids; TPA, 12-O-tetradecanoylphorbol-13-acetate.

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https://doi.org/10.1016/j.sajb.2022.09.020
0254-6299/

ANEXO B

PRIMEIRA PÁGINA DO ARTIGO PUBLICADO NO JOURNAL OF ETHNOPHARMACOLOGY (**ARTIGO 3**)

Disponível em: https://doi.org/10.1016/j.jep.2021.114811

Journal of Ethnopharmacology 284 (2022) 114811

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Evaluation of the anti-inflammatory, antipyretic and antinociceptive activities of the hydroalcoholic extract of *Rhynchospora nervosa* (Vahl) Boeckeler (Cyperaceae)

José Jailson Lima Bezerra [a], João Ricardhis Saturnino de Oliveira [b], Vera Lúcia de Menezes Lima [b], Márcia Vanusa da Silva [b], Daniel Rodrigo Cavalcante de Araújo [c], Antônio Fernando Morais de Oliveira [a,*]

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ARTICLE INFO

Keywords:
Analgesic
Anti-inflammatory activity
Ethnopharmacology
In vivo bioactivity
Medicinal plants
Phenolic compounds

ABSTRACT

Ethnopharmacological relevance: *Rhynchospora nervosa* (Vahl) Boeckeler (Cyperaceae), popularly known as "capim-estrela", is a native species widely distributed in Brazil. The whole plant has been used in local traditional medicine in the form of teas or syrups to treat inflammation, flu, nasal congestion, fever, swelling, and venereal disease. This is the first study to investigate the pharmacological properties of this species. *Aim of the study*: The present study aimed to evaluate the *in vivo* anti-inflammatory, antipyretic and antinociceptive potential of the lyophilized hydroalcoholic extract of *R. nervosa* in heterogenic Swiss mice. In addition to pharmacological studies, the total phenol and flavonoid contents of the extract were determined.

Material and methods: The anti-inflammatory effect was evaluated through carrageenan-induced paw edema and peritonitis models. For the antinociceptive assay, the number of acetic acid-induced writhing responses in the animals was counted. Antipyretic activity was tested by yeast-induced pyrexia in mice and evaluated for 4 h. Nitric oxide (NO) concentration and leukocyte migration in the peritoneal fluid were quantified. The acute toxicity of the extract was also calculated. Quantitative analyses of total phenols and flavonoids in the extract were performed by spectrophotometric methods.

Results: In short, the lyophilized hydroalcoholic extract of *R. nervosa* showed low acute toxicity in the preclinical tests (LD_{50} = 3807 mg/kg). A significant anti-inflammatory effect was observed, with an average reduction of carrageenan-induced paw edema of 96.37%. Comparatively, indomethacin inhibited the development of the carrageenin paw edema by 97.52%. In the peritonitis test, a significant reduction in NO levels was recorded. A reduction in the number of white cells, notably monocytes, was also observed, confirming the anti-inflammatory effect. Writhing was reduced by 86.53%, which indicates antinociceptive activity. As for antipyretic activity, no positive effects of the extract were observed. The lyophilized hydroalcoholic extract of *R. nervosa* presented a high content of phenolic compounds (322.47 μg GAE/mg) and total flavonoids (440.50 μg QE/mg).

Conclusion: The lyophilized hydroalcoholic extract of *R. nervosa* showed significant *in vivo* anti-inflammatory and antinociceptive activity in mice. These preliminary findings support the indication of the use of this species in folk medicine in Brazil for the treatment of inflammation.

1. Introduction

The family Cyperaceae has species distributed in all regions of Brazil and the genera *Cyperus* L., *Eleocharis* R. Br., *Rhynchospora* Vahl, and *Scleria* P. J. Bergius are the most representative (Alves et al., 2009a). Several biological activities have been reported for members of this family, namely, antioxidant (Luo et al., 2014; Popescu et al., 2016), antimicrobial (Nassar et al., 2015; Pagning et al., 2016; Erdem et al., 2018), anti-inflammatory (Owoyele et al., 2015; Dong et al., 2016), anticancer (Nidugala et al., 2016; Pham et al., 2017), anthelmintic (Kasala et al., 2016), antinociceptive (Roy et al., 2019), antidiabetic

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https://doi.org/10.1016/j.jep.2021.114811
Received 12 June 2021; Received in revised form 28 October 2021; Accepted 3 November 2021
Available online 8 November 2021

ANEXO C

PATENTE DEPOSITADA JUNTO AO INSTITUTO NACIONAL DA PROPRIEDADE INDUSTRIAL (INPI)

Número de Registro: **BR 10 2020 017809 1**

República Federativa do Brasil
Ministério da Economia
Instituto Nacional da Propriedade Industrial

(21) BR 102020017809-1 A2

(22) Data do Depósito: 31/08/2020

(43) Data da Publicação Nacional: 15/03/2022

(54) Título: USO DO EXTRATO HIDROALCOÓLICO DE RHYNCHOSPORA NERVOSA COMO AGENTE ANTI-INFLAMATÓRIO E ANTINOCICEPTIVO

(51) Int. Cl.: A61K 36/89; A61K 127/00; A61P 29/00.

(71) Depositante(es): UNIVERSIDADE FEDERAL DE PERNAMBUCO.

(72) Inventor(es): JOSÉ JAILSON LIMA BEZERRA; ANTONIO FERNANDO MORAIS DE OLIVEIRA; JOÃO RICARDHIS SATURNINO DE OLIVEIRA; VERA LÚCIA DE MENEZES LIMA; MÁRCIA VANUSA DA SILVA.

(57) Resumo: USO DO EXTRATO HIDROALCOÓLICO DE Rhynchospora nervosa COMO AGENTE ANTI-INFLAMATÓRIO E ANTINOCICEPTIVO. A presente patente refere-se ao uso do extrato hidroalcoólico a base das partes aéreas de Rhynchospora nervosa como agente anti-inflamatório e antinociceptivo em estudos pré-clínicos. O extrato hidroalcólico de R. nervosa (EHRn) foi utilizado para verificar a toxicidade aguda, o efeito anti-inflamatório (modelo de edema de pata induzido por carragenina) e o potencial antinociceptivo (método de contorções induzidas por ácido acético) em camundongos Swiss. Em síntese, o EHRn apresentou efeito anti-inflamatório, reduzindo 100% do edema de pata induzido por carragenina nos camundongos em todas as doses avaliadas (100, 200 ou 400 mg/kg). O potencial promissor do EHRn também foi observado por meio da atividade antinociceptiva, tendo em vista que na dose referente a 400 mg/kg foi verificada uma redução de 86,53% das contorções nos animais. Além disso, o referido extrato apresentou baixa toxicidade aguda nos testes pré-clínicos (DL50 = 3807.88 mg/kg), indicando previamente seu potencial uso seguro como futuro fitoterápico contra estímulos nociceptivos e processos inflamatórios.

ANEXO D

NORMAS PARA SUBMISSÃO DE MANUSCRITO AO PERIÓDICO **JOURNAL OF HERBAL MEDICINE**

Disponível em: https://www.elsevier.com/journals/journal-of-herbal-medicine/2210-8033/guide-for-authors

ELSEVIER

JOURNAL OF HERBAL MEDICINE

AUTHOR INFORMATION PACK

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ISSN: 2210-8033

DESCRIPTION

The *Journal of Herbal Medicine* is a peer reviewed journal which aims to serve its readers as an authoritative resource on the profession and practice of **herbal medicine**. The content areas of the journal reflect the interests of **Medical Herbalists** and other **health professionals** interested in the clinical and professional application of **botanical medicines**. The objective is to strengthen the research and educational base of **herbal medicine** with research papers in the form of case studies, original research articles and reviews, monographs, clinical trials and relevant in vitro studies. It also publishes policy statements, opinion pieces, book reviews, conference proceedings and profession related information such as **pharmacovigilance** reports providing an information source for not only the **Herbal Practitioner** but any **Health professional** with an interest in **phytotherapy**.

Potentially the premier journal in its field, the journal welcomes papers that stimulate research and interest in **herbal medicine** education and practice that disseminate information about its clinical tradition, best practices, skills and knowledge, e.g. in the area of

- **Traditional medicine, ethnobotany and western herbal medicine**
- **Herbal therapeutics, phytomedicine and herbal preparations**
- **Medicinal plants in healthcare, clinical trials and pilot studies**
- **Biological and pharmacological effects of plant extracts**
- **Medicinal plants and their anti-inflammatory, anti-cholesterol, hypotensive, antispasmodic, anti-diabetic, anticancer, antiviral, antibacterial and antifungal activity**

We do not publish papers
- whereby the focus and primary experimental method involves the use of animals
- where the evidence base of the research paper focuses primarily on animal models and actual descriptions of animal studies are used as the main evidence. In review papers, citations of animal studies should be limited as far as possible
- that only focus on in vitro studies relating to antioxidant activity

AUDIENCE

medical herbalists, pharmacologists, toxicologists, pharmacists, pharmacognosists, phytotherapists (clinicians), biochemists, botanists, general practitioners, CAM practitioners, allied health professionals

ANEXO E

NORMAS PARA SUBMISSÃO DE MANUSCRITO AO PERIÓDICO **SOUTH AFRICAN JOURNAL OF BOTANY**

Disponível em: https://www.elsevier.com/journals/south-african-journal-of-botany/0254-6299/guide-for-authors

ELSEVIER

SOUTH AFRICAN JOURNAL OF BOTANY

An International Interdisciplinary Journal for Plant Sciences

AUTHOR INFORMATION PACK

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ISSN: 0254-6299

DESCRIPTION

The *South African Journal of Botany* publishes original papers that deal with the classification, biodiversity, morphology, physiology, molecular biology, ecology, biotechnology, ethno**botany** and other botanically related aspects of species that are of importance to **southern Africa**. Manuscripts dealing with significant new findings on other species of the world and general **botanical** principles will also be considered and are encouraged.

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AUDIENCE

Plant biochemists, physiologists, molecular biologists,taxonomists, ecologists and ethnobotanists

IMPACT FACTOR

2020: 2.315 © Clarivate Analytics Journal Citation Reports 2021

ANEXO F

NORMAS PARA SUBMISSÃO DE MANUSCRITO AO PERIÓDICO **JOURNAL OF ETHNOPHARMACOLOGY**

Disponível em: https://www.elsevier.com/journals/journal-of-ethnopharmacology/0378-8741/guide-for-authors

ELSEVIER

JOURNAL OF ETHNOPHARMACOLOGY

An Interdisciplinary Journal Devoted to Indigenous Drugs

AUTHOR INFORMATION PACK

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ISSN: 0378-8741

DESCRIPTION

The *Journal of Ethnopharmacology* is dedicated to the exchange of information and understandings about people's use of plants, fungi, animals, microorganisms and minerals and their **biological** and **pharmacological effects** based on the principles established through international conventions. Early people confronted with illness and disease, discovered a wealth of useful **therapeutic agents** in the plant and animal kingdoms. The empirical knowledge of these **medicinal substances** and their toxic potential was passed on by oral tradition and sometimes recorded in herbals and other texts on *materia medica*. Many valuable drugs of today (e.g., atropine, ephedrine, tubocurarine, digoxin, reserpine) came into use through the study of **indigenous remedies**. Chemists continue to use **plant-derived drugs** (e.g., morphine, taxol, physostigmine, quinidine, emetine) as prototypes in their attempts to develop more effective and less toxic medicinals.

In recent years the preservation of local knowledge, the promotion of indigenous medical systems in primary health care, and the conservation of biodiversity have become even more of a concern to all scientists working at the interface of social and natural sciences but especially to ethnopharmacologists. Recognizing the sovereign rights of States over their natural resources, ethnopharmacologists are particularly concerned with local people's rights to further use and develop their autochthonous resources.

Accordingly, today's ethnopharmacological research embraces the multidisciplinary effort in the:

- documentation of **indigenous medical knowledge**,
- scientific study of **indigenous medicines** in order to contribute in the long-run to improved health care in the regions of study, as well as
- search for pharmacologically unique principles from existing indigenous remedies.

The *Journal of Ethnopharmacology* publishes original articles concerned with the observation and experimental investigation of the biological activities of plant and animal substances used in the traditional medicine of past and present cultures. The journal will particularly welcome interdisciplinary papers with an **ethnopharmacological**, an **ethnobotanical** or an **ethnochemical** approach to the study of indigenous drugs. Reports of **anthropological** and **ethnobotanical** field studies fall within the journal's scope. Studies involving **pharmacological** and **toxicological** mechanisms of action are especially welcome. Clinical studies on efficacy will be considered if contributing to the understanding of specific ethnopharmacological problems. The journal welcomes review articles in the above mentioned fields especially those highlighting the multi-disciplinary nature of ethnopharmacology. Commentaries are by invitation only.

ANEXO G

CERTIDÃO DE CADASTRO EMITIDA PELO SISTEMA NACIONAL DE GESTÃO DO PATRIMÔNIO GENÉTICO E DO CONHECIMENTO TRADICIONAL ASSOCIADO (SISGEN)

Número do Cadastro: **A2279F9**

Ministério do Meio Ambiente
CONSELHO DE GESTÃO DO PATRIMÔNIO GENÉTICO

SISTEMA NACIONAL DE GESTÃO DO PATRIMÔNIO GENÉTICO E DO CONHECIMENTO TRADICIONAL ASSOCIADO

Certidão

Cadastro nº A2279F9

Declaramos, nos termos do art. 41 do Decreto nº 8.772/2016, que o cadastro de acesso ao patrimônio genético ou conhecimento tradicional associado, abaixo identificado e resumido, no Sistema Nacional de Gestão do Patrimônio Genético e do Conhecimento Tradicional Associado foi submetido ao procedimento administrativo de verificação e não foi objeto de requerimentos admitidos de verificação de indícios de irregularidades ou, caso tenha sido, o requerimento de verificação não foi acatado pelo CGen.

Número do cadastro:	**A2279F9**
Usuário:	**José Jailson Lima Bezerra**
CPF/CNPJ:	**094.661.484-94**
Objeto do Acesso:	**Patrimônio Genético**
Finalidade do Acesso:	**Pesquisa**
Espécie	
Rhynchospora nervosa	
Título da Atividade:	**ESTUDO QUÍMICO E ATIVIDADES BIOLÓGICAS DE Rhynchospora nervosa (Vahl) Boeckeler (CYPERACEAE)**
Equipe	
José Jailson Lima Bezerra	**Universidade Federal de Pernambuco**
Antônio Fernando Morais de Oliveira	**Universidade Federal de Pernambuco**

Data do Cadastro:	**17/05/2020 19:39:15**
Situação do Cadastro:	**Concluído**

Conselho de Gestão do Patrimônio Genético
Situação cadastral conforme consulta ao SisGen em **17:04** de **11/04/2021**.

SISTEMA NACIONAL DE GESTÃO DO PATRIMÔNIO GENÉTICO E DO CONHECIMENTO TRADICIONAL ASSOCIADO - SISGEN

ANEXO H

PARECER DA COMISSÃO DE ÉTICA NO USO DE ANIMAIS (CEUA/UFPE)

Número do processo: **127/2019**

Universidade Federal de Pernambuco
Centro de Biociências
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Fones: 2126 8842
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Recife, 26 de dezembro de 2019

Ofício nº 122/19

Da Comissão de Ética no Uso de Animais (CEUA) da UFPE
Para: **Prof. Antônio Fernando Morais de Oliveira**
Departamento de Botânica/CB
Universidade Federal de Pernambuco
Processo **nº 127/2019**

Certificamos que a proposta intitulada "**Estudo químico e atividades biológicas de Rhynchospora nervosa (Vahl) Boeckeler (Cyperaceae).", registrado com o nº 127/2019** sob a responsabilidade de **Prof. Antônio Fernando Morais de Oliveira** o que envolve a produção, manutenção ou utilização de animais pertencentes ao filo Chordata, subfilo Vertebrata (exceto humanos), para fins de pesquisa científica (ou ensino) - encontra-se de acordo com os preceitos da Lei nº 11.794, de 8 de outubro de 2008, do Decreto nº 6.899, de 15 de julho de 2009, e com as normas editadas pelo CONSELHO NACIONAL DE CONTROLE DE EXPERIMENTAÇÃO ANIMAL (CONCEA), e foi aprovada pela COMISSÃO DE ÉTICA NO USO DE ANIMAIS (CEUA) DA UNIVERSIDADE FEDERAL DE PERNAMBUCO (UFPE), em reunião de 17/12/2019

Finalidade	() Ensino (X) Pesquisa Científica
Vigência da autorização	17/12/2019 a 17/02/2020
Espécie/linhagem/raça	Camundongo heterogênico
Nº de animais	120
Peso/Idade	25-30/g 8-12 semanas
Sexo	macho (120)
Origem: Biotério de Criação	Laboratório de Imunopatologia Keizo Asami (LIKA) UFPE
Destino: Biotério de Experimentação	Laboratório de Imunopatologia Keizo Asami (LIKA) UFPE

ANEXO I

FICHA DE IDENTIFICAÇÃO BOTÂNICA EMITIDA PELO HERBÁRIO DO INSTITUTO AGRONÔMICO DE PERNAMBUCO

Número de Tombo da Espécie: **93709**

Secretaria de Agricultura e Reforma Agrária
PERNAMBUCO
GOVERNO DO ESTADO

HERBÁRIO IPA – DÁRDANO DE ANDRADE LIMA
FICHA DE IDENTIFICAÇÃO BOTÂNICA

FIB N° 79/2019

	N° de Tombo	Data da coleta	Nome popular	Família	Nome Científico	Identificada por
1	**93709**	29/10/19	Capim estrela	Cyperaceae	*Rhynchospora nervosa* (Vahl) Boeckeler	F. Gallindo

Drª. Rita de Cássia Pereira
Curadora do Herbário IPA

Consulta: José Jailson Lima Bezerra tel.: (83) 987317051
Procedência: PE – Recife – Cidade Universitáriua – Campus da UFPE, em terreno baldio próximo ao Centro de Biociências.
Coletor: o mesmo.
Determinada em: 05/11/2019

Obs.: Material botânico em estudo na UFPE - Deptº de Ciências Biológicas, para fim de pesquisa e tese de Doutorado, sob a orientação do Profº Dr. Antonio Fernando.

Resultado encaminhado por e mail: josejailson.bezerra@hotmail.com em 05/11/2019.

Instituto Agronômico de Pernambuco - IPA
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