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Review article

Health functions and related molecular mechanisms of *Miconia* genus: A systematic review

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ABSTRACT

The *Miconia* genus is traditionally used in folk medicine in Brazil and other tropical American countries and is represented by 282 species in this region. It is a multifaceted genus of medicinal plants widely used to treat rheumatoid arthritis (RA), pain, inflammatory diseases, and many more therapeutic applications. In the present study, we systematically identify and discuss the literature on *in vivo* and *in vitro* studies focusing on the therapeutic potentials and related molecular mechanisms of the *Miconia* genus. The review also assessed phytochemicals and their pharmacological properties and considered safety concerns related to the genus. Literature searches to identify studies on the *Miconia* genus were carried out through four main electronic databases, namely PubMed, Embase, Scopus, and Web of Science limited to Medical Subjects Headings (MeSH) and Descriptores en Ciencias de la Salud (DCS) (Health Sciences Descriptors) to identify studies published up to December 2022. The relevant information about the genus was gathered using the keywords '*Miconia*', 'biological activities', 'therapeutic mechanisms', 'animal model, 'cell-line model', 'antinociceptive', 'hyperalgesia', 'anti-inflammatory', and 'inflammation'. The therapeutic potentials and mechanisms of action of 14 species from genus *Miconia* were

Abbreviations: AAPH, 2,2′-azobis (2-amidinopropane) dihydrochloride; CFA, Complete Freund's Adjuvant; DEMA, a dried extract of *M. albicans*; DPPH, 1,1-diphenyl-2-picrylhydrazyl; GM-CSF, granulocyte macrophage-colony stimulating factor; IL, interleukins; MAEE, *M. albicans* ethanolic leaf extract; MAFRE, *M. albicans* fruits extract; MeSH, Medical Subjects Headings; NFκB, nuclear factor-κB; Nrf2, nuclear factor erythroid-2-related factor 2; OA, oleanolic acid; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RA, rheumatoid arthritis; RNS, reactive nitrogen species; ROS, reactive oxygen species; sTNFR, soluble tumour necrosis factor receptor; TNF-α, tumor necrosis factor-α; UA, ursolic acid; VASP, Visual Analogue Scale of Pain; VEGFR-2, vascular endothelial growth factor receptor-2; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

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examined in 18 *in vitro* studies and included their anti-inflammatory, anticancer, analgesic, antibacterial, cytotoxic, mutagenic, antioxidant, anti-leishmanial, antinociceptive, schistosomicidal, and anti-osteoarthritis potentials, and in eight *in vivo* studies, assessing their analgesic, antioxidant, antinociceptive, and anti-osteoarthritis activities. Some of the main related molecular mechanisms identified are the modulation of cytokines such as IL-1β, IL-6, and TNF-α, as well as the inhibition of inflammatory mediators and prostaglandin synthesis. The limited number of studies showed that commonly available species from the genus *Miconia* are safe for consumption. *Miconia albicans* Sw.Triana and *Miconia rubiginosa* (Bonpl.) DC was the most frequently used species and showed significant efficacy and potential for developing safe drugs to treat pain and inflammation.

1. Introduction

The *Miconia* genus belongs to the Melastomataceae botanical family and comprises various flowering perennial arboreal medicinal shrubs widely distributed in tropical American countries [1]. The genus is distributed mainly in the Cerrado biome, a Brazilian savannah ecosystem in the Atlantic coastal forest of North-Eastern Brazil, occupying the fifth position in respect of species diversity, being represented by about 276 species, of which 121 are endemic [2,3]. Several *Miconia* fruits are edible and rich sources of phenolic compounds [4]. The Brazilian populations commonly use some species of *Miconia* for medicinal purposes to treat different diseases [5]. In traditional medicine, species of the *Miconia* genus, such as *Miconia rubiginosa* (Bonpl.) DC., and *Miconia cinnamomifolia* (DC.) Naudin treats pain, throat infections, colds, and fever [6]. Traditional healers use *Miconia albicans* (Sw.) Triana leaves to treat back pain and rheumatoid arthritis (RA), and its stem has significant antipyretic potential [7,8]. In Brazilian folk medicine, *M. albicans* has been given

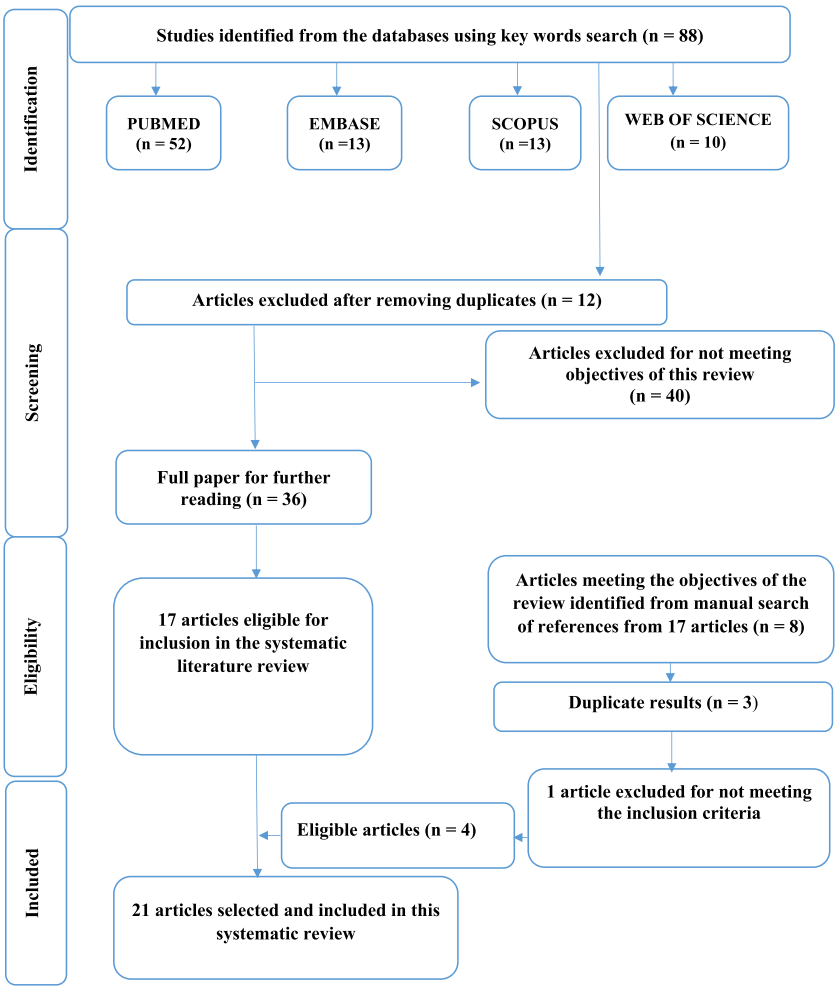


Fig. 1. Flow chart diagram of the selection process of eligible studies.

the popular names of 'Canela-de-velho' and 'branda-fogo' meaning "old man's ankle" or "heat reducer," due to its purported ability to reduce joint pain in old people and the burning sensation of pain in the joints; however, the actual efficacy of many of these treatments has been little studied and/or reported.

Cunha et al. reviewed previous phytochemical investigations and reported 21 investigated species from *Miconia*, viz *Miconia stenostachya* DC., *M. albicans*, *Miconia pepericarpa* Mart. ex DC., *Miconia sellowiana* Naudin, *Miconia fallax* DC., *M. rubiginosa*, *Miconia ligustroides* (DC.) Naudin, *Miconia ferruginata* DC., *Miconia langsdorffii* Cogn., *Miconia macrothyrsa* Benth., *Miconia affinis* DC., *Miconia lepidota* DC., *Miconia pilgeriana* Ule., *Miconia myriantha* Benth., *Miconia alypifolia* Naudin., *Miconia cannabina* Markgr., *Miconia cabucu* Hoehne., *Miconia willdenowii* Klotzsch ex Naudin., *Miconia prasina* (Sw.) DC., *Miconia ioneura* Griseb., *and Miconia trailii* Cogn., containing no less than 79 phytochemicals including flavonoids, triterpenes, steroids, phenolic acids, quinones, tannins, and lignans [9]. The review further reported that flavonoids from the *Miconia* genus are mostly glycosylated with sugar units in the carbons 3 or 7, while others are aglycones such as quercetin, matteucinol, and kaempferol [9]. Among the pentacyclic triterpenes and derivatives isolated from the *Miconia* genus, the main ones are ursolic acid (UA), oleanolic acid (OA), α-amyrin, β-amyrin, α-amyrin acetate, β-amyrin acetate, arjunolic acid, sumaresinolic acid, 2-α-hydroxyursolic acid, and maslinic acid. In addition, constituents such as gallic acid, ellagic acid, primin, casuarictin, schizandriside, and several of their derivatives have also been reported to have been isolated from this genus.

Extracts, compounds, and their derivatives from *Miconia* species have been evaluated *in vivo* and *in vitro* studies regarding their biological and therapeutic potentials. The *Miconia* species showed various biochemical activities such as anti-inflammatory [10], anti-diabetic [11], anti-rheumatic [5], anti-mutagenic and anti-tumor [12–14], anti-microbial [15–19], schistosomicidal [20], anti-oxidant [21–24], analgesic [10,25], anti-malarial [26,27], anti-nociceptive [21]; leishmanicidal [28], trypanocidal [24,26], insecticidal and fungicidal [29,30] activities. However, little is known about their safety, mechanism of action, and systemic toxicity in prolonged use, limiting their clinical use.

The pharmacological characteristics of the genus *Miconia* were also described by da Silva et al. in a recent review [31]. The authors also compiled the phytochemical reports in respect of *Miconia* species. They discovered 148 chemical compounds, including the primary constituents of the *Miconia* species, flavonoids, and phenolic acids. In this systematic review, we examine the phytochemical composition of the species of the *Miconia* genus, their safety, and potential health applications based on the identified *in vivo* and *in vitro* pharmacological studies, and in particular emphasize their related molecular mechanisms.

2. Materials and methods

The current systematic review was designed and performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to detect current *in vivo* and *in vitro* studies linked to the therapeutic mechanisms of the plant species belonging to the *Miconia* genus [32] (Fig. 1).

2.1. Search strategy

Literature searches were conducted using the four main electronic databases, namely PubMed, Embase, Scopus, and Web of Science, and limited to Medical Subjects Headings (MeSH) and Descriptores en Ciencias de la Salud (DCS) (Health Sciences Descriptors) to identify studies published to December 2022. Specific keywords such as '*Miconia'*, 'biological activities', 'therapeutic mechanisms', 'animal model', 'cell-line model', 'antinociceptive', 'hyperalgesia', 'anti-inflammatory', and 'inflammation' were used. Additionally, a

Table 1
Description of the main characteristics of *in vivo* studies using the *Miconia* genus.

Name of the plant	Animal/Strains	Dose/Route	Effects and molecular mechanism	References
Miconia rubiginosa (Bonpl.) DC.	Swiss mice and Wistar rats	100, 200 and 300 mg/kg *intraperitoneal*	↑central and peripheral analgesic; antinociceptive effect	[21]
Miconia albicans Sw. Triana	Swiss albino mice and Wistar rats	200 mg/kg *intraperitoneal*	↓$PGE_2\alpha$ and $PGF_2\alpha$; ↑peripheral-mediated analgesic activity	[25]
M. albicans	Swiss mice and Wistar rats	40 mg/kg *intraperitoneal*	↓inflammatory mediators and inhibition of synthesis of prostaglandins and also the blockage of their receptor sites; ↑peripheral mediated analgesic effect	[10]
Miconia minutiflora (Bonpl.) DC.	Wistar rat and Swiss mice	50, 100 and 200 mg/kg *oral*	reduced inflammatory activity by decrease in cell migration; ↓pro-inflammatory cytokines TNF-α and IL-1β; ↑central and peripheral analgesic effect	[33]
M. albicans	Swiss mice	50 and 100 mg/kg *oral*	↓leukocyte migration; ↓TNF-α, IL-1β, and IL-6; ↓nociceptive and hyperalgesic behaviors; ↓ipsilateral knee edema; ↑mobility and hindpaw grip strength	[36]
M. albicans	Swiss mice	25, 50 and 100 mg/kg *oral*	↓TNF-α and IL-1β; reduced inflammatory nociception and edema; exhibit antioxidant and anti-inflammatory properties	[44]
M. albicans and *Curcuma longa* Linn	Human knee's osteoarthritis	1000 mg/kg *oral*	↓score of WOMAC, VASP; ↑analgesic and exhibit anti-inflammatory effect on knee osteoarthritis	[39]
M. albicans	Swiss mice	2.5 mg/kg on ear edema	↓ear edema and MPO activity; revealed antioxidant and anti-inflammatory effects	[43]

Table 2
Description of the main characteristics of *in vitro* studies using *Miconia* species and its chemical composition.

Plant Used			Plant extract	Chemical composition	Therapeutic properties	Effects and Molecular Mechanism	References
Genus	Species	Plant part					
M.	*rubiginosa*	Aerial parts	Hexane, methylene chloride and ethanol extract	Triterpenes and sterols	Analgesic activity	↑central and peripheral analgesic activity, antinociceptive effect; ↓prostaglandin synthesis	[21]
M.	*albicans*	Aerial parts	Methylene chloride extract	Ursolic acid and oleanolic acid	Analgesic and anti-inflammatory activity	↑analgesic and anti-inflammatory activity; ↓ inflammatory mediators	[10]
Miconia	*salicifolia* (Bonpl. ex Naudin)	Leaves and bark	Ethanolic and aqueous extracts	N/A	Antibacterial activity	ethanol extract has strong antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*	[64]
Miconia	*ligustroides* (DC.) Naudin and isolated triterpene acids	Aerial parts	Methylene chloride extract	Ursolic acid and oleanolic acid	Antimicrobial activity	*M. ligustroides* showed appreciable inhibition against *Bacillus cereus*; ursolic acid displayed efficient activity against *B. cereus*; oleanolic acid exhibited growth inhibitory activity against *B. cereus* and *Streptococcus pneumoniae*	[65]
M. *Miconia* *Miconia* *M.*	*albicans*, *cabucu* Hoehne, *stenostachya* DC., *rubiginosa*	Aerial parts	Methanol extract	Flavonoids and tannins	Mutagenicity and antimutagenicity of the extracts	↑cytotoxic, antimutagenic activity; demonstrated the protective effects against DXR-induced DNA damage	[14]
Miconia	*langsdorffii* Cogn.	Aerial parts	Hydroalcoholic extract	Triterpenes	Antileishmanial activity	↑*in vitro* antileishmanial activity against the promastigote forms of *Leishmania amazonensis*	[28]
M.	*rubiginosa*	Leaves	Aerial parts	Triterpenes, flavonoids and quinones	N/A	N/A	[5]
Miconia	*willdenowii* Klotzsch ex Naudin.	Leaves	Ethanol extract	Benzoquinone	Schistosomicidal activity	↑ crude ethanolic extract of *M. willdenowii* showed the promising results, killing 65% of the *Schistossoma mansoni* worms. Primin as the active metabolite responsible for the observed schistosomicidal effect	[20]
M.	*minutiflora*	Leaves	Methanol extract	Ellagic acid, gallotannin and terpenes	Anti-inflammatory and antinociceptive	↑antioxidant, anti-inflammatory, and antinociceptive activity induced by hydrolyzable tannins; ↓proinflammatory cytokines TNF and IL-1β, decrease edema in both phases of inflammation	[33]
M.	*willdenowii*	Leaves	Ethanol extract	2-methoxy-6-pentyl-benzoquinone	Leishmanicidal and antimicrobial activities	inhibits promastigote forms of *L. amazonensis*; exhibited antimicrobial activity against pathogenic fungi, gram-positive and negative bacteria	[68]
Miconia	*latecrenata* Naudin.	Leaves	Aqueous extract	Tannins	Antioxidant, antibacterial, antimutagenic and antigenotoxic activities	↑antioxidant property due to high total phenolic content; antibacterial activity to gram-positive and negative strains; and	[63]

(*continued on next page*)

Table 2 (*continued*)

Plant Used			Plant extract	Chemical composition	Therapeutic properties	Effects and Molecular Mechanism	References
Genus	Species	Plant part					
						antimutagenic property by decreasing the ROS	
Miconia	*chamissois* Naudin	Leaves	Hydroethanolic extract	Matteucinol	Cytotoxicity and anticancer potential	*M. chamissois* and matteucinol showed cytotoxicity and antitumor potential in glioblastoma cell lines	[77]
M.	*albicans*	Leaves	Ethanol extract	Quercetin and rutin	Antihyperalgesic and anti-inflammatory profile	↓ levels of TNF-α and IL-1β in the joint; ↓ nociceptive and hyperalgesic behaviors	[36]
M.	*albicans*	Leaves	Ethanol extract	Polyphenols, leucoanthocyanins, tannins, steroids and saponins.	*In vitro* antioxidant activity	↑ exhibited strong antioxidant profiles due to enhanced content of polyphenols	[44]
M.	*latecrenata*	Leaves	Organic extract	Phenolic compounds	Antibacterial activity	demonstrated the promising for inhibiting the growth of *S. aureus* and *Pseudomonas aeruginosa*	[69]
Miconia	*burchellii* Triana.	Leaves	Ethanol extract	triterpenes, flavonoids, steroids and pheophorbide	Cytotoxic activity	↑ antiproliferative and demonstrated cytotoxic against leukemia cell lines	[62]
M.	*albicans*	Fruit	Methanol extract	Flavonoids, organic acids, tannins and triterpenes	*In vitro* antioxidant and antiproliferative properties	↑antioxidant, ferrous chelating capacities; non-toxic to VERO cells, ensures cell viability, absence of antiproliferative effect against human tumor cell lines	[43]
Miconia	*ferruginata* DC.	Leaves, stem and flowers	Ethanol extract	flavonoids derivatives of quercetin, catechins, and phenolic acids	anticancer	↑ anticancer; exhibits cytotoxicity against tumor cells of 4T1, A549, and MDA-MB-231	[78]
M.	*albicans*	leaves	Hydroethanolic extract	N/A	anticancer	mixture of plant extracts exhibited cytotoxic potential; ↓ viability of human cancer cell lines	[79]
M.	*chamissois*	leaves					

Abbreviations: Not applicable (N/A); prostaglandin E2α (PGE2α); prostaglandin F2α (PGF2α); tumor necrosis factor alpha (TNF-α); IL-1 beta (IL-1β); interleukin (IL); western Ontario and McMaster universities arthritis index (WOMAC); vasodilator stimulated phosphoprotein (VASP); reactive oxygen species (ROS); doxorubicin (DXR); myeloperoxidase (MPO).

manual search was done online and in Google Scholar searching both academic and preprint literature to detect any articles not found in the databases. The data were collected from online journals published in English, irrespective of the region and publication type.

2.2. Study selection

Initially, two authors (JSSQ and RQG) performed the literature search in the databases. Then the extracted titles, abstracts, and relevant full-text published articles were reviewed independently by three investigators (SRG, JSSQ, and GRG), with any disagreement being settled by consensus or, failing this, by a fifth author (LJQJ); the final selection of articles for systematic review was made in consultation with all co-authors. Only original research papers investigating the *Miconia* genus, its well-defined chemical composition, and its potential therapeutic mechanisms using *in vivo* and *in vitro* experimental models were included in this review. Review articles, meta-analyses, book chapters, conference proceedings, editorials/letters, patents, and case reports were excluded.

2.3. Data extraction

One of the authors (SRG) summarized data extraction from shortlisted studies individually. Tables 1 and 2 summarize the critical information from the selected studies: (a) extracts and natural molecules isolated from the plants' species belonging to the *Miconia* genus, (b) the animals/strains or cell lines used, (c) the doses/routes of administration, (d) the proposed mechanisms of action, (e) the first author's name and year of publication.

3. Results and discussion

3.1. Search results

Fig. 1 shows a PRISMA flow chart showing the process used in this systematic review's database search and articles assessment. According to the PRISMA statement, the systematic investigation included *in vivo* and *in vitro* studies relating to the therapeutic mechanisms of plant species belonging to the *Miconia* genus. Among the 88 potentially relevant articles from four databases (PubMed: 52, Embase: 13, Scopus: 13, Web of Science: 10), 12 were discarded for being duplicates and 40 were excluded after comprehensive screening for the following reasons: (a) studies unrelated to the objectives and aim of this systematic review; (b) studies established to be reviews, editorials, conference proceedings, and meta-analyses. 36 full-text articles were then evaluated independently, with 21 studies being identified that met the eligibility criteria of this review.

3.2. Phytochemical studies

A previous review revealed that 28 glycosylated flavonoids and 10 aglycones (mostly quercetin, matteucinol and kaempferol) had been isolated and identified from plant species belonging to the *Miconia* genus [9]. The major pentacyclic triterpenes isolated from the *Miconia* genus include UA, OA, α-amyrin and, β-amyrin, and several bioactive derivatives. Other isolated phytochemicals include steroids and derivatives (β-sitosterol, stigmasterol, stigmast-4-ene-3,6-dione, campesterol, gallic acid, ellagic acid, and derivatives) [9]. Examination of the leaves from *M. rubiginosa* using high-speed counter-current chromatography showed the presence of phytochemicals including flavonoids, gallic acid, casuarictin, and schizandriside [5]. A study that examined the methanol extract of *Miconia minutiflora* (Bonpl.) DC., using UPLC-DAD-QTOF-MS/MS revealed the presence of ellagic acid, gallotannin, and terpenes [33]. UA and OA are the major secondary metabolites of triterpenes isolated from the plant species from *Miconia*, commonly as an isomeric mixture having a pentacyclic skeleton [34]. Other triterpenes reported are α-amyrin, β-amyrin, lupeol, maslinic acid, epibetulinic acid, and arjunolic acid [11]. *Miconia* plant species revealed the presence of some phytoconstituents such as flavonoid glycosides (quercetin, myricetin, catechin, and kaempferol), a phenolic acid (gallic acid) and bioflavonoids [35]. In addition, HPLC-DAD-ESI-MS/MS analysis of ethanol extract from the leaves of *M. albicans* identified 23 natural molecules, mostly glycoside flavonoids derived from quercetin, and rutin [36]. Phytochemical studies on this genus reported the presence of triterpenes [37], flavones [38], coumarins, and benzoquinones [12]. According to the studies reviewed, Fig. 3A-C depicted the potential phytoconstituents that have been found or extracted from various *Miconia* plant species that are associated with a range of biological functions.

3.3. Evaluation of selected studies

Our review found that the following 11 plant species from this genus have been reported as containing various promising bioactive phytochemicals in reports conducted in both *in vitro* and *in vivo* experiments: *M. albicans, M. rubiginosa, Miconia salicifolia* (Bonpl. ex Naudin) Naudin., *M. ligustroides, M. stenostachya, M. cabucu, M. langsdorffii, M. willdenowii, M. minutiflora, Miconia latecrenata* Naudin., and *Miconia burchellii* Triana. The following biological activities were evaluated in eight *in vivo* studies, including one human

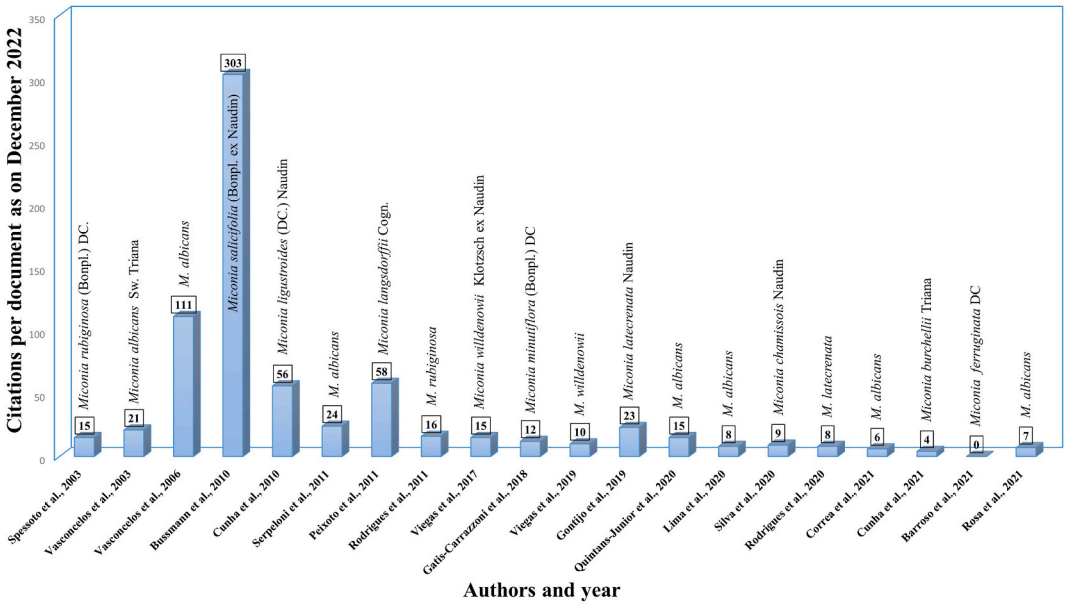


Fig. 2. A bar graph showing the number of articles, their citations, and the year they were published about the genus *Miconia*.

osteoarthritis clinical study by Gomes et al. [39]; antioxidant, antinociceptive, anti-inflammatory, anti-arthritic, and antinociceptive peripheral and central analgesic activity; while the *in vitro* studies investigated the extracts of plant species from *Miconia* for their antibacterial, anti-leishmanial, cytotoxic, mutagenic, schistosomicidal, anti-inflammatory, antioxidant, and anti-proliferative activities. The twenty-one articles reviewed here originated from Brazil (n = 20) and the USA (n = 1). Fig. 2 shows the number of publications with their citations and the year they were reported for each species of *Miconia*. Traditional populations and users of medicinal plants in the Northeast region of Brazil depend on folk medicine widely; most of these species are commonly found for sale in public markets [40]. Our results also show that plant species belonging to the *Miconia* genus that treat joint diseases (those with an inflammatory profile) are more popular with Brazilian folk medicine practitioners than medicinal plants used to treat other illnesses. This is because there is an increase in the elderly population and more people are getting these kinds of diseases [41,42].

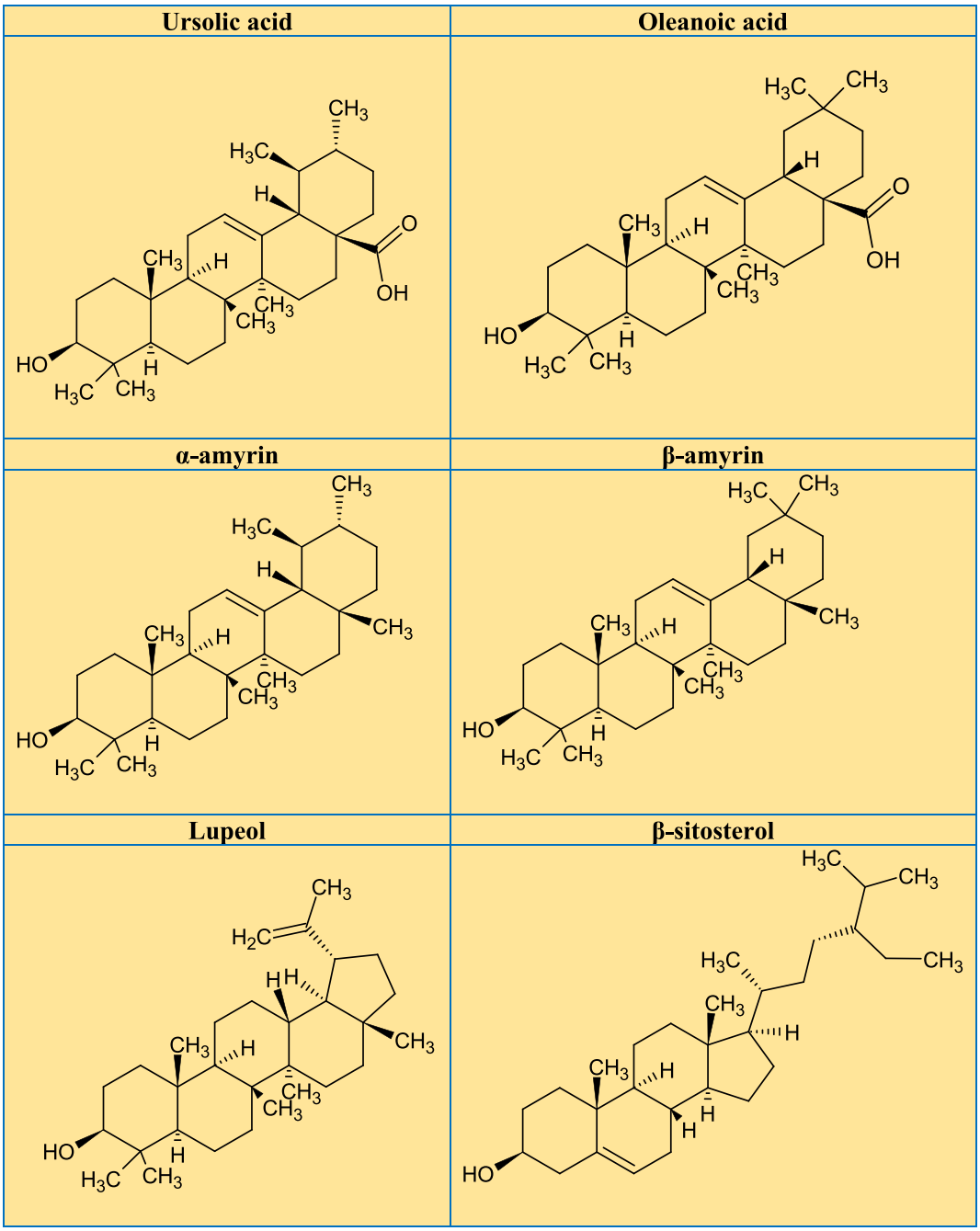


Fig. 3. A–C. Promising phytochemical structures identified/isolated from different *Miconia* plant species that are responsible for a variety of biological functions from the reviewed studies.

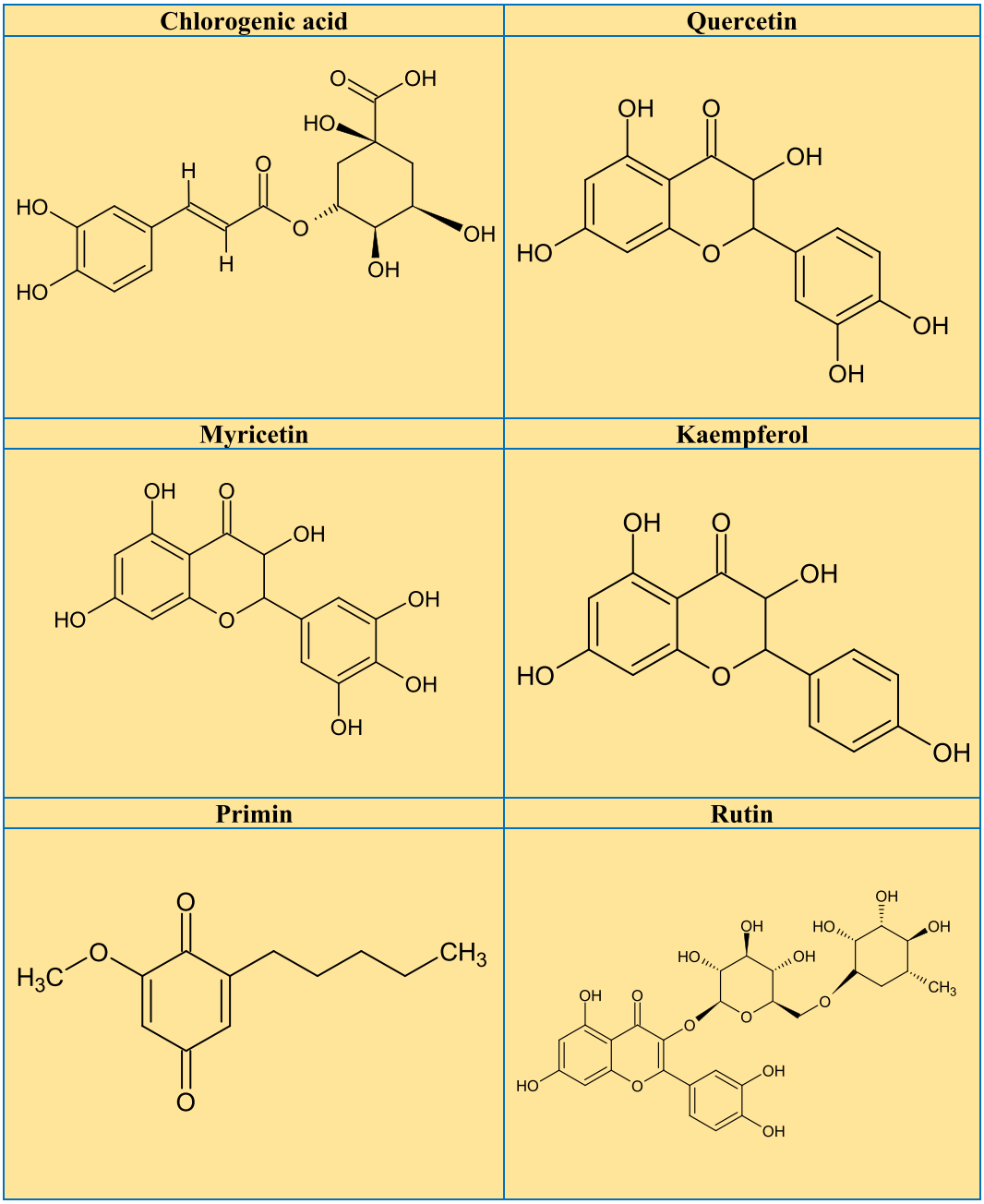
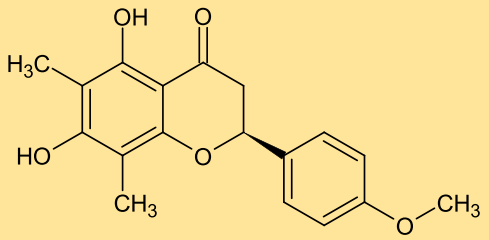
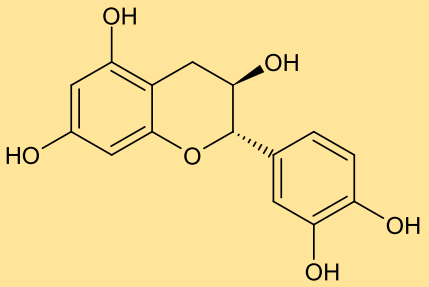


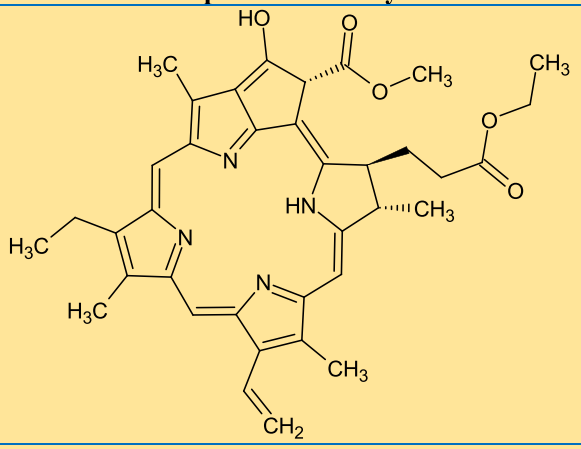
Fig. 3. (*continued*).

3.4. In vivo studies

Our literature search identified 8 *in vivo* studies relating to the biological activities of the extracts and isolated compounds from *Miconia*, the viz analgesic and antioxidant activity of *M. rubiginosa* [21], the antinociceptive and peripheral analgesic activity of *M. albicans* [25], the analgesic and anti-inflammatory activity of *M. albicans* [10], anti-arthritic and anti-inflammatory activity of *M. albicans* [36], antioxidant and anti-inflammatory activity of *M. albicans* [43], anti-inflammatory and antinociceptive of *M. minutiflora* [33], anti-inflammatory and antioxidative effect of *M. albicans* [44], and anti-osteoarthritis activity of *M. albicans* [39]. Most *in vivo* studies in our current review mainly focus on the analgesic and anti-inflammatory methodologies, which might be because plants of the *Miconia* genus are most commonly used to treat pain and inflammation in folk medicine [9].

Matteucinol	Catechin
	

Pheophorbide A ethyl ester



Ellagitannin

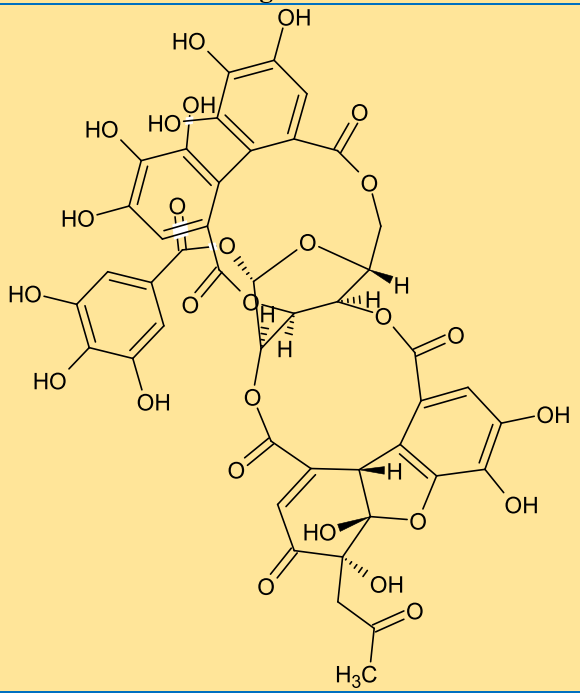


Fig. 3. (*continued*).

3.5. Analgesic and anti-inflammatory activity

The analgesic effect of *M. rubiginosa* extract was studied in rats and mice using the acetic acid-induced writhing and hot plate tests, classical experimental models of analgesic screening were widely used to validate this pharmacological property [21,45]. The extract (200 mg/kg/body wt.) showed a potent increase in the pain threshold and antinociceptive effect and inhibited acetic acid-induced writhing in mice. The presence of triterpenes (UA and OA, α-amyrin and β-amyrin) and sterols (lupeol and β-sitosterol) seems responsible for the central and peripheral analgesic and anti-inflammatory profiles. Previous studies have indicated that these triterpenes play a role in modulating pro-inflammatory mediators and mitigating the deleterious effects of inflammation and cell proliferation [46,47]. The results suggest that the favourable biological mechanism of action might be due to the inhibition of significant levels of prostaglandin, namely, $PGE_{2\alpha}$ and $PGF_{2\alpha}$ synthesis, the two critical prostanoids in the inflammatory cascade following the acetic acid injection, as well as through central inhibitory mechanisms. The synergistic action of natural molecules in the extract could have been accountable for the observed analgesic effect in biological activity studies [47]. Consequently, the analgesic activity study of the crude extracts of aerial parts of *M. rubiginosa* resulted in abdominal writhing inhibition and antinociceptive effects [21]. *M. rubiginosa* crude extracts due to the presence of anti-inflammatory phytochemicals might be involved in the peripheral analgesic activity [48]. Furthermore, the extracts of *M. rubiginosa* significantly reversed the acetic acid-induced writhing in mice. *M. rubiginosa* induced a significant increase in pain threshold throughout the experimental period, with a substantial increase in the percentage of protection. The presence of triterpenes and sterols in *M. rubiginosa* is the essential active principle responsible for the witnessed analgesic effect, possibly mediated by the modulation of prostaglandin synthesis, along with effects on central inhibitory mechanisms. Literature studies report that these compounds have analgesic and anti-inflammatory properties [49]. There is consistent evidence that lupeol and β-sitosterol mitigate tumor necrosis factor-α (TNF-α), vascular endothelial growth factor receptor −2 (VEGFR-2), and pro-inflammatory cytokines activity in cell proliferation, and the production of factors that drive the inflammatory process and, consequently, the pain process [46].

A similar study performed by Vasconcelos et al. using *M. albicans* crude extracts (200 mg/kg/body wt.) in Swiss albino mice and Wistar rats, did not exhibit any analgesic effect on the central nervous system (CNS); however, there were clear peripheral analgesic effects, and a reduction in pain behaviour, and anti-inflammatory activities [25]. Crude extract of the aerial parts of *M. albicans* has been shown to have analgesic effects due to the presence of triterpene acids and β-sitosterol [25]. β-sitosterol has been shown to have outstanding anti-inflammatory properties while reducing critical inflammatory mediators of the pain-related process [50].

The potential analgesic and anti-inflammatory activities of UA and OA, isolated from the aerial parts of *M. albicans* crude methylene chloride extract, were evaluated in a carrageenan-induced paw edema animal model. The compounds produced a significant anti-inflammatory effect and a prostaglandin synthesis inhibition. Thus, they showed a significant reduction in inflammatory pain, which seems to be confirmed by the amelioration of the increase in inflammatory mediators, such as the prostaglandins, induced by carrageenan and the subsequent inhibition of the inflammatory signaling pathways which is one of the main triggers for the pain profile of these animal models. The analgesic effect of the extract was mostly based on its peripheral mediated mechanism, which is compatible with the presence of the UA and OA compounds found [10]. UA and OA are inhibitors of key pro-inflammatory pathways in joint pain, such as the nuclear factor erythroid-2-related factor 2 (Nrf2) and nuclear factor-κB (NFκB) pathways [51,52].

Similarly, Lima et al. demonstrated that *M. albicans* extract possesses an effective treatment profile against RA in carrageenan-induced paw edema [44]. The study revealed that the extract reduced TNF-α, IL-1β, and consequently, the inflammatory nociception and edema caused by carrageenan injection. These results corroborated, at least in part, those reported by Vasconcelos et al. suggesting that *M. albicans* has potential therapeutic uses in chronic, difficult-to-treat conditions that are very disabling for patients, such as arthritis or other joint pain [10]. The chemical study of the extract produced a vast number of flavonoids with polyphenol structures, and the authors suggest that its bioactivity may be explicitly credited to the presence of the composition of flavonoids containing polyphenols structure, such as rutin and quercetin. Flavonoids are anti-inflammatory and are used to mitigate chronic inflammatory diseases [53,54]. Thus, these findings reinforce the use of these anti-inflammatory plants in Brazilian folk medicine to treat joint and related pain [44].

M. minutiflora leaf polyphenols rich-extract has shown anti-inflammatory activity and could reduce edema and the migration of leukocytes towards the site of inflammation, and was associated with suppressed concentrations of the pro-inflammatory cytokines such as TNF-α and IL-1β, while the antinociceptive actions involve central and peripheral mechanisms with the participation of α2-adrenergic receptors. The anti-inflammatory mechanisms of *M. minutiflora* might be related to the decrease in the level of several inflammatory and pro-inflammatory mediators in the edema tissue via the suppression of pro-inflammatory cytokines concentrations [33].

Thus, the major compounds in the studied extracts (especially terpenoids and flavonoids) are known to act directly by mitigating the production and levels of circulating pro-inflammatory cytokines, influencing pathways related to oxidative stress, which are suggested to be responsible for the anti-inflammatory activities of several medicinal plants [53,55]. These therapeutic points of view suggest using plant remedies to recommend these herb species used in traditional medicine to treat inflammation.

3.6. Anti-arthritic and anti-inflammatory activity

Studies have indicated that drugs that modulate or block the pro-inflammatory cytokine TNF-α and its related factors, including interleukins (IL)-1, IL-6, IL-8, and granulocyte macrophage-colony stimulating factor (GM-CSF) have been considered as one of the preferred treatments for the management of RA [56–58]. *M. albicans* ethanolic leaf extract (MAEE), in doses of 50 and 100 mg/kg/body wt., was assessed for its anti-hyperalgesic and anti-inflammatory profiles in a carrageenan-induced arthritis-like model. The results

showed that MAEE significantly lessened leukocyte migration in the pleurisy model and suppressed TNF-α and IL-1β in pleural lavage. Moreover, in the Complete Freund's Adjuvant (CFA) mice model, a primary animal model that mimics the signs and symptoms of RA in humans, MAEE administration in rats resulted in a significant decrease in nociceptive pain and hyperalgesic actions in the rearing test and decreased mechanical hyperalgesia. Moreover, MAEE significantly improved mobility in the open-field test and increased hind paw grip strength without any apparent damage to the liver. MAEE drastically reduced the volume of CFA-induced ipsilateral knee edema, the solid anti-inflammatory potency could be related to its positive effect on IL-6 and TNF-α in the knee joint [36]. Moreover, a dried extract of *M. albicans* (DEMA) reduced the carrageenan-induced edema of the paw. It ameliorated the inflammatory reactions by downregulating TNF-α and IL-1β and reducing antioxidant parameters, consequently reducing inflammatory nociception, important factors in reducing the inflammatory cascade [44]. Similarly, the *in vivo* anti-inflammatory effect of *M. albicans* fruits methanol extract, which is rich in phenolic compounds, flavonoids, hydroxybenzoic acids, terpenoids, ellagitannins, chlorogenic acid, and fatty acids was assessed in croton oil-induced ear edema in mice and was reported to have potential health benefits [43].

An important aspect in these recent studies with different extracts of *M. albicans* [36,43,44] is the possible ability of the extracts to reduce RA symptoms, mitigate pro-inflammatory pathways, and reduce oxidative stress by acting as a potential anti-RA agent, similar to RA blockers which reduce TNF-α, IL-1β and IL-6 levels [59,60]. Moreover, TNF-α and IL-6 are cytokines at high levels in the synovial fluid of RA patients. The reduction of these cytokines has been directly related to improvements in the general condition of patients, especially in respect of joint pain that produces the greatest disability in these persons [61]; thus the fact that the studied extracts of *M. albicans* seem to be able to act as TNF-α, IL-1β and IL-6 blockers are encouraging in respect of their potential use. Fig. 4 depicts the role of phytochemicals derived from the *Miconia* genus plant species in exhibiting their anti-inflammatory effect by modulating vital inflammatory mediators, which might be related to their antioxidative mechanism involving the normalization of oxidative stress-stimulated biomarkers.

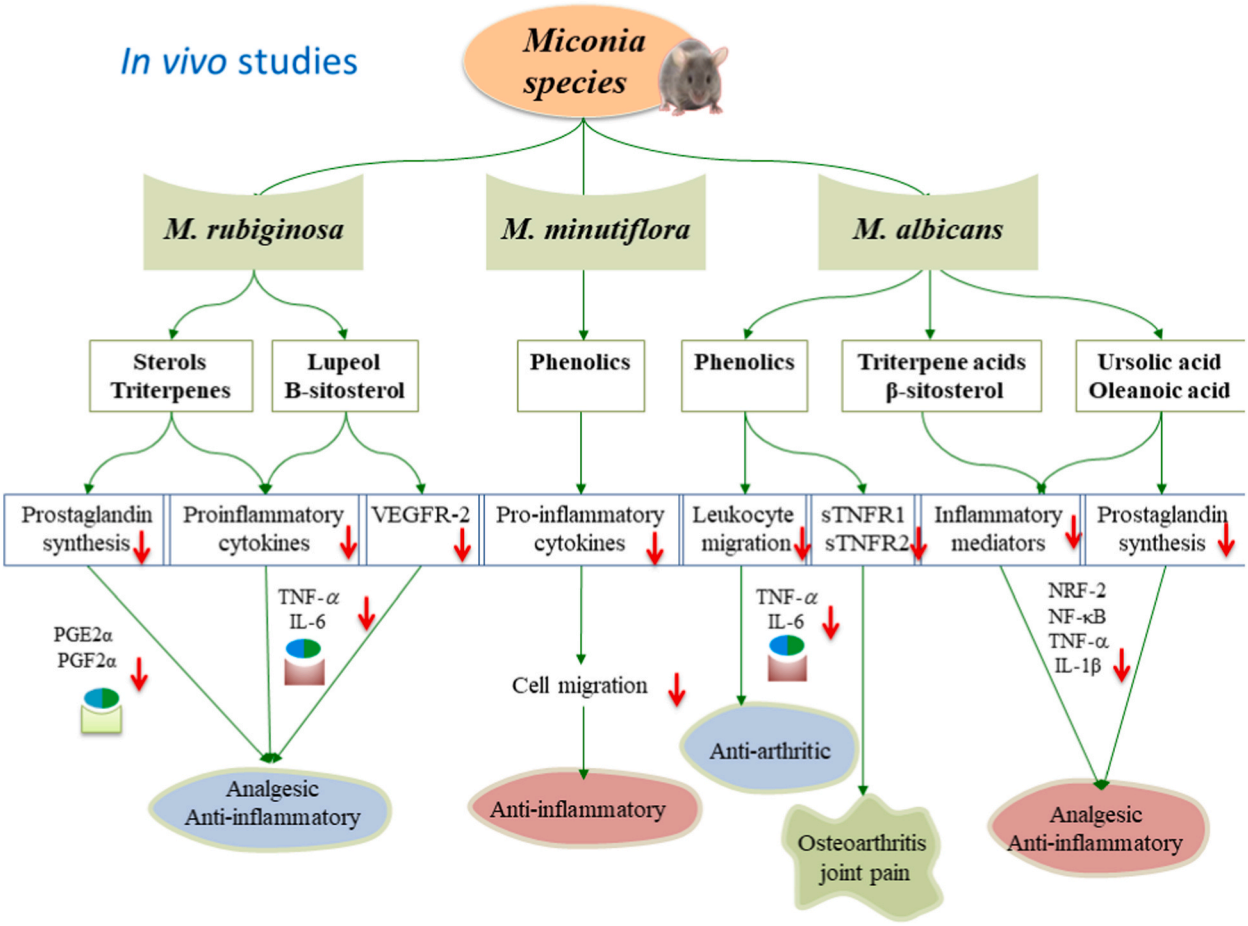


Fig. 4. The *in vivo* biological studies evaluated the therapeutic potentials of the *Miconia* species, such as their analgesic, anti-inflammatory activity, anti-arthritis, joint pain, and anti-osteoarthritis activities The extracts and secondary metabolites from *Miconia* species, such as phenolic compounds, hydroxybenzoic acids, flavonoids, terpenoids, triterpenes, sterols, ellagitannins independently or synergistically, might have contributed to strong antioxidant and anti-inflammatory activities through cytokine-mediated responses. Pro-inflammatory and anti-inflammatory cytokine production might have modulated various ILs-mediated cellular responses to the tested diseases, especially for treating osteoarthritis, and joint pain.

3.7. Osteoarthritis and joint pain

Interestingly, a clinical study conducted to assess the analgesic and immunomodulatory potential of *M. albicans* in knee osteoarthritis revealed its capability to lessen joint pain and inflammation and improve function [39]. This is probably the first clinical study using *M. albicans* for a common disease and provides further evidence for its use in traditional medicine. In the study, the oral administration of the extract at 1000 mg/day/body wt. for 30 days reduced the patients' pain, decreased Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analogue Scale of Pain (VASP) scores, and knee joint effusion resulting in functional improvement. This clinical study demonstrated the analgesic and anti-inflammatory effect of *M. albicans* on knee osteoarthritis, correlating with changes in the expression of inflammatory mediators in the synovial fluid. Moreover, the treatment decreased the expression of resist in and soluble TNF-α receptors (soluble tumour necrosis factor receptor (sTNFR)1 and sTNFR2 and increased the expression of adiponectin and leptin. In this study, the authors demonstrated the analgesic efficacy of *M. albicans* and their possible mechanisms concerning pain modulation, reduced inflammation, and improved function in knee osteoarthritis. The study also corroborated the clinical safety of using this plant species and its therapeutic benefits [39].

Although this study lacked a more careful analysis of possible toxicity and did not evaluate the inflammatory mediators involved (blood levels of cytokines, inflammatory mediators common in osteoarthritis, among others) more systemically, it is the first study in humans to provide evidence that supports the popular use of *M. albicans* and shows that it can be effective for diseases such as osteoarthritis and RA. This is, therefore, a fundamental study and provides a reasonable basis for further controlled and randomized clinical trials.

In summary, eight *in vivo* studies of the biological efficacy of the various extracts and their natural molecules from the *Miconia* genus were found to have potential health benefits, including analgesic, antioxidant, antinociceptive, and anti-osteoarthritis activities. Most importantly, *M. albicans* fruit extract has higher concentrations of flavonoids (quercetin, myricetin, kaempferol), terpenoids, and fatty acids such as palmitic, stearic, arachidic, behenic, elaidic, oleic, eicosenoic, and linoleic acids, as well as others, which might have contributed to the strong antioxidant and anti-inflammatory activities [43]. But there is still a lack of scientific evidence about some clinical aspects (molecular information, acute and chronic toxicity, effectiveness, etc.) and the possible effects of long-term use of pharmaceutical preparations that contain extracts from *Miconia* genus plants or their isolated compounds. This is an area that needs to be looked into more.

3.8. In vitro studies

In our systematic search, we identified 18 *in vitro* studies of the pharmacological activities of the plant species from the *Miconia* genus with enriched bioactives (Fig. 5), viz., the antioxidant property of *M. albicans* [43], the cytotoxic activity of *M. burchellii* [62], the antioxidative effect of *M. albicans* [44], a chemo profile study of *M. albicans* [36], the antioxidant, the antibacterial and antimutagenic activity of *M. latecrenata* [63], the phytochemistry, anti-inflammatory and antinociceptive properties of *M. minutiflora* [33], the schistosomicidal activity of *M. willdenowii* [20], the phytochemistry of *M. rubiginosa* [5], the anti-leishmanial activity of *M. langsdorffii* [28], the cytotoxic and mutagenic activity of *M. albicans, M. cabucu*, and *M. stenostachya* [14], the antibacterial activity of *M. salicifolia*

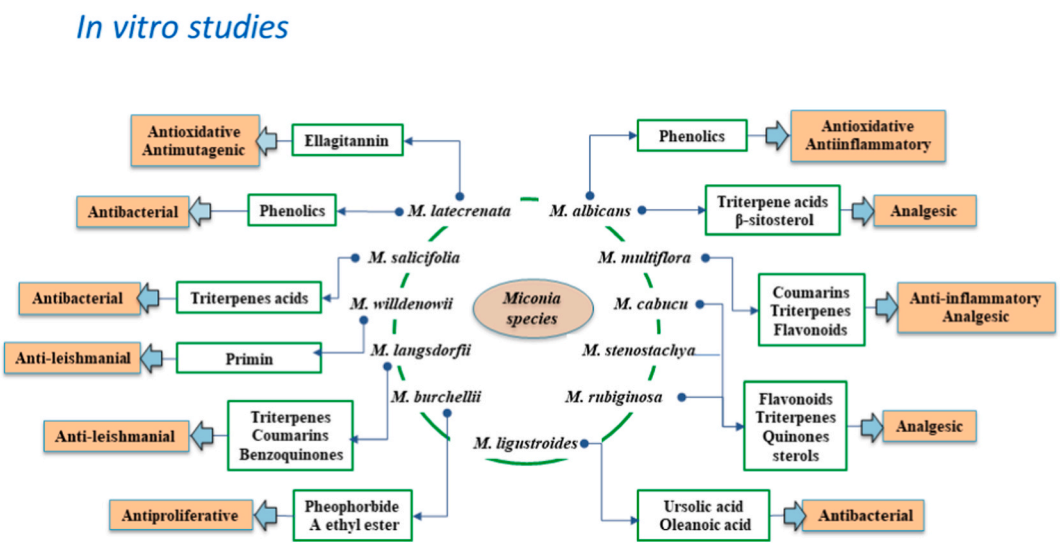


Fig. 5. *In vitro* pharmacological studies of *Miconia* species showed several crucial health benefits, mainly focused on anti-inflammatory, antioxidant, analgesic, antibacterial, anti-leishmanial, antinociceptive, schistosomicidal, anti-osteoarthritis, cytotoxic, and mutagenic activities. Phenolic compounds, hydroxybenzoic acids, flavonoids, terpenoids, ellagitannins, chlorogenic acids, fatty acids, and many more, might have contributed to the aforementioned therapeutic potentials of *Miconia* species. Evidence indicates that the extracts and secondary metabolites from *Miconia* species are also safe for consumption and could be explored further for managing diseases.

[64], the antibacterial activity of *M. ligustroides* [65], and the phytochemical and antioxidant activity of *M. rubiginosa* [21].

3.9. Antibacterial and antifungal activities

A study conducted by Bussmann et al. reported that various solvent extracts prepared from 51 Peruvian medicinal plant species had antibiotic and inhibitory activity regarding microbial growth [64]. The extracts inhibited *Escherichia coli* and *Staphylococcus aureus.* The ethanolic extracts exhibited higher inhibitory potential than the aqueous extracts against tested microorganisms. *M. salicifolia,* had the lowest MIC values, indicating its antibacterial activity. Several triterpene acids have great potential as antimicrobial compounds in treating infectious diseases [66]. UA and OA from *M. ligustroides* have anti-microbial activity against some multi-resistant bacteria but not against many others [65,67]. A synergetic effect was noted when different concentrations of various UA derivatives were evaluated to inhibit the growth of *Bacillus cereus*, *Vibrio cholerae*, *Salmonella choleraesuis*, *Klebsiella pneumoniae*, and *Streptococcus pneumonia,* and was found to have an antimicrobial effect against some of the microbes. The antimicrobial activity of several species from *Miconia* against various microorganisms has already been reported in the literature [15]. The leaves of *M. latecrenata,* which contain copious amounts of ellagitannin, presented higher antibacterial effects against some gram-positive and negative strains. On the other hand, the phenolic-rich *M. latecrenata* show antimicrobial activity against antibiotic-resistant bacteria, which cause some significant infections to human health [63]. The *M. willdenowii* leaves collected from the Brazilian Atlantic forest have antibacterial properties, and evidence would suggest that primin, the component with the highest concentration, is the main bioactive metabolite in the plant. Additionally, the findings reveal for the first time the extract's potent antibacterial and antifungal effects on *S. aureus*, *Candida krusei*, and *Candida glabrata* [68]. The phenolic compounds extracted from *M. latecrenata* leaves acquired from the Brazilian Atlantic forest showed the greatest potential for preventing the growth of *S. aureus* and *Pseudomonas aeruginosa*. Following bio-guided fractionation of the extract, the fraction demonstrated synergism with ampicillin and tetracycline for *S. aureus* and *P. aeruginosa,* respectively. These results imply that *M. latecrenata* leaf extracts and fractions may be employed as therapeutic antibacterial agents [69].

3.10. Anti-leishmanial and schistosomicidal activities

The extract was prepared from the aerial parts of *M. langsdorffii* and was evaluated for their potential against promastigotes, mainly *Leishmania amazonensis*, the major parasite responsible for leishmaniasis in humans [70]. Bioassay-guided fractionation of this extract revealed the presence of an extensive concentration of triterpenes. The compounds, UA and OA were observed to be the primary compounds in the plant extracts. Among the UA-derived substances, the C-28 methyl ester derivative exhibited the best activity [70]. The study results showed that UA and OA are highly potent compounds of antileishmanial action and can be effective agents against leishmania in the clinical location. An acute toxicity study of the molecules found they were safe even at high concentrations, but further studies using animal models are warranted to screen these compounds for developing new antiprotozoal agents [28].

The crude ethanolic extract from *M. willdenowii* was assessed for its schistosomicidal activity [20]. The extract showed greater schistosomicidal activity against *S. mansoni* worms than praziquantel. The ethanolic extract was further subjected to fractionation to identify its active lead molecule(s), with the hexane sub-fraction having considerably greater schistosomicidal activity against the adult worms. Moreover, chromatographic isolation of this active sub-fraction led to the isolation of 2-methoxy-6-pentyl-benzoquinone, also known as primin. This activity may be attributed to this significant bioactive metabolite. The authors reported that *M. willdenowii* extracts containing its active lead molecule primin showed important antischistosomal activity. Thus, these substances could be novel candidates for the treatment and management of microbes and could also act as a less toxic natural remedy against schistosomiasis [20]. The leishmanicidal activity of primin-containing ethanolic extract of *M. willdenowii* was also reported by Viegas et al. which demonstrated inhibition of 99.7% of the promastigote forms of *L. amazonensis* at a concentration of 80 μg/mL [68].

3.11. Cytotoxic and mutagenic effects

Knowledge of plant genotoxicity and potential mutagenic effects is necessary to develop plant-based phytochemical products and drugs. Extracts of plant species from *Miconia* were prepared and assessed for their cytotoxicity, mutagenicity, and protective effects on Chinese hamster lung fibroblast cell cultures (V79). The cytotoxicity study indicated a remarkable decline in cell viability at higher concentrations of plant extracts from *Miconia*, suggesting that the mixtures of polyphenols present in these extracts could contribute to the dose-dependent cytotoxicity potential of this plant and should be further validated by the pharmaceutical industry due to its ever-growing number of nutraceutical properties [71].

The plant extracts found to be the most active as pro- or anti-oxidants revealed the presence of a copious amount of phenolic compounds. Hence, the reports of the study suggest that the plant extracts prepared from the *Miconia genus* containing large amounts of phenolics are responsible for the antioxidant activity *in vitro* due to their free radical scavenging properties. Phenolic components in fruits, vegetables, and medicinal herbs have been proposed to be active secondary metabolites and have antioxidant and anticancer properties [72]. The interactions and potential synergistic properties of various plant extract polyphenols and their beneficial effects were reported in the study by Feinstein et al. including regarding doxorubicin (XDR)-induced damage [73]. In addition to XDR, the DNA-damaging potential of adriamycin has been reported [73]. Adriamycin is a substance that causes excessive production of free radicals, resulting in the generation of oxidative injuries to DNA and the production of oxidative stress-mediated lipid peroxidation [74]. The amelioration of DNA impairment reported in the study suggests that *Miconia* extracts containing phenolics may have protective effects on XDR-induced DNA damage by neutralizing the free radicals-mediated inflammatory reactions. Polyphenols have been shown as worthy quenchers of circulating free radicals, and therefore they inhibit DNA damage and act as vital antioxidant

molecules [75]. The most outstanding feature of the present study is the indication of a therapeutic role of *Miconia* extracts in the recovery of XDR-induced DNA damage by enhancing DNA-repair efficiency in the damaged cells, which has been attributed to the presence of high levels of bioactive polyphenols [14]. Therefore, this study suggests *Miconia* species rich in polyphenols have anti-oxidant effects and high anti-mutagenic activity.

3.12. Anti-inflammatory and antioxidant properties

This study summarizes the recent investigations into the anti-inflammatory effect of *M. albicans* fruit extract (MAFRE). The chemical profile showed a high concentration of phenolic compounds, flavonoids, and fatty acids, that benefit the counter-inflammatory response with less toxicity on VERO cells. Flavonoids are the predominant substances in MAFRE and it has been shown that they are natural immunomodulators of pro and anti-inflammatory molecules [53]. Nine fatty acids have been found in MAFRE, in addition to linoleic acid, which is one of its major constituents. The phytochemical contents of *M. albicans* fruit have been previously investigated and shown to contain untapped resources of phytochemicals with effective pharmacological actions beneficial for pharmaceutical and nutritional purposes [43]. *M. albicans* extract exhibited potent antioxidant activity, probably due to the high concentration of flavonoids, tannins, saponins, leucoanthocyanins, and, steroids. Significant levels of total phenolic (551.3 mg gallic acid equivalent/g of dried extract) and flavonoid contents (367.19 mg catechin equivalent/g of dried extract) have been identified. A study using HPLC-PDA revealed the presence of rutin and quercetin as two major flavonoids in the extract which act strongly to inhibit levels of nitric oxide, the intracellular reactive oxygen species (ROS) pathway, and pro-inflammatory cytokines, thus reducing, for example, the levels of TNF-α and IL-6, whilst also mitigating the oxidative imbalance common in the inflammatory process and tissue injury [76]. Regarding the antioxidant activity of this standardized extract, it has been shown that the anti-inflammatory phytochemicals rutin and quercetin present in *M. albicans* appears to exhibit profound activity in modulating the damaging effects of reactive oxygen species [44].

The primary pharmacological activities of *M. latecrenata* support its therapeutic potential concerning ROS/reactive nitrogen species (RNS) related anti-inflammatory disorders. Furthermore, the phenolic compounds from *M. latecrenata* significantly contribute to minimizing or inhibiting biological macromolecule damage, especially to DNA molecules. Phytochemical analysis of *M. latecrenata* revealed a high total phenolic content, especially ellagitannins, demonstrating a potential pharmacological activity. In addition, the extract's high antioxidant, antibacterial, and antimutagenic activities were observed in different tests. Therefore, this ellagitannin-rich extract can accelerate and reduce costs in the search for new therapeutic agents [63].

3.13. Anticancer and antiproliferative activity

The *in vitro* anticancer potential of *Miconia chamissois* Naudin for treating glioblastomas was examined in the study by Silva et al. [77]. The hydroethanolic extract of *M. chamissois* and its chloroform partition were tested for cytotoxicity in glioblastoma cell lines. A single molecule, matteucinol, was identified in the fraction. In the adult glioblastoma cell lines, matteucinol induced intrinsic apoptosis, which induced cell death [77]. Additionally, matteucinol markedly decreased the tumour cells' invasion, migration, and clonogenicity. In an *in vitro* study, *M. burchellii* leaves were reported to have antiproliferative activity with the ethyl acetate fraction showing potent cytotoxic activity against four of the five tumor cell lines tested. The cytotoxic activity was attributed to the strong presence of pheophorbide A ethyl ester in the respective fraction, which is projected to be effective against leukemia cell lines. The investigation showed that neither the fractions nor the compounds from *M. burchellii* contributed significantly to the antiproliferative potential [62]. Additionally, *M. ferruginata*, a native Brazilian plant from the Cerrado biome known as "pixirica" or "babatena," which is rich in flavonoid derivatives from quercetin, catechins, and phenolic acids, showed potential cytotoxicity against tumor cells of 4T1, A549, and MDA-MB-231 in association with minimal cell toxicity against fibroblasts and should be taken into consideration for further research against the treatment of cancer [78]. Hydroethanolic extracts from the leaves of *M. albicans* and *M. chamissois;* reduced the viability of human cancer cell lines. They exhibited cytotoxic potential, leading to the discovery of novel chemotherapeutic agents for cervical cancer [79].

To summarize, the *in vitro* studies reported that extracts from the *Miconia* genus and isolated compounds had anti-proliferative, anticancer, analgesic, antibacterial, cytotoxic, mutagenic, anti-leishmanial, antinociceptive, schistosomicidal and anti-osteoarthritic properties. The presence of phenolic compounds, hydroxybenzoic acids, flavonoids, terpenoids, ellagitannins and chlorogenic acids, and fatty acids such as palmitic, stearic, arachidic, behenic, elaidic, oleic, eicosenoic, linoleic acids in the *Miconia* genus may have contributed to the strong antioxidant, anti-cancer, and anti-inflammatory activities [43].

4. Safety of *Miconia*

Several *in vivo* experiments indicate that extracts from certain *Miconia* species and their isolated phytochemicals are safe for medical use, at least in the doses and routes assessed in our survey. However, there is a lack of studies demonstrating safety in controlled clinical trials. The consumption of *Miconia* extracts and biomolecules from the aerial parts of the plants has not been reported to cause any undesirable outcome. *M. albicans* methanol fruit extract has strong antioxidant and anti-inflammatory properties and contains phenolic compounds, flavonoids, terpenoids, ellagitannins, and chlorogenic acid, and is potentially non-toxic to VERO cells, with 95% cell viability [43]. Moreover, no untoward outcomes were reported in a recently published clinical trial in patients with knee osteoarthritis. Patients received *M. albicans* extracts (1000 mg/day/body wt. orally for 30 days) [39]. An acute toxicity study of *M. minutiflora* leaf methanolic extract (2000 mg/kg/body wt., orally) in experimental models *in vivo* showed no significant changes in

weight, or food and water intake, and did not produce any deaths or treatment-linked adverse reactions [33].

In general, *in vitro* studies reveal the antioxidant potential of plants from the *Miconia* species [43,44,63]. The n-butanol fraction and the isolated flavonoids from the methanolic extract of *M. albicans* leaves had significant antioxidant activities with a scavenging capacity against 2,2′-azobis (2-amidinopropane) dihydrochloride (AAPH) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) [24]. The strong occurrence of phytochemicals, such as steroids, triterpenes, alkaloids, anthraquinones, glycosides, flavonoids, leucoanthocyanins, tannins, and saponins present in *Miconia* species, are known to have significant free radical scavenging capacity.

Therefore, the *in vitro* and *in vivo* studies suggested that the consumption of a limited number of the species from the *Miconia* genus is safe and can be used for clinical and therapeutic purposes; this is supported by the fact that it has been used in folk medicines around the globe for a long period without any adverse outcomes being reported.

5. Conclusion

Miconia species is of growing public interest and considered one of the largest genera of angiosperms belonging to the Melastomataceae family, with 1050 species distributed in the South American continent, with more than 282 species in Brazil alone, of which 121 are endemic [80]. Although it occupies a large area, has a widespread distribution, and is associated with several traditional uses, studies of its phytochemical and biological activity are scarce. Here, we reviewed all current studies of the *Miconia* genus and its phytochemical and pharmacological properties to provide an up-to-date understanding of its therapeutic potential. *In vitro* pharmacological studies were mainly focused on its anti-inflammatory, analgesic, antibacterial, cytotoxic, mutagenic, antioxidant, anti-leishmanial, antinociceptive, schistosomicidal, and anti-osteoarthritic properties. The *in vivo* biological studies mostly evaluated its therapeutic potential regarding its analgesic, antioxidant, antinociceptive, and anti-osteoarthritic properties. The identification and authentications of phenolic compounds; hydroxybenzoic acids; flavonoids; terpenoids; ellagitannins; chlorogenic acid; fatty acids such as palmitic, stearic, arachidic, behenic, elaidic, oleic, eicosenoic, and linoleic acids, among many others, has sparked increasing interest in these species as a strong antioxidant and anti-inflammatory agents. In addition, analysis of the phytochemical composition of this species yielded eight bioactive phytomolecules: pheophorbide an ethyl ester, kaempferol, kaempferol-3-*O*-β-glucopyranoside, kaempferol-3-*O*-β-galactopyranoside, OA, UA, lupeol, and β-sitosterol that added therapeutic value to each plant belonging to the *Miconia* species. Phytochemical and pharmacological studies focused on the aerial parts belonging to *M. albicans, M. rubiginosa, M. salicifolia*, *M. ligustroides, M. stenostachya, M. cabucu, M. langsdorffii, M. willdenowii, M. minutiflora, M. latecrenata,* and *M. burchellii.* There is sufficient *in vitro* and *in vivo* evidence to suggest that the extracts and natural molecules from *Miconia* are safe for consumption for clinical and therapeutic purposes, which is supported by the fact that no adverse outcomes have been reported regarding their traditional use. Given the variety of their effects and potential health benefits, future investigations are warranted, particularly studies that examine the most effective delivery mechanisms and more randomized studies of more species and controlled clinical trials to further examine their potential beneficial effects.

Ethics approval

Not applicable.

Availability of data and materials

Not applicable to this article.

Consent to participate

Not applicable.

Consent for publication

All the authors have approved the manuscript for publication.

Author contribution statement

SRG, LJQJ, RQG, and JSSQ: Conceived and designed the study; SRG, GRG, SAC, LJQJ, and RQG: Analyzed and interpreted the data; SRG, GRG, PJA, and LJQJ: Wrote the original draft; VEH, LJQJ, and RQG: Reviewed and edited the final draft; GH and YL: Performed the graphical abstract, figures 4 and 5 using image editing software. All authors have read and agreed to the published version of the manuscript.

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Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare no conflict of interest.

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