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Ximenia americana L. From Popular Use to Anti-Inflammatory Activities: A Comprehensive Review

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ABSTRACT

Ximenia americana (L.), known as “yellow plum,” “sea lemon,” or “Brazilian plum,” is a tropical/subtropical plant widely used in traditional medicine. Its roots, leaves, flowers, stem, and fruits are traditionally employed to treat various inflammatory disorders. To review the ethnomedicinal uses, phytochemical profile, and biological-pharmacological properties of *X. americana* related to inflammation. This systematic review followed the Cochrane Handbook and preferred reporting items for systematic review and meta-analysis (PRISMA) guidelines. The research question was whether traditional uses of *X. americana* are supported by its phytochemical and biological properties in nonclinical studies. Article searches were conducted in Medline, Embase, Web of Science, Scopus, Virtual Health Library, SciELO, and Google Scholar. Two reviewers independently selected eligible studies, extracted data, and assessed risk of bias. Ninety-six articles met the inclusion criteria: 21 in vivo (521.2%), 16 in vitro (39%), and four with both approaches (9.8%). *X. americana* is used in folk medicine for treating toothaches, respiratory and gastrointestinal disorders, and general inflammation. Scientific studies support these uses, showing anti-inflammatory, antinociceptive, gastroprotective, and antioxidant properties. A total of 181 compounds have been identified, including 31 oil and fat compounds, 22 terpenes, 18 flavonoids, three phenolic acids, one alkaloid, one polyphenol, and 105 others. *X. americana* has validated anti-inflammatory and gastroprotective potential, supported by its rich phytochemical composition. It represents a promising natural source for identifying novel bioactive molecules for treating inflammatory diseases, with strong potential for pharmaceutical development.

Abbreviations: AA, arachidonic acid; AAPH, 2,2'-azodiisobutyramidine dihydrochloride; ABTS, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid); BK, bradykinin; CB2, receptors involving cannabinoid type 2; COX, cyclooxygenase; DPPH, 2,2-diphenyl-1-picrylhydrazyl; FRAP, ferric reducing/antioxidant power; IC₅₀, inhibitory concentration 50; IL-1 β , interleukin-1 β ; IL-6, interleukin-6; KC, keratinocyte-derived chemokine; LOX, lipoxygenase; MPO, myeloperoxidase; NO, nitric oxide; NSAIDs, non-steroidal anti-inflammatory drugs; OH, hydroxyl; PGE₂, prostaglandin E₂; PM, Mo-phosphate; RC₅₀, efficiency concentration; TAC, total antioxidant capacity; TNF- α , tumor necrosis factor-alpha.

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1 | Introduction

The word “inflammation” has its origins in the Latin “inflammation,” a term coined by the Roman physician Aulus Cornelius Celsus in the 1st century AD, with the meaning of “to ignite” or “to set fire” (Bai et al. 2021). The inflammatory response is usually described by five main signs: heat, redness, edema, pain, and loss of function. Inflammatory lesions stimulate the release of systemic mediators, such as cytokines and chemokines, which coordinate cellular infiltration and help in the resolution of inflammation, restoring tissue integrity. However, persistent inflammatory stimuli or failures in resolution mechanisms can result in chronic inflammation (Maione et al. 2016). Chronic inflammation is frequently associated with several diseases, both physiological and pathological, including obesity, atherosclerosis, rheumatoid arthritis (RA), gout, AD, depression, Parkinson’s disease (PD), and cancer (Bai et al. 2021).

Despite rapid advances in the development of treatments for inflammation, the efficacy and tolerability of conventional anti-inflammatory and analgesic drugs can be compromised by undesirable side effects. Research on natural compounds, based on ethnopharmacological knowledge, has played an important role in the improvement of drugs and opened new possibilities for the development of pharmacological alternatives in the treatment of inflammatory conditions (Maione et al. 2016; Allegra 2019; Bai et al. 2021). The importance of medicinal plants as potential sources of drugs is evidenced by the global commercialization of effective drugs derived from several plant species (Khumalo et al. 2022).

Piowowski et al. (2015) suggest that exploring little-known traditional herbs that are not part of conventional medicine may be a promising strategy for the development of innovative and sustainable medicines in the future. The study of the phytochemical and pharmacological properties of herbal remedies plays an essential role in research on medicinal plants and indigenous knowledge systems. Validating the connections between ethnobotanical uses, bioactive compounds, and their biological and pharmacological effects will be critical to ensuring the continued use of these medicines, especially given their increasing popularity due to their affordable cost and increasing reliance on traditional herbal treatments.

Considering the growing interest in natural products, the genus *Ximenia* consists of 10 species, namely, *X. americana* L., *X. caffra* Sond., *X. coriacea* Engl., *X. glauca* (DeFillips) Bentouil, *X. parviflora* Benth., *X. perrieri* Cavaco & Kerauderen, *X. pubescens* Standl., *X. roigii* León, *X. horrida* Urb. & Ekman, and *X. intermedia* (Chodat & Hassl.) DeFilippis (Maroyi 2016) with tropical and subtropical distribution (Maroyi 2016). Among these species, *X. americana* stands out, a pantoplistic species, which has several medicinal properties, used in the treatment of different inflammatory diseases in several countries (Bussmann et al. 2020).

Popularly known in Australia and Asia as “yellow plum” or “sea lemon” and wild plum in the Americas, *X. americana* is a semiclimbing shrub or small deciduous tree, with diverse habitats, found mainly in semiarid savannahs, in many types of dry forest, open sandy forest, dry mountainous areas, coastal

native forest, and along watercourses and on rocky slopes (Mevy et al. 2006; Hunde Feyssa et al. 2012). The bark, inner bark, fruits, leaves, roots, and seeds of the “wild plum” are used in the treatment of different inflammatory diseases in several countries. In traditional medicine, *X. americana* is also known by other popular names, such as “wild plum,” “Ababoni,” and “Brazilian plum” (Bussmann et al. 2020).

Previous research has demonstrated that *X. americana* possesses antioxidant, gastroprotective, antiparasitic, wound healing, antiedematogenic, anti-inflammatory, and antinociceptive biological properties (Souza Neto Junior et al. 2019; da Silva et al. 2023; Pessoa et al. 2024). Considering that *X. americana* is a popular medicinal plant widely used and studied by the scientific community, this literature review aimed to provide a better understanding of the potential of *X. americana*, focusing on its ethnopharmacological characteristics, phytochemistry, and biological-pharmacological activities correlated with inflammation.

2 | Materials and Methods

2.1 | Methods Protocol

This systematic review was conducted following the recommendations of the Cochrane Collaboration Handbook and the preferred reporting items for systematic review and meta-analysis (PRISMA) statement (Shamseer et al. 2015; Higgins and Thomas 2020).

2.2 | Identification and Selection of Studies

Two independent reviewers (ESS, JELB) screened all studies identified using the specified search terms. After removing duplicates, titles and abstracts were assessed to determine whether articles met the inclusion criteria. When studies were considered eligible, the full text and reference lists of selected articles were also reviewed. Any disagreement was resolved through discussion or, in the absence of consensus, by a third reviewer (MGLS). If the full text of an article was not accessible, an email was sent to the corresponding author.

2.3 | Review Question, Population, Intervention, Control, Outcomes, and Type of Study (PICOS) Strategy, and Search Strategy

The central question of the review was: do the traditional use of *X. americana*, its chemical compounds, and its antioxidant activity prove its anti-inflammatory action in vitro and in vivo? The PICOS strategy was formulated as follows: P: animals with pathologies, chemical compounds, traditional medicine, or free radicals; I: treatment with *X. americana*; C: no treatment; O: antioxidant, traditional use in the treatment of inflammation, phytochemistry, and/or reduction of pathologies; S: experimental studies in vitro and in vivo. The studies were independently selected by two reviewers (ESS, JELB), using the following search terms: *X. americana* and ethnopharmacology; *X. americana* and phytochemistry; *X. americana* and antioxidant; and *X. ameri-*

cana and anti-inflammatory. The research was conducted in the electronic databases Medline (via PubMed), Embase, Web of Science, Scopus, Virtual Health Library (VHL), and Google Scholar, covering all sources up to October 2025.

2.4 | Inclusion and Noninclusion Criteria

All studies that addressed the medicinal use, phytochemistry, antioxidant activity, and experiments that evaluated the anti-inflammatory effects of *X. americana* were included, regardless of the extraction method used. Studies that used isolated compounds extracted from *X. americana* extract were excluded, as well as those that combined this extract with others or with therapies involving *X. americana*. Studies conducted in humans, review articles, editorials, conference abstracts, and contents of theses and dissertations published in scientific journals and conference proceedings were also excluded.

2.5 | Study Selection and Data Extraction

For ethnomedicinal use in the treatment of inflammatory diseases, the following information was extracted: popular use, parts of the plant used, location/country, and year of publication. For in vivo studies, the following data were extracted: the activity or effect assessed, the experimental or test model used, the part of the plant and the extraction method employed, the characteristics of the animals (species, weight, group, dose, concentration, routine, and time of administration), the results/targets, and the conclusion, in addition to the names of the authors, year, and country of publication. In the case of in vitro studies, the following information was extracted: model used, part of the plant and extraction method, concentration and incubation time, experimental methods for determining RC_{50} and inhibitory concentration 50 (IC_{50}) values, results and targets, conclusion, and the names of the authors, year, and country of publication.

2.6 | Risk of Bias

The risk of bias of the included studies was independently assessed by two investigators (ADS, ASO) using tools from the Systematic Review Center for Laboratory Animal Experimentation (SYRCLE) (Hooijmans et al. 2014). The following domains were considered: (1) random sequence generation; (2) baseline characteristics; (3) allocation concealment; (4) random housing; (5) blinding of caregivers and investigators; (6) random outcome assessment; (7) blinding of outcome assessors; (8) incomplete data; (9) selective reporting of results; and (10) other sources of bias (whether studies mentioned the chemical compounds of essential oils and extracts). For in vitro studies, methodological quality was assessed using a modified version of the SYRCLE risk of bias tool, with nine domains: (1) random sequence generation; (2) baseline characteristics; (3) allocation concealment; (4) blinding of caregivers and investigators; (5) random assessment of outcomes; (6) blinding of outcome assessors; (7) incomplete outcome data; (8) selective reporting of outcomes; and (9) other sources of bias, as per Chan et al. (2017). All analyses were performed and exported to RevMan-Review Manager to prepare the figures used in this study.

3 | Results

3.1 | Search Results

The initial search resulted in 934, of which 709, 75, 68, 39, 29, and 22 were found in Google Scholar, Embase, Scopus, Web of Science, PubMed, and VHL, respectively. Of these, 112 were excluded due to duplication. After title and abstract analysis, another 731 reports were excluded, resulting in 100 studies. Of these, four studies were excluded after reading the full text—two due to associated use with other substances and because they were about a different plant species, resulting in 94 articles. In addition, two studies were identified after a manual search of the references, resulting in 96 included studies (Figure 1). Reliability/agreement ($\kappa = 0.853$) was almost perfect between reviewers after screening the titles and abstracts (Landis and Koch 1977).

Among the selected articles with antioxidant and anti-inflammatory properties, 21 (51.2%) reported in vivo experiments, 16 (39%) in vitro studies, and 4 (9.8%) in vitro and in vivo experiments. The articles were produced in eleven countries, with Brazil presenting the highest number of publications with 14 articles (35%), followed by Nigeria with five articles (12.5%), Kenya with five (12.5%), Burkina Faso with four (10%), Mali with four (10%), Ethiopia with two (5%), France with one (2.5%), India with one (2.5%), Togo with one (2.5%), Cameroon with one (2.5%), and Ivory Coast (2.5%).

3.2 | Risk of Bias and Quality of Included Studies

Risk of bias in in vitro studies was assessed using a modification of the SYRCLE tool. None of the studies provided sufficient data to allow us to assess the domains related to blinding of animal caretakers and researchers, random assessment of outcomes, and blinding of the outcome assessor. Some studies provided sufficient information to assess bias in other domains and were classified as having low risk of bias regarding the domains related to baseline characteristics (95.55%), allocation concealment (100%), incomplete outcome data (85.58%), selective reporting of outcomes (80.52%), and other sources of bias (75.00%). In contrast, 12.50% of the studies showed high risk of bias regarding random sequence generation, as they provided information on the dose used, and 12.50% did not provide data on the phytochemical composition of *X. americana* and were classified as having high risk of bias (Figure 2A).

Similarly, most domains of the SYRCLE tool for in vivo studies were classified as uncertain: random sequence generation (60.00%), allocation concealment (100.00%), random housing (65.00%), blinding of caregivers and researchers (90.00%), random outcome assessment (95.00%), blinding of the assessor of the results (78.00%), incomplete data (95.00%), and selective result report (90.00%) due to a lack of information in the articles. Some studies provided sufficient information and were classified as having a low risk of bias in respect of the random sequence generation (40.00%), baseline characteristics (100.00%), and other sources of bias (80.00%) domains. In contrast, 20.00% of the studies did not provide data on the phytochemical composition of *X. americana* and were classified as having a high risk of bias in the other bias domain (Figure 2B).

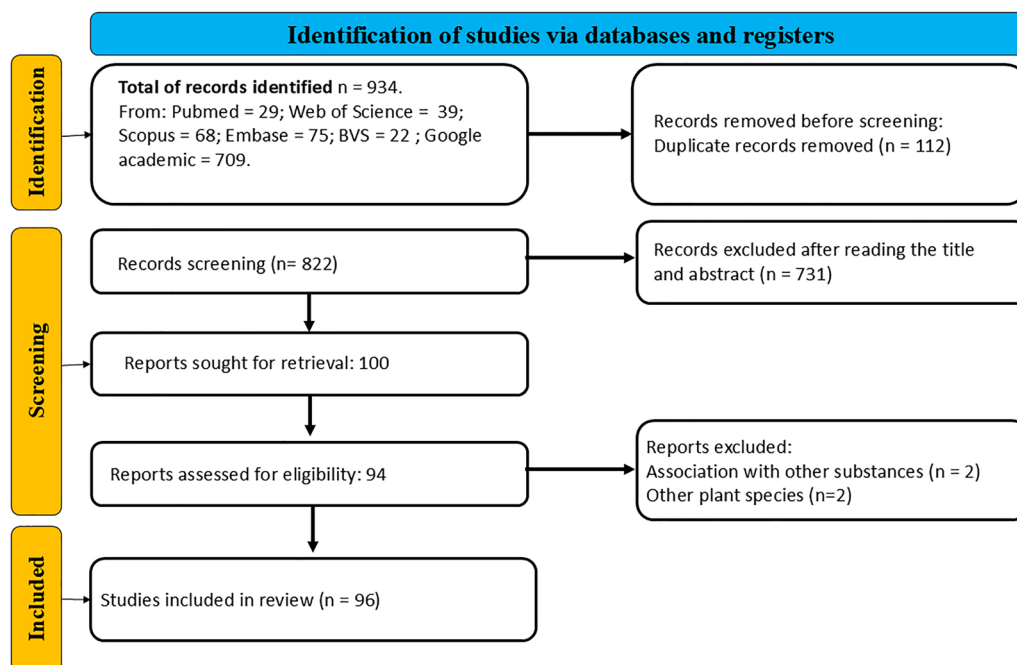


FIGURE 1 | Flowchart of included studies in the systematic review.

3.3 | Characterization and Botanical Distribution

X. americana L. is a member of the family Ximeniaceae, formerly Olacaceae. Ximeniaceae is a monophyletic group consisting of four genera, *Curupira* G. A. Black, *Douradora* Sleumer, *Malania* Chun and Lee, and *Ximenia* L (Nickrent et al. 2010). According to Maroyi (2016), the seeds of the genus *Ximenia* contain unusual glycerides in the form of ethanoic acids, which are cis-hexacos-17-enoic acid of C_{26} acid and cis-triacont-21-enoic acid of C_{30} acid. The genus *Ximenia* consists of 10 species, namely, *X. americana* L., *X. caffra* Sond., *X. coriacea* Engl., *X. glauca* (DeFillips) Bentouil, *X. parviflora* Benth., *X. perrieri* Cavaco & Kerauderen, *X. pubescens* Standl., *X. roigii* León, *X. horrida* Urb. & Ekman, and *X. intermedia* (Chodat & Hassl.) DeFilipps (Maroyi 2016) with tropical and subtropical distribution. This genus was first described by Linnaeus in 1753. The generic name *Ximenia* is a tribute to a Spanish priest Francisco Ximénez who wrote about the plants of Mexico in the 17th century and *americana* was another tribute to an Italian merchant Amerigo Vespucci (Hollsten 2012).

Botanical synonyms of *X. americana* L. include *Amyris arborescens* P. Browne, *Heymassoli inermis* Aubl., *Heymassoli spinosa* Aubl., *Persicaria odorata* Raf., *Ximenia aculeata* Crantz, *X. americana* fo. *inermis* (Aubl.) Engl., *X. americana* fo. *inermis* S. Moore, *X. americana* var. *ovata* DC., *X. arborescens* Tussac ex Walp., *X. fluminensis* M. Roem., *X. inermis* L., *X. montana* Macfad., *X. multiflora* Jacq., *X. oblonga* Lam. ex Hemsl., *X. spinosa* Salisb., and *X. verrucosa* M. Roem (das Chagas Dourado de Sousa 2015).

According to Hunde Feyssa et al. (2012) and Bussmann et al. (2020), *X. americana* is a semiclimbing shrub or small deciduous tree, heliophilous to semi-sciophilous, monoecious or dioecious, and up to 2–7 m tall. The trunk is inclined or tortuous, and

in most cases the trunk diameter does not exceed 10 cm in diameter at breast height (DBH); the wood is heavy, pink to yellowish, fragrant, gray to brownish, thick, irregularly divided, and flaky. The bark is dark brown to light gray and smooth to scaly. Its branches are reddish-purple with a waxy bloom, and the tree is usually armed with straight, sharp, slender spines that transform into brachyblasts (short branches). Sometimes there is a semiparasitic nature with haustoria in the roots. The leaves are simple, alternate, lanceolate to elliptical, 3–8 or 1.5–4 cm, variable thickness (semi-succulent to thin), obtuse or emarginate, with three to seven pairs of veins, discrete. The petioles are short, thin, up to 6 mm long, and canaliculate and have grayish-green, hairless, leathery, or thin flesh. When crushed, the young leaves smell like bitter almonds. The flowers are yellow-green, white, or pink, which develop in branched, dichlamydeous, tetramerous or pentamerous, androgynous or functionally unisexual, fragrant, 1.5–2 cm long inflorescences. Pedicel 8–12 mm long; calyx short; corolla with villous petals on the inner side; androecium with 6–10 stamens; superior ovary. Fruit globose to elliptical, two to three 1.8–2.2 cm, monospermous, with thin epicarp ranging from yellow to reddish at maturity, juicy mesocarp at this stage, and hard endocarp, generally beige in color. Seed globose to elliptical, yellowish or beige, oily, and much smaller than the fruit (see Figure 3).

X. americana is native to Australia and Asia, commonly known as yellow plum or sea lemon. However, it is a cosmopolitan plant found in tropical and subtropical regions of the world, with wild occurrence, and can be found in Africa, India and Southeast Asia, Pacific Islands, West Indies, New Zealand, Central America, and South America (Mevy et al. 2006; Hunde Feyssa et al. 2012). It is a noncultivated fruit tree and uncommon in nature. In the American continent, the southern limit of its distribution is the central region of Argentina, and it can be commonly found in Brazil spontaneously in the states of Para, Minas Gerais, Mato

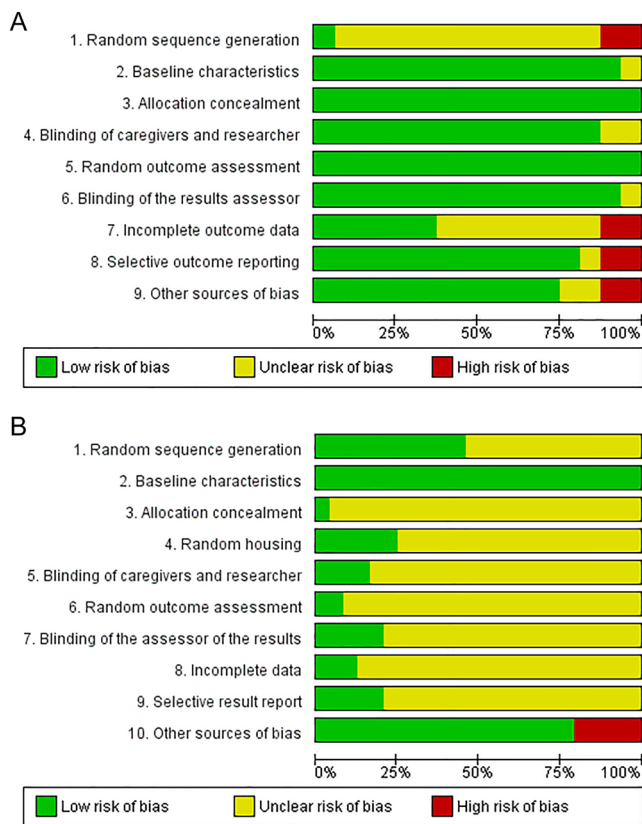


FIGURE 2 | Graph of risk of bias in included studies: in vitro studies (A) and in vivo studies (B).

Grosso, and several regions of the Northeast states such as Bahia, Rio Grande do Norte, and Ceara (Hunde Feyssa et al. 2012; da Silva et al. 2018, 2023; Bussmann et al. 2020) (see Figure 4).

It is a plant of diverse habitats, found mainly in semiarid scrubland, in many types of dry forest, open sandy forest, dry mountainous areas, coastal native forest, and along watercourses and on rocky slopes (Hunde Feyssa et al. 2012). In the state of Ceará, *X. americana* is part of the shrub-tree stratum of the Caatinga, figuring as one of the main species. In the dry season, when most Caatinga species lose their leaves, this plant stands out for having completely green leaves, which characterizes a drought-resistant plant (Hollsten 2012; Hunde Feyssa et al. 2012; Bussmann et al. 2020).

3.4 | Popular Use of *X. americana* for the Treatment of Inflammation

The bark, inner bark, fruits, leaves, roots, and seeds of the “wild plum” have several medicinal properties and are used in the treatment of different inflammatory diseases in several countries through infusion, maceration, decoction, or in combination with other substances. In traditional medicine, *X. americana* is also known by other popular names, such as “ameixa-do-mato,” “ababoni,” and “ameixa-do-brasil” (Bussmann et al. 2020).

Table 1 presents a summary of the traditional use of *X. americana* in the treatment of various inflammatory conditions. The plant



FIGURE 3 | *Ximenia americana* flowers, fruits, leaves, branches, and thorns. Source: Bekele-Tesemma (2007).

is used to combat different types of inflammation, both acute and common, such as edema and gingivitis, and chronic and complex, such as arthritis. The roots are frequently used in various countries to treat problems such as asthma, edema, fever, pain, inflammation, scarring, dysmenorrhea, vaginitis, hemorrhoids, and joint inflammation (James et al. 2008; Maikai et al. 2008; Maikai et al. 2010; Le et al. 2012; De Carvalho Nilo Bitu et al. 2015; Aliyu et al. 2022). In Northwestern Nigeria, the decoction of the roots of *X. americana* is applied externally in the treatment of conjunctivitis and edema (Aliyu et al. 2022). In Ethiopia, the stone of this plant is used by the Suri, with the oily substance being applied to skin cuts and after bone surgeries to prevent infections (Abbink 1995). The fruit is eaten raw to treat gastritis (Berihun and Molla 2017).

In Kenya, the leaves and roots are used to treat venereal diseases, gynecological pain, and toothache. The roots are chewed (Pakia and Cooke 2003). Kaluwa Kaingu et al. (2014) report that the roots are used for the treatment of diarrhea using the decoction method to treat the symptoms. The bark is boiled or mixed with milk to treat anemia and diarrhea in children (Chalo et al. 2016). According to Wanzala et al. (2016), the roots of *X. americana* are used in the form of decoction/infusion for the treatment of gonorrhea, hematuria, RA, edema, jaundice, menorrhagia, abscesses, syphilis, diarrhea, amoebic dysentery, measles, and pneumonia. The bark and stem bark are used in the form of a concoction for the treatment of cough, throat infection, amenorrhea, wound healing, and pain (Mailu et al. 2020).

According to Inngjerdingen et al. (2004), in Mali, the bark and roots are used topically for insect bites that cause boils, a curse (“Yaanga-kein”). The roots and leaves are the most commonly used parts, in decoction and powdered forms. The decoction is usually used for bathing and/or drinking. The powder is usually dispersed in water and used for bathing and/or drinking, or the

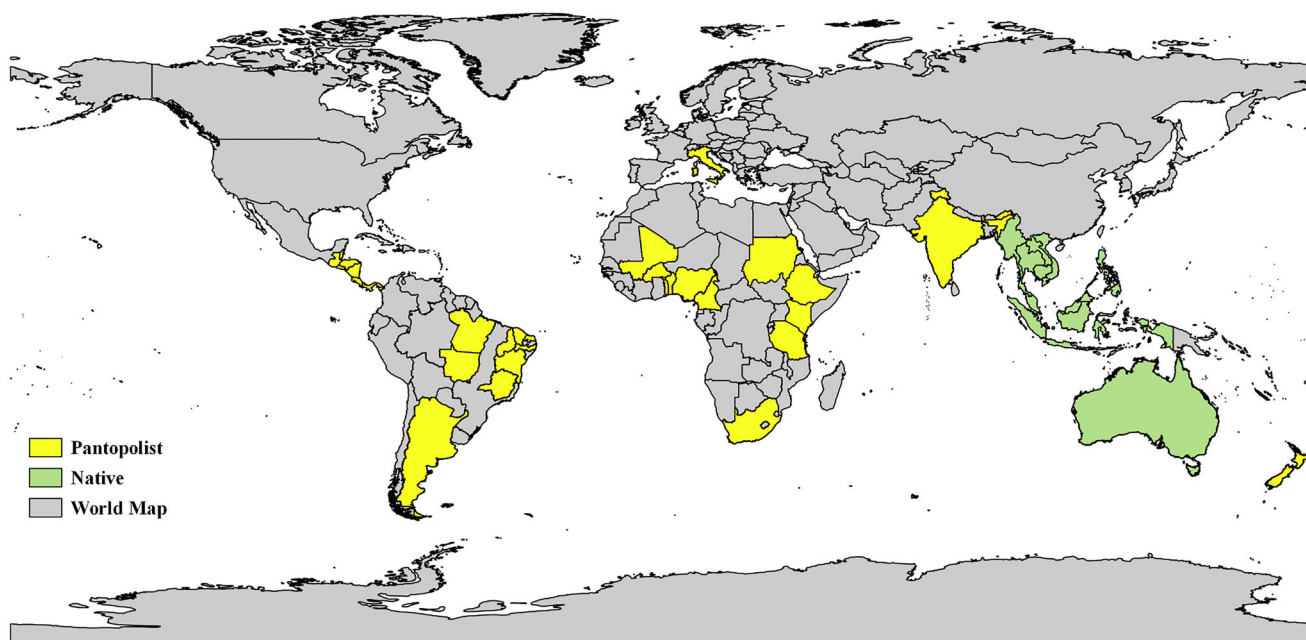


FIGURE 4 | Geographical distribution of *Ximenia americana*.

powder is thrown into a fire and the smoke is inhaled. The consensus of healers is less consistent for *X. americana*, and therefore it is more difficult to say which medical indication is the most important. Plum root is used in Nigeria for stomatitis and toothache. For swelling of the face, the powdered root is inhaled in Senegal in a mixture with *Maerua angolensis* (Capparaceae), and the root powder massaged into the gums is used in Ivory Coast and Burkina Faso for stomatitis and toothache (Grønhaug et al. 2008). The fruits, leaves, root, root-bark, stem, seeds, and stem bark are used in the form of decoction, powder, or maceration for the treatment of dysmenorrhea, *Candida* infection, vaginitis, toothache, backache, gastric ulcer, anemia (children), inflammation, throat infection, toothache, tonic, gingivitis, tonic (children), amenorrhea, gastric diseases, gastric pain, urinary tract infection, arthritis, conjunctivitis, cough, flu, internal wounds, sinusitis, tonic (children), and dermatitis (Le et al. 2012).

In Argentina the seeds are roasted and then decocted in 2 L of water. A cup of tea is drunk once a day until the dysentery symptoms disappear (Scarpa 2004). In Nigeria, the whole plant is used to treat symptoms of toothache and headache (Adamu et al. 2005). According to Umar and Babalola (2016), the leaves, roots, and bark are used in decoction/maceration form for the treatment of inflamed breast, toothache, bladder infection, and cystitis. Maceration, decoction, boiling, or a cold preparation mixture of the stem bark and leaves are used to treat typhoid fever (Abdulsalami et al. 2017). Jumare et al. (2022) reported that the bark and leaves are used for snakebite and ulcer treatment.

Tapsoba and Deschamps (2006) report that the leaves, roots, and bark of *X. americana* (Burkina Faso) are used in the form of decoction or inhalation to treat toothache, gingivitis, and wounds. In Brazil, the bark, stem bark, bast, roots, and fruits are used in the form of decoction, infusion, bottled, juice, lick, and topical use for the treatment of injuries, inflammation in general, and back pain

(de Albuquerque et al. 2007; de Oliveira et al. 2021; Júnior et al. 2011; Paulino et al. 2012; Souza et al. 2014; Ribeiro et al. 2014; De Carvalho Nilo Bitu et al. 2015; N. F. Da Silva et al. 2019; Vandesmet et al. 2020; de Oliveira et al. 2021).

In India, the roots are used in the form of decoction and powder of dried parts for the treatment of gum problems. The mode of use of these plants is in the form of gargling the decoction of the plant part(s), powder of the dried material, or toothbrush (Ganesan 2008). According to Reddy et al. (2010), the bark of the stem, stem, seed, and fruit are used for the treatment of diabetes, body pains, and gastric problems. In addition, Rama Krishna et al. (2014) reported that the leaves are used for the treatment of gastric problems. The stem bark is used for the treatment of venereal diseases, jaundice, diarrhea, febrifuge, astringent, wounds, laxative (Gritto et al. 2015), and RA (Mutyalu Naidu 2015).

The stem of *X. americana* is used for the treatment of rheumatic pain in Sudan (Doka and Yagi 2009). Urso et al. (2016) reported that the bark, leaves, and seeds are used in communities for snake and scorpion bites, body and hair care, burns and wounds, cough, food poisoning, joint pain, measles, otitis, stomach pain, and varicose veins. In Tanzania, the roots are used for dysmenorrhea, hormones, libido disorder, and irregular menstrual period (Hilonga et al. 2019), and its leaves and bark in the form of infusion are used for the treatment of worm infestation, diarrhea, abdominal pain and gastric ulcers, stomach pain in children, food, tonic, constipation, and back pain (Kingo and Maregesi 2020).

In South Africa, the roots and leaves are used in ground, decoction, or infusion form for the treatment of measles, jaundice, headaches, and as an antiseptic (Mudau et al. 2020), skin infections and inflamed eyes (Mahlo and Shikwambana 2020), and eye infections (Eiki et al. 2022). According to Abdoulaye et al. (2022), the roots, trunk bark, and leaves are used in Benin for the treatment of tooth decay and gingivitis (see Table 1).

TABLE 1 | Folk use of parts of *Ximenia americana* for the treatment of inflammatory conditions.

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
Abbink (1995)	Ethiopia	<i>Lomáy, orsu</i>	Plant stone	The stone from this plant is used by the Suri, with the oily substance being applied to cuts in the skin and after bone surgeries to prevent infections	Oil	Topical application
Pakia and Cooke (2003)	Kenya	<i>Mutundukula; Mdhoto; Mtundukula</i>	Roots and leaves	Veneral diseases, gynecological pain, and toothache	Not specified	Chewing the roots
Inngierdingen et al. (2004)	Mali	<i>Onombani (domno soo)</i>	Roots and barks	Insect sting leading to boils, a curse (“Yaanga-kein”)	Not specified	Topical application
Scarpa (2004)	Argentina	<i>Pata</i>	Seeds	Dysentery	A handful of the seeds is toasted. Then it is decocted in 2 L of water. A teacup is drunk once a day until symptoms disappear	Orally
Adamu et al. (2005)	Nigeria	<i>Tsa’ada</i>	Whole plant	Toothache and headache	Not specified	Not specified
Tapsoba and Deschamps (2006)	Burkina Faso	<i>Leenga</i>	Leaves, roots, and bark	Toothache, gingivitis, and sores	Decoction and inhalations	To treat toothache, the roots are boiled with red and white stones for inhalation. Some healers advise against gargling due to the risk of losing healthy teeth. Inhalations with fresh leaves and roots can be done

(Continues)

TABLE 1 | (Continued)

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
De Albuquerque et al. (2007)	Brazil	<i>Ameixa; ameixa de espinho</i>	Bark and bast	Injury, inflammations in general, back pain	Not specified	Not specified
Ganesan (2008)	India	<i>Chiru-illanthai</i>	Root	Gum trouble	Decoction and powder of dry parts	The mode of utilization of these plants is either in the form of gargle of the decoction of the plant part (s), powder of dried material or toothbrush
Grønhaug et al. (2008)	Mali	<i>Ntonkè</i>	Leaves, bark, and roots	Throat infection, ulcers, fever, diarrhea, stomatitis, jaundice, toothache, and dysmenorrhea	Decoction and preparation of a powder	Topical application, orally, sprayed, and associated with other medications

(Continues)

TABLE 1 | (Continued)

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
Doka and Yagi (2009)	Sudan	<i>Umm Medeka</i>	Stem	Rheumatic pains	Not specified	Smoke
Reddy et al. (2010)	India	<i>Nakkeri; nakkeri</i>	Stem bark, stem, seed, and fruit	Diabetes, body pain, and gastric problems	Not specified	Orally and topical application
Oliveira et al. (2010)	Brazil	<i>Ameixa</i>	Bark	Inflammation of the uterus and ovaries, healing, cleansing the uterus, cleansing the blood, abortion, anemia, ulcer, cancer, urinary tract infection, stomach problems, itching, wound, burn, diarrhea, gastritis, fracture	Decoction, infusion, bottled, juice, lick, and topical use	Orally and topical application
Ferreira-Júnior et al. (2011)	Brazil	<i>Ameixa-branca</i>	Barks	Pain in the uterus, headache	Not specified	Not specified
Paulino et al. (2012)	Brazil	<i>Ameixa</i>	Stem-bark	Anti-inflammatory and healing	Decoction and aroeira's water are very used as anti-inflammatory. Alone or mixed with stem bark of other species	Orally
Le et al. (2012)	Mali	<i>Onombani (donno soo); Ntonké</i>	Fruits, leaves, root, root bark, stem, seeds, and stem bark	Dysmenorrhea, <i>Candida</i> infection, vaginitis, toothache, back pain, gastric ulcer, anaemia (children), inflammation, throat infection, toothache, tonic, gingivitis, tonic (children), amenorrhea, gastric diseases, gastric pain,	Decoction, powder, and maceration	Not specified

(Continues)

TABLE 1 | (Continued)

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
Kaingu et al. (2014)	Kenya	<i>Muntuntuda; mtundukula; huda hudo</i>	Roots	urinary tract infection, arthritis, conjunctivitis, cough, flu, internal wounds, sinusitis, tonic (children), and dermatitis	Roots boiled in water and decoction	Taken orally half a glass for 5 days
Krishna et al. (2014)	India	<i>Nakkerā</i>	Leaves	Gastric trouble	Not specified	Two teaspoons of tender tips paste administered with one cup of milk
Souza et al. (2014)	Brazil	<i>Ameixa</i>	Bark and bast	Dermatitis, wound healing, flu, antipyretic, headache, diabetes, uterine inflammation, boils, ovary inflammation, and edema	Not specified	Not specified
Ribeiro et al. (2014)	Brazil	<i>Ameixa</i>	Stem-bark	Inflammation of the skin, healing, spine pain, wound, gynecological inflammation, inflammation of internal organs, throat inflammation, kidney pain, bone bruise, gallbladder, prostate problems, blow	Immersed in water, decoction, in “cachaça”*	Baths, oral ingestion, applied at the affected site
Bitu et al. (2015)	Brazil	<i>Ameixa</i>	Bark, roots, and fruit	Pain, obesity, inflammation, wound healing, diabetes, cough, hoarseness,	Infusion, sauce, pods, and mash	Not specified

(Continues)

TABLE 1 | (Continued)

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
Gritto et al. (2015)	India	<i>Chiru-illanthai</i>	Stem-bark	constipation, venereal disease, and osteoporosis	Not specified	Not specified
Aniel-Kumar et al. (2015)	India	<i>Kondanakkera</i>	Stem-bark	Veneral diseases, jaundice, diarrhea, febrifuge, astringent, sores, and laxative	Decoction	Stem bark decoction is taken orally once a day till cure
Duncan et al. (2016)	Kenya	<i>Olamai</i>	Bark	Anemia, stop infant diarrhea	Not specified	Boil bark drink liquid (cut bark into pieces), can mix with milk), used for children, mothers, and new babies
Urso et al. (2016)	Italia	<i>Omumpeke</i>	Bark, leaves, and seed	Snakes and scorpions bites, body and hair care, burns, and wounds, cough, food poisoning, joint pain, measles, otitis, stomachache, and varicose veins	Not specified	Baths, oral ingestion, applied at the affected site
Umar and Babalola (2016)	Nigeria	<i>Sourplum; Tsada; Dadun</i>	Leaves, root, and bark	Inflamed breast, toothache, bladder infection, and cystitis	Decoction and maceration	Grind and rub the paste on the breast

(Continues)

TABLE 1 | (Continued)

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
Wanzala et al. (2016)	Kenya	<i>Mutula; Kitula</i>	Root	Gonorrhoea, haematuria, rheumatoid arthritis, edema, jaundice, menorrhagia, abscesses, syphilis, diarrhea, amoebic dysentery, measles, and pneumonia	Decoction and infusion	Root decoction is drunk for diarrhea, haematuria, rheumatoid arthritis, edema, jaundice, menorrhagia, abscesses, and syphilis. Root infusion is used for diarrhea and amoebic dysentery. Leaf decoction is bathed with for measles. Root decoction is used as a remedy for pneumonia
Abdulsalami et al. (2017)	Nigeria	<i>Wild olive; Tsaada; Igo</i>	Stem-bark and leaves	Typhoid fever	Maceration, decoction, boiling or a cold concoction mixture	Not specified
Berihun and Molla (2017)	Ethiopia	<i>Meyo</i>	Fruit	Gastritis	Not specified	The fruit is eaten raw
Da Silva et al. (2019)	Brazil	<i>Ameixa</i>	Bark, weaves, fruit	Tune your blood, anemia, healing, diabetes, bellyache, headache, stomach ache, gastritis, inflammation of woman	Not specified	Not specified

(Continues)

TABLE 1 | (Continued)

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
Hilonga et al. (2019)	Tanzania	<i>Ngomai</i>	Root	Dysmenorrhoea, hormones, libido disorder, and irregular menstrual period	Not specified	Not specified
Kingo and Maregesi (2020)	Tanzania	<i>Busantu</i>	Leaves and bark	Treatment of worm's infestation, diarrhoea, abdominal pains, and gastric ulcers. Stomachache in kids, food, tonic, constipation, and backache	Infusion	Orally
Mailu et al. (2020)	Kenya	<i>Oleno</i>	Roots or stem-bark	Cough, throat infection, amenorrhea, wound healing, and pain	Concoction	Orally
Mudau et al. (2020)	South Africa	<i>Tshitanzwawanzwa</i>	Roots	Antiseptic, measles, jaundice, and headaches	Ground	Orally
Shikwambana and Mahlo (2020)	South Africa	<i>Ntsenghele</i>	Roots and leaves	Skin infections and inflamed eyes	Decoction	Orally and topically
Vandesmet et al. (2020)	Brazil	<i>Ameixa</i>	Sapwood	Inflammation, throat inflammation, numbness, dizziness, malaise, gas, body aches, fever, allergy, weight loss, and fever children	Not specified	Not specified
De Oliveira et al. (2021)	Brazil	<i>Ameixa</i>	Bark	Female inflammations, uterine bleeding, and healing	Juice smoothie, topical use (powder), and infusion	Orally and topically

(Continues)

TABLE 1 | (Continued)

References	Country	Local name/Vernacular name	Part used	Diseases treated	Preparation modes	Utilization modes
Abdoulaye et al. (2022)	Benin	<i>Kibovwe; so munoro</i>	Root, trunk bark, and leaves	Tooth decay and gingivitis	Infusion	Mouthwash
Eiki et al. (2022)	South Africa	<i>Tallow wood</i>	Leaves	Eye infections	Leaf infusion	Topical
Jumare et al. (2022)	Nigeria	<i>Tsada</i>	Bark and leaves	Snake bite, ulcer	Dry grind into powder and drink to Kunu (gruel), also apply the powder on the wound	Orally and topically

*Alcoholic distillate obtained by fermentation and distillation of the residual molasses from sugarcane; sugarcane spirit.

3.5 | Phytochemistry

3.5.1 | Terpenes

Terpenes are among the most common classes of natural products in plants (González-Coloma et al. 2011). These compounds present great structural diversity, resulting from the head-to-tail bonding of five-carbon units, known as isoprene units. The chemical structures formed by the union of two, three, four, five, six, and eight isoprene units are called mono-, sesqui-, di-, sester-, tri-, and tetraterpenes, respectively (Ben Salha et al. 2021). Among these classes, monoterpenes, triterpenoids, and sesquiterpenes are the main constituents of *X. americana*, which are highlighted in Table 2, with their structures illustrated in Figure 5.

3.5.2 | Flavonoids, Phenolic Acids, Alkaloid, and Polyphenol

Flavonoids are polyphenolic compounds of secondary metabolism, characterized by a basic structure composed of three rings (C6–C3–C6), which are called A, B, and C. These compounds are widely found in plants, both in free form (aglycones) and linked to sugars (glycosides) (Shen et al. 2022). Research indicates that flavonoids have several pharmacological effects, including anti-inflammatory and antioxidant activities (Chiorcea-Paquim 2023).

Phenolic acids are a class of organic acids that have phenolic groups directly linked to aromatic rings. These compounds are abundant in plants and are present in a wide variety of medicinal and edible species and are essential secondary metabolites. Currently, phenolic acids have several applications in sectors such as the food industry, pharmaceuticals, health supplements, and cosmetics. They are used as natural preservatives and antioxidants and play the role of therapeutic agents or adjuvants in the treatment of inflammatory conditions (Xie et al. 2024).

Alkaloids are basic organic compounds containing nitrogen and are found mainly in plants, being rare in fungi and animals. It is estimated that there are about 12,000 different types of alkaloids, which are mainly divided into organic amines, quinolines, isoquinolines, indoles, pyrrolidines, and piperidines. These compounds have a wide range of physiological and pharmacological activities, such as analgesic, anti-inflammatory, antioxidant, antitumor, and antibacterial effects, offering vast potential for the development of new drugs (Bai et al. 2021, Kawo, 2011).

Polyphenolic compounds constitute a significant group of bioactive substances. This family of compounds is characterized by the presence of multiple hydroxyl (OH) groups, with structures ranging from simple molecules to complex polymers. These compounds are naturally present in small amounts in a variety of foods, such as tea, grapes, vegetables, wine, cereals, coffee, and medicinal shrubs and plants such as eucalyptus and neem. Polyphenols are known for their antioxidant, anticarcinogenic, anti-inflammatory, and antimicrobial properties (Sridhar et al. 2021).

TABLE 2 | Chemical structure of terpenes from of *Ximenia americana*.

Number	Compounds	Molecular formula	Class	References
1	Sesquiterpene lactone	C ₁₅ H ₂₀ O ₄	Sesquiterpene	Abebe et al. (2024)
2	Furano-sesquiterpene	C ₁₇ H ₂₄ O ₅	Sesquiterpene	de Araújo et al. (2009)
3	Ximonican	C ₁₅ H ₂₂ O ₂	Sesquiterpene	de Araújo et al. (2009)
4	Linalool	C ₁₀ H ₁₈ O	Monoterpene	Mevy et al. (2006)
5	<i>trans</i> -Linalool oxide	C ₁₀ H ₁₈ O ₂	Monoterpene	Mevy et al. (2006)
6	<i>cis</i> -Linalool oxide	C ₁₁ H ₁₉ NO ₃	Monoterpene	Mevy et al. (2006)
7	Terpinen-4-ol	C ₁₀ H ₁₈ O	Monoterpene	Mevy et al. (2006)
8	α -Terpineol	C ₁₀ H ₁₈ O	Monoterpene	Mevy et al. (2006)
9	Geraniol	C ₁₀ H ₁₈ O	Monoterpene	Mevy et al. (2006)
10	β -Cyclocitral	C ₁₀ H ₁₆ O	Monoterpene	Mevy et al. (2006)
11	β -Ionone	C ₁₃ H ₂₀ O	Monoterpene	Mevy et al. (2006)
12	Epoxy- β -ionone	C ₁₃ H ₁₈ O ₂	Monoterpene	Mevy et al. (2006)
13	Caryophyllene oxide	C ₁₅ H ₂₄ O	Sesquiterpene	Mevy et al. (2006)
14	Humulene oxide II	C ₁₅ H ₂₄ O	Sesquiterpene	Mevy et al. (2006)
15	γ -Eudesmol	C ₁₅ H ₂₆ O	Sesquiterpene	Mevy et al. (2006)
16	β -Eudesmol	C ₁₅ H ₂₆ O	Sesquiterpene	Mevy et al. (2006)
17	α -Eudesmol	C ₁₅ H ₂₆ O	Sesquiterpene	Mevy et al. (2006)
18	Campherenone	C ₁₅ H ₂₄ O	Sesquiterpene	Mevy et al. (2006)
19	Abscisic acid	C ₁₅ H ₂₀ O ₄	Sesquiterpene	de Araújo et al. (2009), Olanrewaju et al. (2019)
20	Lupeol	C ₃₀ H ₅₀ O	Triterpenoid	Da Silva et al. (2016)
21	Betulinic acid	C ₃₀ H ₄₈ O ₃	Triterpenoid	de Araújo et al. (2009)
22	Oleanolic acid	C ₃₀ H ₄₈ O ₃	Triterpenoid	de Araújo et al. (2009)

To date, 18 types of flavonoids, three phenolic acids, one alkaloid, and one polyphenol have been identified in *X. americana*, which are highlighted in Table 3, with their structures represented in Figure 6.

3.5.3 | Compounds of Oils and Fats

Fatty acids are polyunsaturated and can be divided into two groups, namely, omega-3 (v-3) and omega-6 (v-6). Essential fatty acids contain a carboxyl group (–COOH) at one end, so they are among the group of compounds known as carboxylic acids. Essential fatty acids can also be classified according to the number of carbon atoms (C4–C36) and double bonds (Roncone et al. 2010). To date, 28 types of fatty acids have been identified in *X. americana*, followed by two sterols and one phytosterol that are highlighted in Table 4, with their structures represented in Figures 7 and 8.

3.5.4 | Other Components

In addition to the flavonoids, phenolic acids, alkaloids, polyphenols, terpenes, and oil and fat compounds mentioned above, another 105 compounds found in the species *X. americana*

are summarized in Table 5, with their structures illustrated in Figures 9–15.

3.6 | Antioxidant Activity

Reactive species are associated with the development of several diseases, including cancer, PD, diabetes, cardiovascular diseases, inflammation, and aging (Wang and Wang 2020). One of the well-recognized properties of plants is their ability to capture these reactive species, which contributes to their use in the treatment and prevention of several conditions (Pérez-Torres et al. 2021; Meleh Umar et al. 2023). Antioxidant agents are substances that neutralize reactive species, decreasing their ability to damage cells. These agents can act by enzymatic mechanisms, such as catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), or by nonenzymatic mechanisms, such as vitamins A and C and reduced glutathione (Kiran et al. 2023).

The 2,2-diphenyl-1-picrylhydrazyl (DPPH) test is the oldest indirect method for determining antioxidant activity that is based on the ability of the stable free radical 2,2-diphenyl-1-picrylhydrazyl to react with hydrogen donors, including phenols. The 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) test

TABLE 3 | Chemical structure of alkaloids, flavonoids, polyphenol, and phenolic acids from of *Ximenia americana*.

Number	Compounds	Molecular formula	Class	References
23	Gallic acid	C ₇ H ₆ O ₅	Phenolic acid	Lamien-Meda et al. (2008), Le et al. (2012), Aragão et al. (2018), da Silva et al. (2018), Olanrewaju et al. (2019), Pare et al. (2019), Bazezew et al. (2021, 2022), Pessoa et al. (2023, 2024)
24	Quercetin	C ₁₅ H ₁₀ O ₇	Flavonoids	Lamien-Meda et al. (2008), Le et al. (2012), Aragão et al. (2018), da Silva et al. (2018), Pare et al. (2019), Olanrewaju et al. (2019), Bazezew et al. (2021, 2022), Pessoa et al. (2023, 2024)
25	Yohimbine	C ₂₁ H ₂₆ N ₂ O ₃	Alkaloids	Aragão et al. (2018)
26	Procyanidin	C ₃₀ H ₂₆ O ₁₃	Flavonoids	Aragão et al. (2018), Barrera-Vázquez et al. (2023)
27	Catechin/Epicatechin	C ₁₅ H ₁₄ O ₆	Flavonoids	Aragão et al. (2018), Da Silva et al. (2018), Barrera-Vázquez et al. (2023), Pessoa et al. (2023)
28	Rutin	C ₂₇ H ₃₀ O ₁₆	Flavonoids	Da Silva et al. (2018), Barrera-Vázquez et al. (2023), Pessoa et al. (2024)
29	Isoquercetin	C ₂₁ H ₂₀ O ₁₂	Flavonoids	Barrera-Vázquez et al. (2023)
30	Avicularin	C ₂₀ H ₁₈ O ₁₁	Flavonoids	Le et al. (2012), Barrera-Vázquez et al. (2023)
31	Kaempferol 3- <i>o</i> -glucoside	C ₂₁ H ₂₀ O ₁₁	Flavonoids	Barrera-Vázquez et al. (2023)
32	Kaempferol 3-neohesperidoside	C ₂₇ H ₃₀ O ₁₅	Flavonoids	Barrera-Vázquez et al. (2023)
33	Quercetin pentoside	C ₁₆ H ₁₂ O ₇	Flavonoids	Barrera-Vázquez et al. (2023)
34	Quercetin rhamnoside	C ₂₁ H ₂₀ O ₁₁	Flavonoids	Barrera-Vázquez et al. (2023)
35	Kaempferol 3- <i>o</i> -arabinoside	C ₂₀ H ₁₈ O ₁₀	Flavonoids	Barrera-Vázquez et al. (2023)
36	Kaempferol pentoside	C ₂₀ H ₁₈ O ₁₀	Flavonoids	Barrera-Vázquez et al. (2023)
37	Chlorogenic acid	C ₁₆ H ₁₈ O ₉	Phenolic acid	Da Silva et al. (2018), Pessoa et al. (2023)
38	Caffeic acid	C ₉ H ₈ O ₄	Phenolic acid	Da Silva et al. (2018), Pessoa et al. (2023, 2024)
39	Ellagic acid	C ₁₄ H ₆ O ₈	Polyphenol	Da Silva et al. (2018), Pessoa et al. (2023)
40	Quercitrin	C ₂₁ H ₂₀ O ₁₁	Flavonoids	Le et al. (2012), Da Silva et al. (2018), Pessoa et al. (2023, 2024)
41	Kaempferol	C ₁₅ H ₁₀ O ₆	Flavonoids	Da Silva et al. (2018), Pessoa et al. (2023, 2024)
42	(–)Epicatechin	C ₁₅ H ₁₄ O ₆	Flavonoids	Dias et al. (2018), Sousa-Carvalho et al. (2020)
43	Quercetin-3- <i>O</i> -β-xylopyranoside	C ₂₀ H ₁₈ O ₁₁	Flavonoids	Le et al. (2012)
44	Quercetin-3- <i>O</i> -(6"-galloyl)-β-glucopyranoside	C ₂₈ H ₂₄ O ₁₆	Flavonoids	Le et al. (2012)
45	Kaempferol-3- <i>O</i> -(6"-galloyl)-β-glucopyranoside	C ₂₈ H ₂₄ O ₁₅	Flavonoids	Le et al. (2012)
46	(–)Catechin	C ₁₅ H ₁₄ O ₆	Flavonoids	Pessoa et al. (2024)

TABLE 4 | Chemical structure of fatty acids from of *Ximenia americana*.

Number	Compounds	Molecular formula	Class	References
47	9,12-Octadecadienoic acid (Z,Z)-	C ₁₈ H ₃₂ O ₂	Fatty acid	Da Silva et al. (2016)
48	<i>trans</i> -9-Octadecenoic acid	C ₁₈ H ₃₄ O ₂	Fatty acid	Da Silva et al. (2016)
49	Ethanedioic acid	C ₂ H ₂ O ₄	Dicarboxylic acid	Da Silva et al. (2016)
50	Nonadioic acid	C ₉ H ₁₆ O ₄	Fatty acid	Da Silva et al. (2016)
51	Hexadecanoic acid	C ₁₆ H ₃₂ O ₂	Fatty acid	Da Silva et al. (2016), Shettar et al. (2017)
52	<i>cis</i> -9-Octadecenoic acid	C ₁₈ H ₃₄ O ₂	Fatty acid	Da Silva et al. (2016)
53	<i>trans</i> -9-Octadecenoic acid	C ₁₈ H ₃₄ O ₂	Fatty acid	Da Silva et al. (2016)
54	Octadecanoic acid	C ₁₈ H ₃₆ O ₂	Fatty acid	Da Silva et al. (2016), Shettar et al. (2017), Dahiru et al. (2022)
55	Linolenic acid	C ₁₈ H ₃₀ O ₂	Fatty acid	Da Silva et al. (2016)
56	9,12-Octadecadiynoic acid	C ₁₈ H ₂₈ O ₂	Fatty acid	Da Silva et al. (2016), Shettar et al. (2017)
57	Tetracosanoic acid	C ₂₄ H ₄₈ O ₂	Fatty acid	Da Silva et al. (2016)
58	<i>cis</i> -15-Tetracosenoic acid	C ₂₄ H ₄₆ O ₂	Fatty acid	Da Silva et al. (2016)
59	β -Sitosterol	C ₂₉ H ₅₀ O	Phytosterol	Da Silva et al. (2016)
60	Methyl palmitate	C ₁₇ H ₃₄ O ₂	Fatty acid	Dahiru et al. (2022)
61	Oleic acid	C ₁₈ H ₃₄ O ₂	Fatty acid	Shettar et al. (2017), Dahiru et al. (2022)
62	Palmitic acid	C ₁₆ H ₃₂ O ₂	Fatty acid	Dahiru et al. (2022)
63	Stearic acid	C ₁₈ H ₃₆ O ₂	Fatty acid	Dahiru et al. (2022)
64	<i>cis</i> -Vaccenic acid	C ₁₈ H ₃₄ O ₂	Fatty acid	Dahiru et al. (2022)
65	<i>n</i> -Pentadecanoic acid	C ₁₅ H ₃₀ O ₂	Fatty acid	Dahiru et al. (2022)
66	Stigmasterol	C ₂₉ H ₄₈ O	Sterol	de Araújo et al. (2009), Dahiru et al. (2022)
67	3- <i>O</i> -(β -D-Glucopyranosyl) sitosterol	C ₃₅ H ₆₀ O ₆	Sterol	de Araújo et al. (2009)
68	Hexadecanoic acid, methyl ester	C ₁₇ H ₃₄ O ₂	Fatty acid	Bazezew et al. (2021)
69	9-Octadecenoic acid (Z)-, methyl ester	C ₁₉ H ₃₆ O ₂	Fatty acid	Bazezew et al. (2021)
70	9-Octadecenoic acid, methyl ester (E)	C ₁₉ H ₃₆ O ₂	Fatty acid	Bazezew et al. (2021)
71	Methyl stearate	C ₁₉ H ₃₈ O ₂	Fatty acid	Bazezew et al. (2021)
72	Methyl octadeca-9-yn-11- <i>trans</i> -enoic acid	C ₁₉ H ₃₂ O ₂	Fatty acid	Bazezew et al. (2021)
73	3-Olean-12-enyl palmitate	C ₃₃ H ₅₄ O ₂	Fatty acid	Fatope et al. (2000)
74	Linoleate	C ₁₈ H ₃₂ O ₂	Fatty acid	Freiberger et al. (1998)
75	α -Linolenate	C ₁₈ H ₂₉ O ₂	Fatty acid	Freiberger et al. (1998)
76	Non-decanoic acid	C ₁₉ H ₃₈ O ₂	Fatty acid	Shettar et al. (2017)
77	8,11,14-Eicosatrienoic acid	C ₂₀ H ₃₄ O ₂	Fatty acid	Shettar et al. (2017)

TABLE 5 | Chemical structure of other compounds extracted from *Ximenia americana*.

	Compounds	Molecular formula	References
78	1,2-Bis(trimethylsiloxy)ethane	$C_8H_{22}O_2Si_2$	Da Silva et al. (2016)
79	Disiloxane, hexamethyl-	$C_6H_{18}OSi_2$	Da Silva et al. (2016)
80	Glycerol	$C_3H_8O_3$	Da Silva et al. (2016)
81	β -D-Galactofuranoside	$C_6H_{12}O_6$	Da Silva et al. (2016)
82	D-Fructose	$C_6H_{12}O_6$	Da Silva et al. (2016)
83	Mannonic acid, lactone	$C_6H_{10}O_6$	Da Silva et al. (2016)
84	Sorbopyranose, L-	$C_6H_{12}O_6$	Da Silva et al. (2016)
85	D-Galactose	$C_6H_{12}O_6$	Da Silva et al. (2016)
86	Inositol, scyllo-	$C_6H_{12}O_6$	Da Silva et al. (2016)
87	α -D-Glucopyranose	$C_6H_{12}O_6$	Da Silva et al. (2016)
88	D-Mannitol	$C_6H_{14}O_6$	Da Silva et al. (2016)
89	D-Glucose	$C_6H_{12}O_6$	Da Silva et al. (2016)
90	Inositol, myo-	$C_6H_{12}O_6$	Da Silva et al. (2016)
91	D(+)-Sucrose	$C_{12}H_{22}O_{11}$	Da Silva et al. (2016)
92	14,17-Nor-3,21-dioxo- β -amyrin, 17,18-didehydro-3-dehydroxy-	$C_{28}H_{40}O_2$	Da Silva et al. (2016)
93	Silane, (9,19-cyclo-9 β -lanost-24-en-3 β -yloxy)trimethyl-	$C_{33}H_{58}OSi$	Da Silva et al. (2016)
94	Disiloxane, hexamethyl-	$C_6H_{18}OSi_2$	Da Silva et al. (2016)
95	Pentasiloxane, dodecamethyl-	$C_{12}H_{36}O_4Si_5$	Da Silva et al. (2016)
96	Glycerol	$C_3H_8O_3$	Da Silva et al. (2016)
97	<i>trans</i> -Octadec-11-en-9-ynoic acid, 8-trimethylsilyloxy-, methyl ester	$C_{22}H_{44}O_3Si$	Da Silva et al. (2016)
98	1-Monooleoylglycerol	$C_{21}H_{40}O_4$	Da Silva et al. (2016)
99	Catechol	$C_6H_6O_2$	Dahiru et al. (2022)
100	Pyrrolidine, 1-(1-butenyl)-	$C_8H_{15}N$	Dahiru et al. (2022)
101	2-Isopropoxyphenol	$C_9H_{12}O_2$	Dahiru et al. (2022)
102	3-methyl-1 <i>H</i> -pyridazin-6-one	$C_5H_6N_2O$	Dahiru et al. (2022)
103	Hydroquinone	$C_6H_6O_2$	Dahiru et al. (2022)
104	Tridecane	$C_{13}H_{28}$	Dahiru et al. (2022)
105	1,2,3-Benzenetriol	$C_6H_6O_3$	Dahiru et al. (2022)
106	1,2,4-Benzenetriol	$C_6H_6O_3$	Dahiru et al. (2022)
107	3-Methyl-1 <i>H</i> -pyrazole-5-carboxylic acid	$C_5H_6N_2O_2$	Dahiru et al. (2022)
108	Ascorbyl dipalmitate	$C_{38}H_{68}O_8$	Dahiru et al. (2022)
109	2,6-Heptanedione	$C_7H_{12}O_2$	Dahiru et al. (2022)
110	3,8-Dimethyldecane	$C_{12}H_{26}$	Dahiru et al. (2022)
111	1-Methylidene-2 (phenylsulfonyl)cyclopropane	$C_{12}H_{12}O_3S$	Dahiru et al. (2022)
112	3,4-Dimethylcyclohexanol	$C_8H_{16}O$	Dahiru et al. (2022)

(Continues)

TABLE 5 | (Continued)

	Compounds	Molecular formula	References
113	2-Dodecoxyethanol	C ₁₄ H ₃₀ O ₂	Dahiru et al. (2022)
114	5-Acetoxyethyl-2-furaldehyde	C ₈ H ₈ O ₄	Dahiru et al. (2022)
115	1,3,5-Benzenetriol	C ₆ H ₆ O ₃	Dahiru et al. (2022)
116	3-Methyl-1 <i>H</i> -pyrazole-5-carboxylic acid	C ₅ H ₆ N ₂ O ₂	Dahiru et al. (2022)
117	5-Butylnonane	C ₁₃ H ₂₈	Dahiru et al. (2022)
118	1,2,3-Benzenetriol	C ₆ H ₆ O ₃	Dahiru et al. (2022)
119	4,4-Dimethylcyclohex-2-en-1-ol	C ₈ H ₁₆ O	Dahiru et al. (2022)
120	Tetradec-13-enal	C ₁₄ H ₂₆ O	Dahiru et al. (2022)
121	9-Tetradecenal, (<i>Z</i>)-	C ₁₄ H ₂₆ O	Dahiru et al. (2022)
122	7,11-Hexadecadien-1-ol, acetate, (7 <i>Z</i> ,11 <i>Z</i>)-	C ₁₈ H ₃₂ O ₂	Dahiru et al. (2022)
121	(<i>E</i>)-Hexadec-11-enal	C ₁₆ H ₃₀ O	Dahiru et al. (2022)
124	14-Methyl- <i>Z</i> -8-hexa-decen-1-al	C ₁₇ H ₃₂ O	Dahiru et al. (2022)
125	(<i>Z</i>)-11-Hexadecenal	C ₁₆ H ₃₀ O	Dahiru et al. (2022)
126	Octadecanal	C ₁₈ H ₃₆ O	Dahiru et al. (2022)
127	3β-Hydroxycycloart-24(<i>E</i>)-ene-26-oic acid	C ₃₀ H ₄₈ O ₄	de Araújo et al. (2009)
128	(<i>Z</i>)-Hexen-3-ol	C ₆ H ₁₂ O	Mevy et al. (2006)
129	(<i>E</i>)-2-Hexenol	C ₆ H ₁₂ O	Mevy et al. (2006)
130	4-Methylpentanol	C ₆ H ₁₄ O	Mevy et al. (2006)
131	Benzaldehyde	C ₇ H ₆ O	Mevy et al. (2006)
132	6-Methylhept-6-en-2-one	C ₈ H ₁₄ O	Mevy et al. (2006)
133	(<i>E,E</i>)-2,4-Heptadienal	C ₇ H ₁₀ O	Mevy et al. (2006)
134	Isophorone	C ₉ H ₁₄ O	Mevy et al. (2006)
135	3,5-Octadien-2-one	C ₈ H ₁₂ O	Mevy et al. (2006)
136	Methyl benzoate	C ₈ H ₈ O ₂	Mevy et al. (2006)
137	6-Methylhepta-3,5-dien-2-one	C ₈ H ₁₂ O	Mevy et al. (2006)
138	3-Oxa-2,2,4-trimethyl-4-vinylcyclohexanone	C ₁₁ H ₁₆ O ₂	Mevy et al. (2006)
139	Allyl hexanoate	C ₉ H ₁₆ O ₂	Mevy et al. (2006)
140	Hydroxybenzyl cyanide	C ₈ H ₇ NO	Mevy et al. (2006)
141	(2 <i>E</i> ,4 <i>E</i>)-Nonadienal	C ₉ H ₁₄ O	Mevy et al. (2006)
142	Geranyl acetone	C ₁₃ H ₂₂ O	Mevy et al. (2006)
143	Dihydroactinidiolide	C ₁₁ H ₁₆ O ₂	Mevy et al. (2006)
144	Actinidiolide	C ₁₁ H ₁₄ O ₂	Mevy et al. (2006)
145	(<i>Z</i>)-3-Hexenyl benzoate	C ₁₃ H ₁₆ O ₂	Mevy et al. (2006)
146	Nonadecane	C ₁₉ H ₄₀	Bazew et al. (2021)
147	2-Chloro- <i>N</i> -(hydroxymethyl)acetamide	C ₃ H ₆ ClNO ₂	Bazew et al. (2021)

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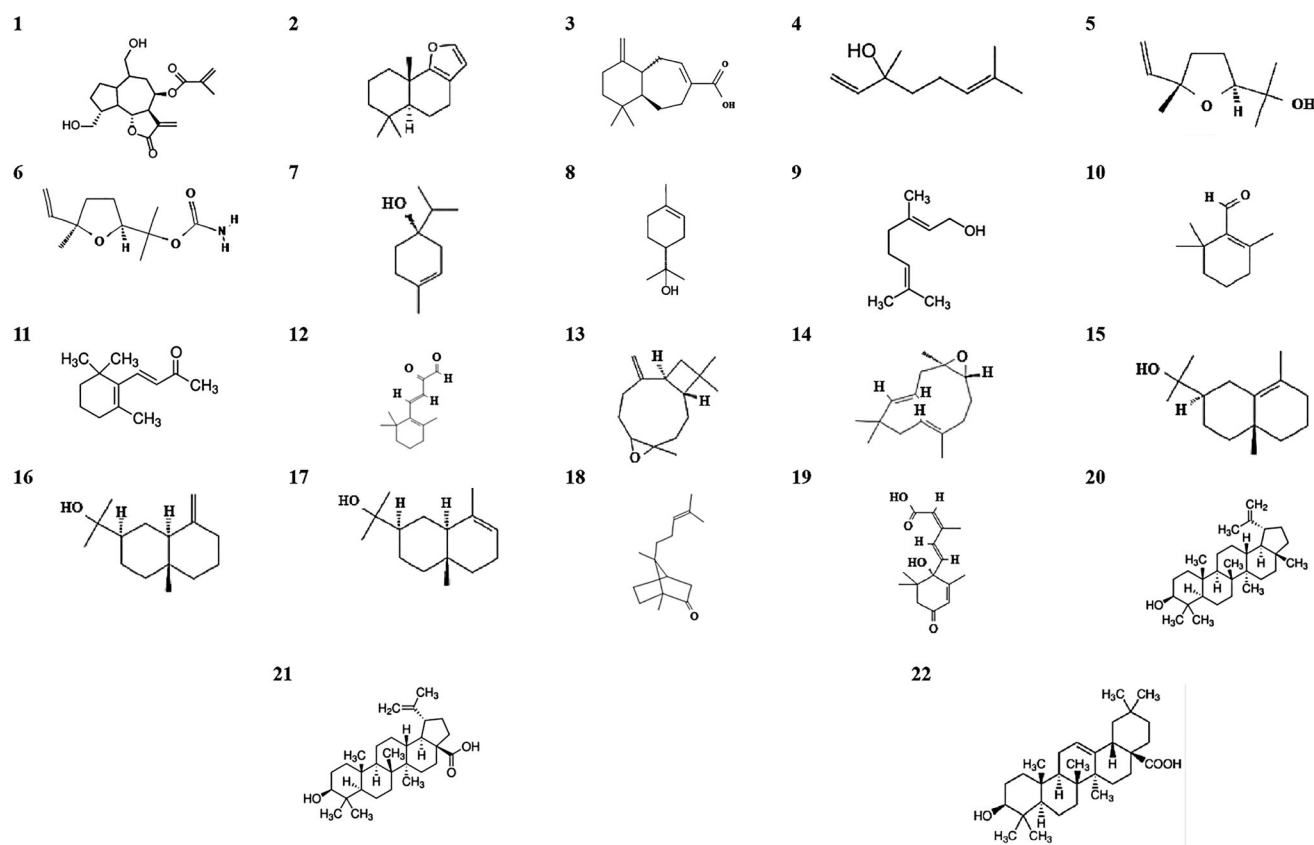


FIGURE 5 | Chemical structure of terpenes from *Ximenia americana* (1–22).

measures the relative antioxidant capacity of fruits to scavenge the ABTS⁺ radical cation produced by the oxidation of 2,2'-azinobis-3-ethylbenzothiazoline-6-sulfonate (Lamien-Meda et al. 2008).

Regarding the antioxidant effect of *X. americana*, in vitro experiments revealed that it acts by donating H⁺ ions, which bind to the DPPH radical, reducing it to hydrazyl, or by sequestering the ABTS⁺ radical, reducing ABTS. Its antioxidant capacity against these radicals was evaluated using the acetone and methanol extract of the fruits, presenting a percentage of inhibition (PI) of 4025.17 (mg AEAC/100 g of fw—methanol extract), 5015.25 (mg AEAC/100 g of fw—acetone extract) (DPPH), 310 (μmol AEAC/100 g of fw—methanol extract), and 342.5 (μmol AEAC/100 g of fw—acetone extract) (ABTS) (Lamien-Meda et al. 2008); aqueous extract—IC₅₀: >2500 μg/mL demonstrating no antioxidant effect at the dose tested (DPPH) (Kumar-Roiné et al. 2009); methanol extract—RC₅₀: 82.50 μg/mL (DPPH) (Maikai et al. 2010); ethanolic, aqueous, and butanoic extract—IC₅₀: 19.2, 10.8, and 20.5 μg/mL (DPPH) (Le et al. 2012); aqueous extract—IC₅₀: 68.04, 70.29, 76.12, 78.07, and 80.39 μg/mL and methanol extract—IC₅₀: 63.48, 64.94, 66.51, 70.32, and 73.96 μg/mL (DPPH) (Shettar et al. 2015); fruit fractions (green and ripe)—329.85 g/g, 344.68 g/g and seeds—373.80 g/g (DPPH) and fruit fractions (green and ripe)—348.96 μmol, 221.05 μmol and seeds—279.96 μmol (ABTS) (Darcio and Sarmiento 2015) (see Table 6).

Almeida et al. (2016) demonstrated the antioxidant effect of the extract and pulp of *X. americana* fruits, revealing

489.40 ± 108.04 g fruit/g (green), 1222.25 ± 87.94 g fruit/g (ripe) (DPPH), 198.77 ± 0.99 μmol (green), and 48.09 ± 0.39 μmol (ripe) (ABTS). The antioxidant activities measured in ethanolic and aqueous extracts obtained using ABTS and DPPH assays, it was observed that the lower concentration for the higher PI increases and varies. The PI has values ranging from 60.46% to 96.37% (ABTS) and 31.91% to 89.77% (DPPH) (Mariko et al. 2017). The ethanolic extract of the stem bark with a PI of more than 90% (100 μg/mL). The ethanolic extract of the stem wood presented a PI = 78.29% (250 μg/mL). At a concentration of 100 μg/mL, the ethanolic extracts of the stem bark, leaves, and stem wood presented a percentage of DPPH radical inhibition of 94.75%; 57.27%, and 42.83%, respectively. The ethyl acetate fractions of the stem bark and leaves at a concentration of 100 μg/mL reduced DPPH by 93.49% and 92.33%, respectively (Uchôa et al. 2016). According to Pare et al. (2019), the ethanolic extract demonstrated an antioxidant effect equal to 62.32% (DPPH).

The red flesh of *X. americana* fruit showed higher radical scavenging (97%) as compared to the yellow *X. americana* flesh (94%) at 200 μg/mL concentration. The red *X. americana* seed had higher scavenging activity (75%) than the yellow *X. americana* seed (68%). The IC₅₀ for the red pulp of *X. americana* was 99 μg/mL; for the yellow pulp of *X. americana*, it was (102 μg/mL). The red seed of *X. americana* also showed greater antioxidant capacity (IC₅₀ 1/4 147 μg/mL) compared to the yellow seed (IC₅₀ 1/4 154 μg/mL) without significant variations (DPPH) (Bazewez et al. 2021). It was noted that the quadratic effects of the liquid: solid ratio (X₃², 13.13%) and liquid: solid ratio (X₄², 21.70%), the linear effects of liquid: solid ratio (X₃, 17.14%) strongly influence the DPPH radical

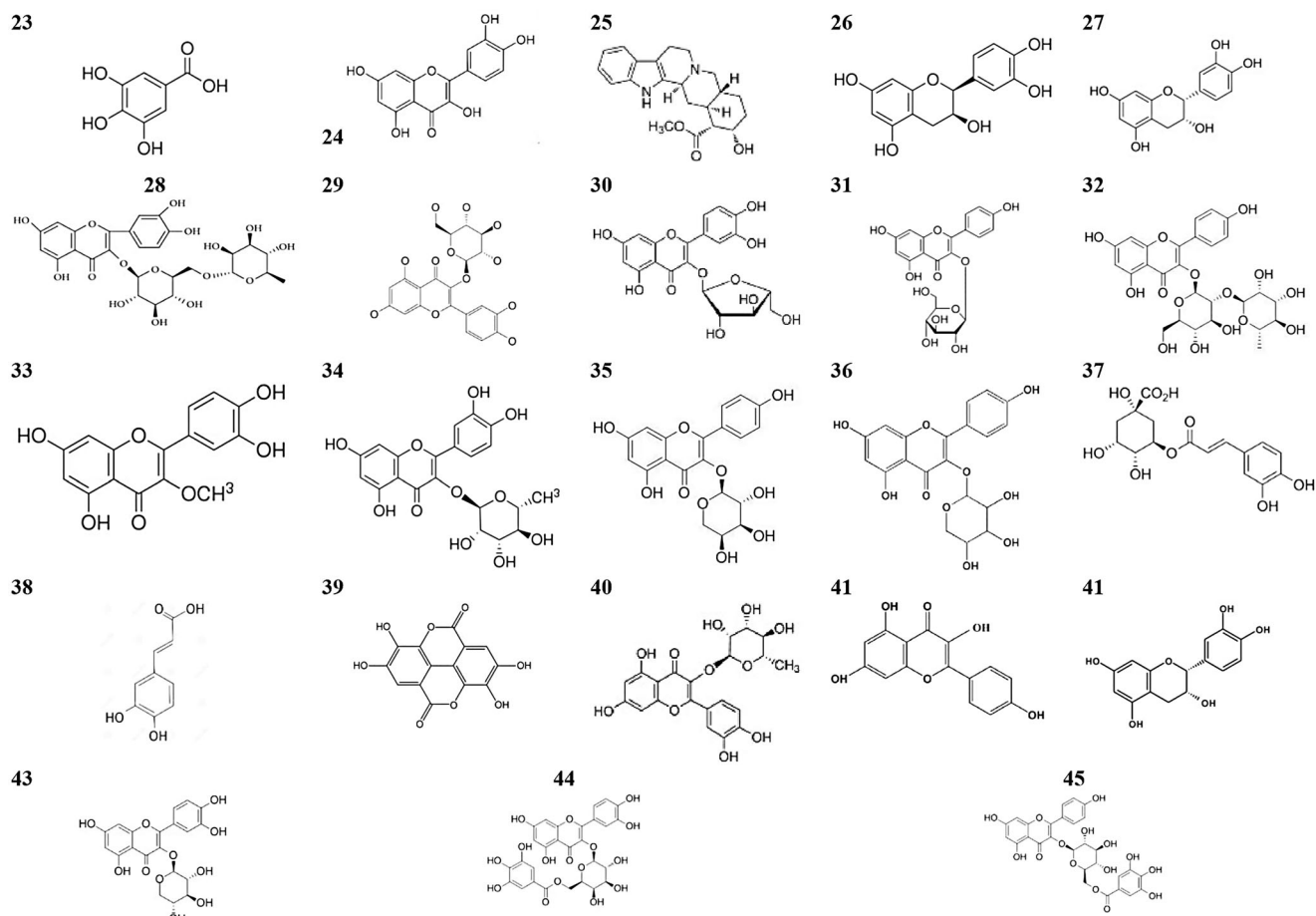


FIGURE 6 | Chemical structure of alkaloids, flavonoids, phenolic acid, and polyphenol from *Ximenia americana* (23–45).

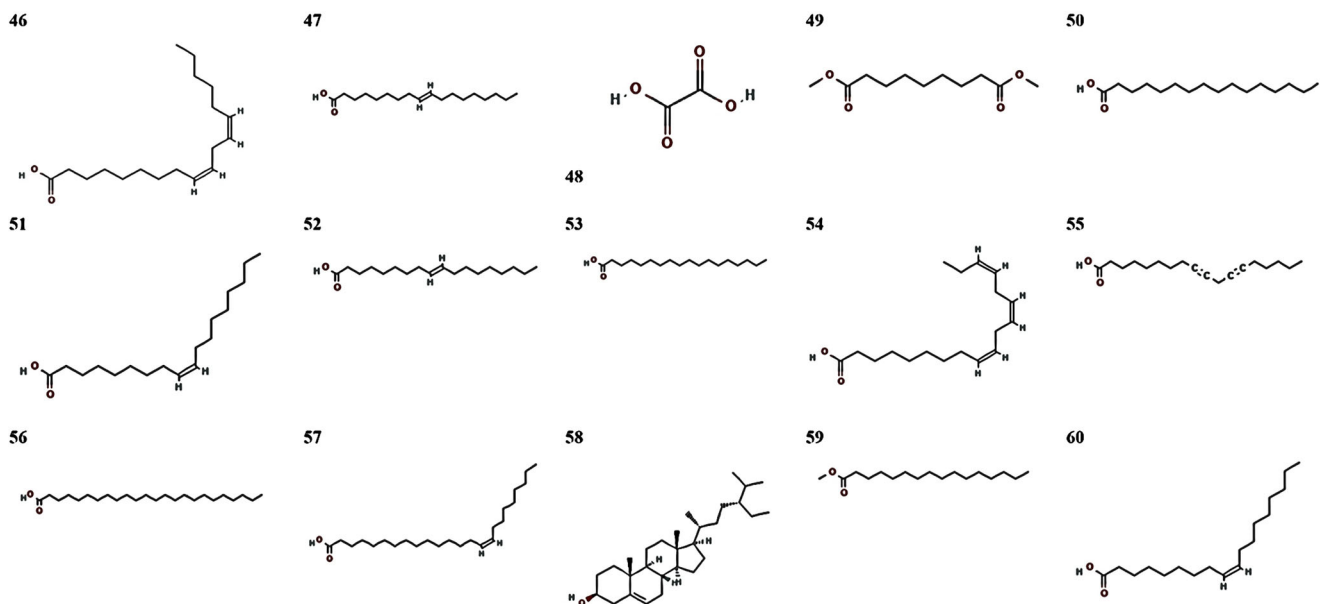


FIGURE 7 | Chemical structure of fatty acids from *Ximenia americana* (46–60).

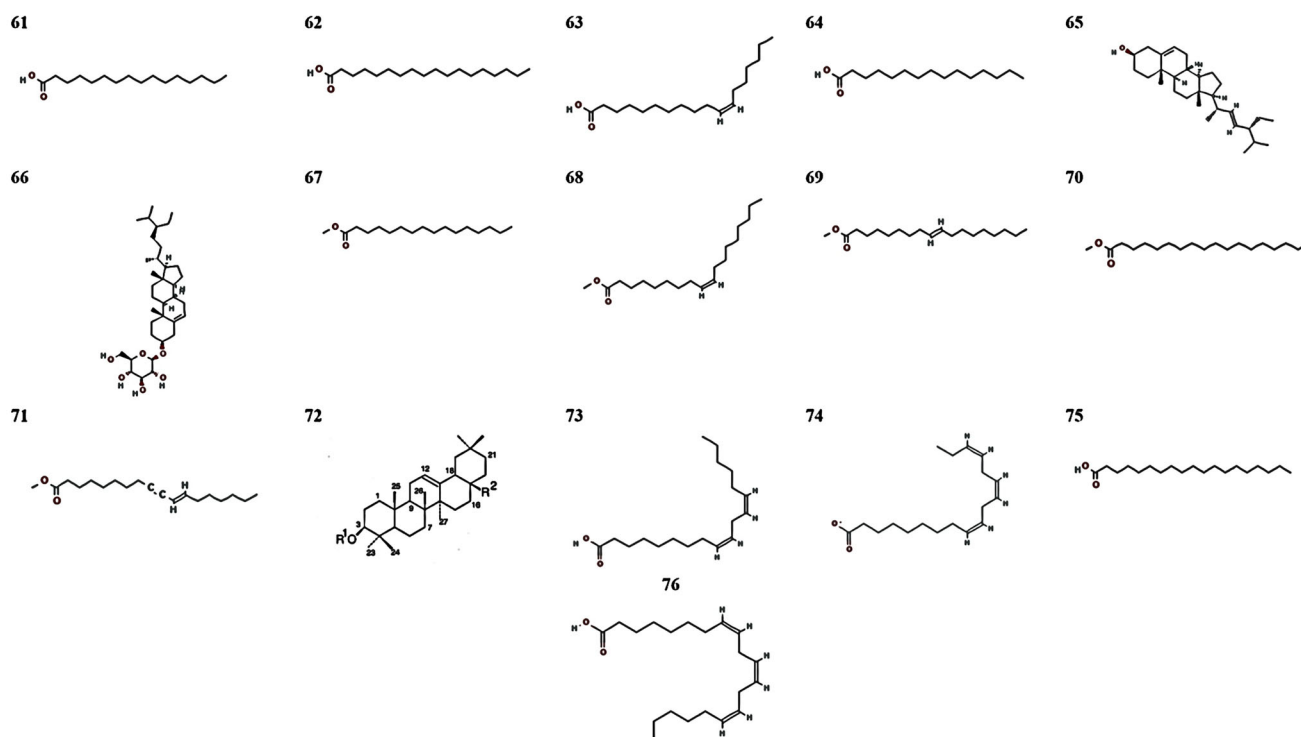


FIGURE 8 | Chemical structure of fatty acids from *Ximenia americana* (61–76).

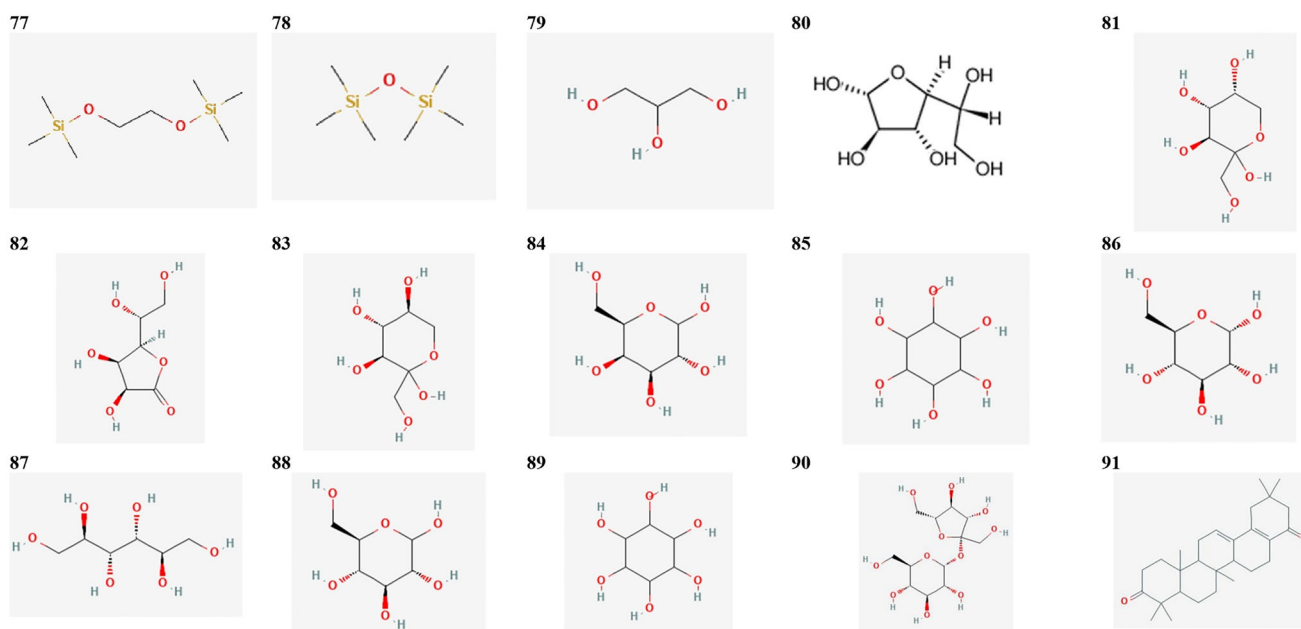


FIGURE 9 | Chemical structure of other compounds from *Ximenia americana* (77–91).

scavenging activity (Sidonie Beatrice et al. 2021). The antioxidant assay revealed that the antioxidant capacity varies according to the type of solvent used. When comparing the acetone extract with the methanolic extract, it was observed that the methanolic extract presented a higher inhibition rate, probably due to the higher concentration of phenolic compounds, flavonoids, and vitamin C. In both cases, the inhibition percentage increased as the concentration was increased (Bazezew et al. 2022).

Aqueous extracts, *n*-hexane, ethyl acetate, and methanol demonstrated IC_{50} : *n*-hexane—51.3 $\mu\text{g/mL}$; ethyl acetate—28.4 $\mu\text{g/mL}$; methanol—22.4 $\mu\text{g/mL}$, and water—67.6 $\mu\text{g/mL}$ (DPPH) (Meleh Umar et al. 2023). Delma et al. (2023) demonstrated that the aqueous ethanolic extract presented an IC_{50} : 5.01 $\mu\text{g/mL}$.

Another antioxidant mechanism described for *X. americana* was the reduction of nitric oxide (NO) production (Kumar-

TABLE 5 | (Continued)

	Compounds	Molecular formula	References
148	Octadecane, 2,6,10,14-tetramethyl	C ₂₂ H ₄₆	Bazezew et al. (2021)
149	Bis(2-ethylhexyl) phthalate	C ₂₄ H ₃₈ O ₄	Bazezew et al. (2021)
150	2-Aminobutanedioic acid	C ₂₄ H ₄₂ N ₆ O ₂₄	Freiberger et al. (1998)
151	Glutamate	C ₅ H ₇ CaNO ₄	Freiberger et al. (1998)
152	L-Serine	C ₃ H ₇ NO ₃	Freiberger et al. (1998)
153	Glycine	C ₂ H ₅ NO ₂	Freiberger et al. (1998)
154	Histidine	C ₆ H ₁₀ ClN ₃ O ₂	Freiberger et al. (1998)
155	Arginine	C ₆ H ₁₄ N ₄ O ₂	Freiberger et al. (1998)
156	Threonine	C ₄ H ₉ NO ₃	Freiberger et al. (1998)
157	Alanine	C ₃ H ₇ NO ₂	Freiberger et al. (1998)
158	Proline	C ₅ H ₉ NO ₂	Freiberger et al. (1998)
159	Tyrosine	C ₉ H ₁₁ NO ₃	Freiberger et al. (1998)
160	Valine	C ₅ H ₁₁ NO ₂	Freiberger et al. (1998)
161	Methionine	C ₅ H ₁₁ NO ₂ S	Freiberger et al. (1998)
162	Isoleucine	C ₆ H ₁₃ NO ₂	Freiberger et al. (1998)
163	Leucine	C ₆ H ₁₃ NO ₂	Freiberger et al. (1998)
164	Phenylalanine	C ₉ H ₁₁ NO ₂	Freiberger et al. (1998)
165	Lysine	C ₆ H ₁₄ N ₂ O ₂	Freiberger et al. (1998)
166	Cysteine	C ₃ H ₇ NO ₂ S	Freiberger et al. (1998)
167	Tryptophan	C ₁₁ H ₁₂ N ₂ O ₂	Freiberger et al. (1998)
168	3-Undecene	C ₁₁ H ₂₂	Shettar et al. (2017)
169	Tridecene	C ₁₃ H ₂₆	Shettar et al. (2017)
170	Trifluoroacetoxy tetradecene	C ₁₆ H ₂₁ F ₉ N ₄ O ₃	Shettar et al. (2017)
171	<i>trans</i> -11-Tetradecenylacetate	C ₁₆ H ₃₀ O ₂	Shettar et al. (2017)
172	Trichloroacetic acid-3-tridecyl-ester	C ₁₅ H ₂₇ Cl ₃ O ₂	Shettar et al. (2017)
173	1-Tetracosanol	C ₂₄ H ₅₀ O	Shettar et al. (2017)
174	Behenyl alcohol	C ₂₂ H ₄₆ O	Shettar et al. (2017)
175	1-Hexacosanol	C ₂₆ H ₅₄ O	Shettar et al. (2017)
176	Octadecanal	C ₁₈ H ₃₆ O	Shettar et al. (2017)
177	4-Piperidine propanoic acid	C ₈ H ₁₅ NO ₂	Shettar et al. (2017)
178	α -D-Mannofuranoside	C ₇ H ₁₄ O ₆	Shettar et al. (2017)
179	7-Tetradecanal	C ₁₄ H ₂₈ O	Shettar et al. (2017)
180	1-Ocytyn-3-ol-4-ethy	C ₁₀ H ₁₈ O	Shettar et al. (2017)
181	Uronic acid	C ₉ H ₁₀ N ₂ O ₇	Silva-Leite et al. (2017)
182	Gluconic acid	C ₆ H ₁₂ O ₇	Pessoa et al. (2024)
183	D-Gluconic acid	C ₆ H ₁₀ O ₇	Pessoa et al. (2024)

Roiné et al. 2009). It is known that, when generated in large quantities, this molecule can interact with the superoxide anion, forming peroxynitrite, a substance capable of nitrating several cellular components, such as proteins and DNA, impairing their functions (Iova et al. 2023; Wang et al. 2023).

Furthermore, *X. americana* has demonstrated the ability to reduce iron (ferric reducing/antioxidant power [FRAP]) and Mo-phosphate (PM) (Lamien-Meda et al. 2008; Shettar et al. 2015; Ballo et al. 2023; Delma et al. 2023). Under oxidative stress, Fe³⁺ ions can react with superoxide ions, generating

TABLE 6 | General characteristics of the studies in vitro related to the antioxidant properties of *Ximenia americana* included in this review.

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Lamien-Meda et al. (2008), Burkina Faso	DPPH FRAP ABTS	Fruit Methanol extract Acethone extract	Extracts: 100 g of fruit DPPH: mg AEAC/100 g of fw FRAP: mmol AEAC/100 g of fw ABTS: Ascorbic acid: no related	DPPH NC: no related PC: ascorbic acid FRAP NC: no related PC: ascorbic acid ABTS NC: no related PC: ascorbic acid	DPPH Methanol extract: 4025.17 (mg AEAC/100 g of fw) Acethone extract: 5015.25 (mg AEAC/100 g of fw) Ascorbic acid: $R^2 = 0.9997$ FRAP Methanol extract: 13.20 (mmol AEAC/100 g of fw) Acethone extract: 17.57 (mmol AEAC/100 g of fw) Ascorbic acid: $R^2 = 0.9999$ ABTS Methanol extract: 310 (μ mol AEAC/100 g of fw) Acethone extract: 342.5 (μ mol AEAC/100 g of fw) Ascorbic acid: $R^2 = 0.9990$	The study reveals that <i>X. americana</i> fruits can be used as potential antioxidants and states that the strong antioxidant capabilities of these fruit extracts were due to their high phenolic contents
Kumar-Roiné et al. (2009), France	DPPH	Roots Aqueous extract	Extract: 0.025, 0.025, 0.25, 2.5 g/L DPPH: 0.3 mM	DPPH NC: no related PC: no related	DPPH IC50: >2.500 μ g/mL	The aqueous extract of <i>X. americana</i> bark did not show significant antioxidant activity

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Maikai et al. (2010), Nigeria	DPPH	Stem-bark Methanol extract, flavonoid portion, and saponnin portion	Extract: 20, 40, 60, 80, 100, 200, and 500 µg/mL DPPH: 1 mL of 0.002% Ascorbic acid: 1–100 µg/mL	DPPH NC: no related Naive: DPPH PC: ascorbic acid	DPPH Methanol extract: 82.50 ± 3.60 µg/mL Flavonoid portion: 8.20 ± 1.10 µg/mL Saponnin portion: 148.70 ± 4.35 µg/mL Ascorbic acid: 10.60 ± 2.20 µg/mL	The study reveals that <i>X. americana</i> could be used as a potential antioxidant
Le et al. (2012), Mali	DPPH Xanthine oxidase	Leaves Ethanol, aqueous, and butanol extract	Extracts: no related DPPH: no related Xanthine oxidase: no related	DPPH NC: water PC: quercetin Xanthine oxidase NC: water PC: quercetin	DPPH Ethanol extract: 19.2 ± 0.8 µg/mL Aqueous extract: 10.8 ± 0.3 µg/mL Butanol extract: 20.5 ± 0.6 µg/mL Xanthine oxidase Ethanol extract: 19.6 ± 2.0 µg/mL Aqueous extract: 16.1 ± 1.2 µg/mL Butanol extract: >83 µg/mL	This study showed the content of high amounts of phenolic compounds that contribute to the antioxidant effects of <i>X.</i> <i>americana</i> leaves
Shettar et al. (2015), India	DPPH FRAP PM	Leaves Aqueous extract Methanol extract	Extracts: 100, 200, 300, 400, and 500 µL DPPH: 100 µL of a DPPH radical solution in ethanol (60 µmol/L) FRAP: 2.5 mL of trichloroacetic acid and 0.5 mL of ferric chloride PM: 1 mL molybdate Ascorbic acid: 100, 200, 300, 400, and 500 µL	DPPH NC: no related PC: ascorbic acid FRAP NC: no related PC: ascorbic acid PM NC: no related PC: ascorbic acid	DPPH Aqueous extract: 68.04% ± 0.35%, 70.29% ± 0.34%, 76.12% ± 0.35%, 78.07% ± 0.26%, and 80.39% ± 0.34% Methanol extract: 63.48% ± 0.28%, 64.94% ± 0.28%, 66.51% ± 0.40%, 70.32% ± 0.51%, and	The results confirm that the aqueous extract of <i>X. americana</i> exhibits high antioxidant activity

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Sarmiento et al. (2015), Brazil	DPPH ABTS	Fruits (green and mature) and seeds Fractions	Extract: pulp DPPH: A methanol solution containing 0.06 mM DPPH was prepared and aliquots of 100 µL ABTS: ABTS stock solution 7 with 140 mM of potassium persulfate	DPPH NC: no related PC: no related ABTS NC: no related PC: no related	73.96% ± 0.23% Ascorbic acid: 69.06% ± 0.30%, 76.16% ± 0.29%, 78.44% ± 0.23%, 80.69% ± 0.23%, and 83.87% ± 0.46% FRAP	The edible fraction (pulp + peel) of the X. <i>americana</i> fruit, the edible part of the green fruit and the seeds of the fruits have high antioxidant activity related to their chemical composition
					In the results obtained, aqueous extract showed higher activity than the methanol extract which was comparable to standard ascorbic acid PM	
					Aqueous extract showed the highest activity among methanol extract and standard ascorbic acid	
					Seeds: 373.80 g/g Fruit green: 329.85 g/g Fruit mature: 344.68 g/g ABTS Seeds: 279.96 µmol Trolox/g Fruit green: 348.96 µmol Trolox/g Fruit mature: 221.05 µmol Trolox/g	

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Almeida et al. (2016), Brazil	DPPH ABTS Antioxidant enzymes: Ascorbate peroxidase Catalase Superoxidase dismutase	Fruit (green and mature) Extract: pulp and skin	Extract: concentration varies according to the assay. For DPPH 100 μ L and ABTS 10 μ L DPPH: 3.6 mL (0.06 mM in methanol) ABTS: 3 mL (7 mM with 140 mM of potassium persulfate) Ascorbate peroxidase: mol of ascorbate is required for a reduction of 1 mol of hydrogen peroxide (H ₂ O ₂) Catalase: One unit of CAT activity (UA) was defined as the amount of enzyme required to decompose H ₂ O ₂ Superoxide dismutase: no related	DPPH NC: no related PC: no related ABTS NC: no related PC: no related Ascorbate peroxidase NC: no related PC: no related Catalase NC: no related PC: no related Superoxidase dismutase NC: no related PC: no related	DPPH Green: 489.40 $\pm$ 108.04 g fruit/g Mature: 1222.25 $\pm$ 87.94 g fruit/g ABTS Green: 198.77 $\pm$ 0.99 μ mol Trolox/g Mature: 48.09 $\pm$ 0.39 μ mol Trolox/g Ascorbate peroxidase Pulp green: 0.207 $\pm$ 0.09 μ mol H ₂ O ₂ /mg protein/min Pulp mature: 0.069 $\pm$ 0.01 μ mol H ₂ O ₂ /mg protein/min Skin green: 0.139 $\pm$ 0.03 μ mol H ₂ O ₂ /mg protein/min Skin mature: 0.118 $\pm$ 0.02 μ mol H ₂ O ₂ /mg protein/min CAT Pulp green: 159.85 $\pm$ 1.03 μ mol H ₂ O ₂ /mg protein/min Pulp mature: 58.27 $\pm$ 0.51 μ mol H ₂ O ₂ /mg protein/min Skin green: 67.55 $\pm$ 0.51 μ mol	The results indicate that the fruits may be a promising source of antioxidants, with possible applications in pharmacology, medicine and/or as a food to combat cellular oxidation in the human body caused by free radicals. Although this study provides relevant data and information on the nutritional properties of the fruits of <i>X. americana</i> , further investigation is needed in other areas of research

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Mariko et al. (2017), Mali	DPPH ABTS	Leaves Ethanollic and aqueous extracts	Extracts: 2, 3, 4, and 5 µg/mL DPPH: 3.2 mL (4 mg DPPH with 100 mL of ethanol) ABTS: 2 mL (38.4 mg of ABTS and 6.75 mg potassium persulfate each with 2.5 mL of distillated water) Ascorbic acid: 2, 3, 4, and 5 µg/mL	DPPH NC: no related PC: ascorbic acid ABTS NC: no related PC: ascorbic acid	H ₂ O ₂ /mg protein/min Skin mature: 51.57 ± 3.09 µmol H ₂ O ₂ /mg protein/min SOD	The study reveals that <i>X. americana</i> could be used as a potential antioxidant
					Pulp green: 731.61 ± 1.51 UAE/mg protein Pulp mature:	
					586.50 ± 6.04 UAE/mg protein	
					Skin green:	
					618.81 ± 9.28 UAE/mg protein	
					Skin mature:	
					551.51 ± 11.6 UAE/mg protein	
					Antioxidant activities measured in ethanolic and aqueous extracts obtained using ABTS and DPPH assays were measured three times to test the reproducibility of the assays. In general, it is observed that the lowest concentration to the highest percentage of inhibition increase and varies. Percent inhibitions have values ranging from 60.46% to 96.37% (ABTS); 31.91% to 89.77% (DPPH test)	

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Uchôa et al. (2016), Brazil	DPPH	Stem-bark, stem wood, and leaves Ethanol extracts and fractions (leaves and stem-bark)	Extracts: 25, 50, 100, 150, 200, and 250 µg/mL Rutin: 25, 50, 100, 150, 200, and 250 µg/mL Fractions stem-bark and leaves: 100 µg/mL	DPPH NC: no related PC: rutin	with the standard and the extracts tested. The inhibitory activity of each extract is greater with ABTS than DPPH. Absorbance is inversely proportional to the percent inhibition The ethanolic extract of the stem bark was the most effective in scavenging the DPPH radical, with a PI of over 90% (100 µg/mL). The ethanolic extract of the stem wood showed a PI = 78.29% (250 µg/mL). At concentration of 100 µg/mL, the ethanolic extracts of the stem bark, leaves, and stem wood showed a percentage of DPPH radical inhibition of 94.75 ± 0.27, 57.27 ± 4.20, and 42.83 ± 2.43, respectively. The ethyl acetate fractions of the stem bark and leaves at a concentration of 100 µg/mL reduced DPPH by 93.49% ± 2.85% and 92.33% ± 3.12%, respectively	The results indicate that <i>X. americana</i> extracts, ethyl acetate fractions from the stem bark and leaves, present high antioxidant activity related to their chemical composition

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Pare et al. (2019), Burkina Faso	DPPH FRAP	Leaves Ethanol extract	Extract: 1 mg/mL DPPH: 20 mg/L (in methanol) FRAP: 0.1% (25 µL) Gallic acid: no related Quercetin: no related	DPPH NC: methanol and DPPH PC: gallic acid FRAP NC: no related PC: ascorbic acid	DPPH 62.32% ± 0.17% FRAP 3.45 ± 0.97 mmol EAA/10 g	The extract from the leaves of <i>X. americana</i> has good antioxidant activity
Togbossi et al. (2020), Togo	TAC Metal chelating assay APPH	Stem-bark Hydro-alcoholic extract	Extract for TAC: 1 mg/mL Extract for metal chelating assay: 50–250 µg/mL Extract for AAPH: 100–500 µg/mL EDTA: 50–250 µg/mL APPH: no related Ascorbic acid: 0.3 mg/mL and 50–250 µg/mL	TAC NC: no related PC: ascorbic acid Metal chelating assay NC: no related PC: EDTA AAPH NC: no related PC: ascorbic acid	TAC 303.081 ± 4.946 mg equivalent of ascorbic acid/g of extract Metal chelating assay Extract and metals chelate by EDTA in a concentration- dependent manner. IC ₅₀ analysis indicates that the chelate capacity of the extract is superior to that of EDTA AAPH It was inhibited in the presence of hydroalcoholic extract of the stem bark of <i>X. americana</i> and in a manner dependent on the concentration of ascorbic acid	The in vitro evaluation of antioxidant activity showed that the hydroalcoholic extract of the stem bark of <i>X. americana</i> has a total antioxidant capacity and it was found that the extract inhibits hemolysis and chelates metals in a concentration-dependent manner

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Bazezew et al. (2021), Ethiopia	DPPH	Fruit flesh (includes exocarp and mesocarp) and seed Raw extracts	Extracts: 20, 40, 80, 120, 160, and 200 µg/mL Ascorbic acid: 20, 40, 80, 120, 160, and 200 µg/mL	DPPH NC: no related PC: ascorbic acid	The red flesh of <i>X. americana</i> fruit showed higher radical scavenging (97%) as compared to the yellow <i>X. americana</i> flesh (94%) at 200 µg/mL concentration. The red <i>X. americana</i> seed had higher scavenging activity (75%) than the yellow <i>X. americana</i> seed (68%). The IC ₅₀ for the red pulp of <i>X. americana</i> was 99 µg/mL, for the yellow pulp of <i>X. americana</i> it was (102 µg/mL). The red seed of <i>X. americana</i> also showed greater antioxidant capacity (IC ₅₀ ¼ 147 µg/mL) compared to the yellow seed (IC ₅₀ ¼ 154 µg/mL) without significant variations	Therefore, the fruit and seeds of <i>X. americana</i> can be applied for value addition in the food processing and pharmaceutical industries due to their high free radical scavenging activities as they demonstrate high antioxidant activity
Sidonie Beatrice et al. (2021), Cameroon	DPPH	Roots Hydro-alcoholic extract	Extract: no related DPPH: 100 µM	DPPH NC: no related PC: no related	It was noted that the quadratic effects of the liquid:solid ratio (X ₃ ² , 13.13%) and liquid:solid ratio (X ₄ ² , 21.70%), the linear effects of liquid:solid ratio (X ₃ , 17.14%) strongly influence the DPPH	<i>X. americana</i> extract has high antioxidant activity. The obtained extracts might be used as natural bioactive compounds in several industrial applications

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Bazezew et al. (2022), Ethiopia	DPPH	Seeds Extract acetone and methanol of mucilage	Extract: 0.01, 0.1, 1.0, 2.0, and 5 mg/mL Ascorbic acid: 0.01, 0.1, 1.0, 2.0, and 5 mg/mL DPPH: 1 mM	DPPH NC: methanol and PC: ascorbic acid	$1.6156X_3X_4 - 2.3309X_1^2 - 2.9077X_2^2 - 6.1462X_3^2 - 10.1551X_4^2$ The antioxidant assay indicated that the antioxidant capacity varies according to the type of solvent used. When compared to the acetone extract, the methanolic extract showed a higher inhibition rate, possibly due to the higher concentration of phenolic compounds, flavonoids, and vitamin	radical scavenging activity. Thus, attention must also be paid not only on main effects but also on quadratic factors. The equation of the model for the response, including the interaction and quadratic terms of each controlled factor were: % DPPH = 84.0963 + 2.3848X₁ + 1.5669X₂ + 5.7673X₃ - 8.0214X₄ + 0.72562X₁X₂ - 0.5756X₁X₃ + 2.0994X₁X₄ - 1.7494X₂X₃ + 0.7431X₂X₄ - 1.6156X₃X₄ - 2.3309X₁² - 2.9077X₂² - 6.1462X₃² - 10.1551X₄² X. americana extracts demonstrate high antioxidant activity

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Meleh Umar et al. (2023), Nigeria	DPPH	Stem-bark <i>n</i> -Hexane, ethyl acetate, methanol, and water extracts	Extracts: 10, 25, 50, 100, 125, 250, 300, and 500 µg/mL DPPH: 0.004% Ascorbic acid: 10, 25, 50, 100, 125, 250, 300, and 500 µg/mL	DPPH NC: no related PC: ascorbic acid	C in the methanolic extract. In both cases, the inhibition percentage increased as the concentration was increased <i>n</i> -Hexane PI (µg/mL): 10—11.6%; 25—41.3%; 50—56.9%; 100—71.3%; 125—80.4%; 250—83.3%; 300—85.8%, and 500—85.8% Ethyl acetate PI (µg/mL): 10—26.7%; 25—55.9%; 50—70.2%; 100—84.9%; 125—86.4%; 250—88.0%; 300—89.9%, and 500—90.5% Methanol PI (µg/mL): 10—27.6%; 25—56.3%; 50—70.9%; 100—86.1%; 125—87.9%; 250—89.2%; 300—90.5%, and 500—90.8% Water PI (µg/mL): 10—21.6%; 25—50.5%; 50—60.3%; 100—78.4%; 125—80.9%; 250—84.4%; 300—86.9%, and 500—87.6%	The extent of antioxidant activities recorded for the <i>X. americana</i> stem bark is adequate to protect cells and tissues from destruction by free radicals

(Continues)

TABLE 6 | (Continued)

Author (year), country	Model	Part of the plant/Extraction method	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Ballo et al. (2023), Mali	FRAP Hydrogen peroxide scavenging	Roots Aqueous and hydroethanolic extract	Extract: 0.1–200 µg/mL FRAP: 1% H ₂ O ₂ scavenging: 40 mM Ascorbic acid: no related	FRAP NC: no related PC: ascorbic acid Hydrogen peroxide NC: no related PC: ascorbic acid	Ascorbic acid PI (µg/mL): 10–35.9%; 25–47.5%; 50–63.1%; 100–81.9%; 125–86.2%; 250–87.5%; 300–88.9%, and 500%–89.2%	<i>X. americana</i> extract has high antioxidant activity
					IC ₅₀ (µg/mL) compared to ascorbic acid: ascorbic acid—38.9; <i>n</i> -hexane—51.3; ethyl acetate—28.4; methanol—22.4, and water—67.6	
					Aqueous extract: <i>R</i> ² —0.992 and IC ₅₀ —44.85 µg/mL	
					Hydroethanolic extract: <i>R</i> ² —0.996 and IC ₅₀ —29.00 µg/mL	
					Ascorbic acid: <i>R</i> ² —0.997 and IC ₅₀ —8.42 µg/mL	
					H ₂ O ₂ scavenging Aqueous extract: IC ₅₀ —42.97 ± 1.6	
					Hydroethanolic extract: IC ₅₀ —53.54 ± 1.34	
					Ascorbic acid: IC ₅₀ —21.76 ± 1.64	

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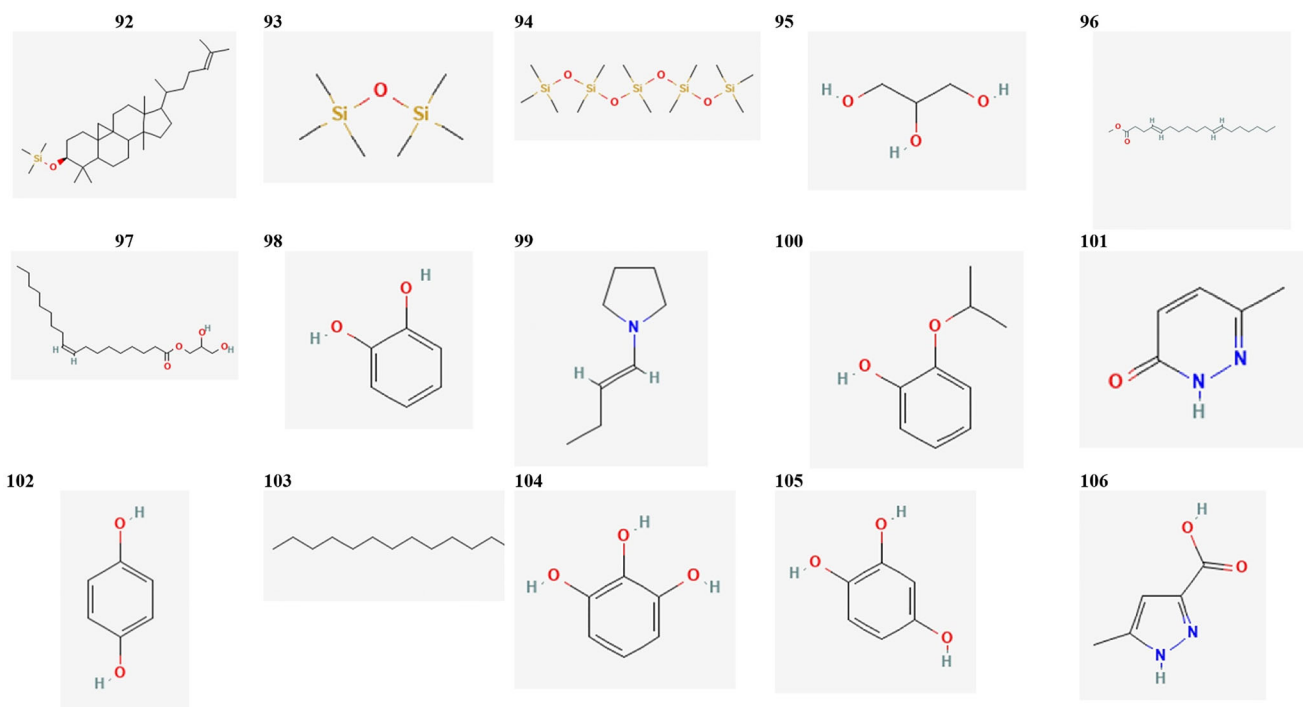


FIGURE 10 | Chemical structure of other compounds from *Ximenia americana* (92–106).

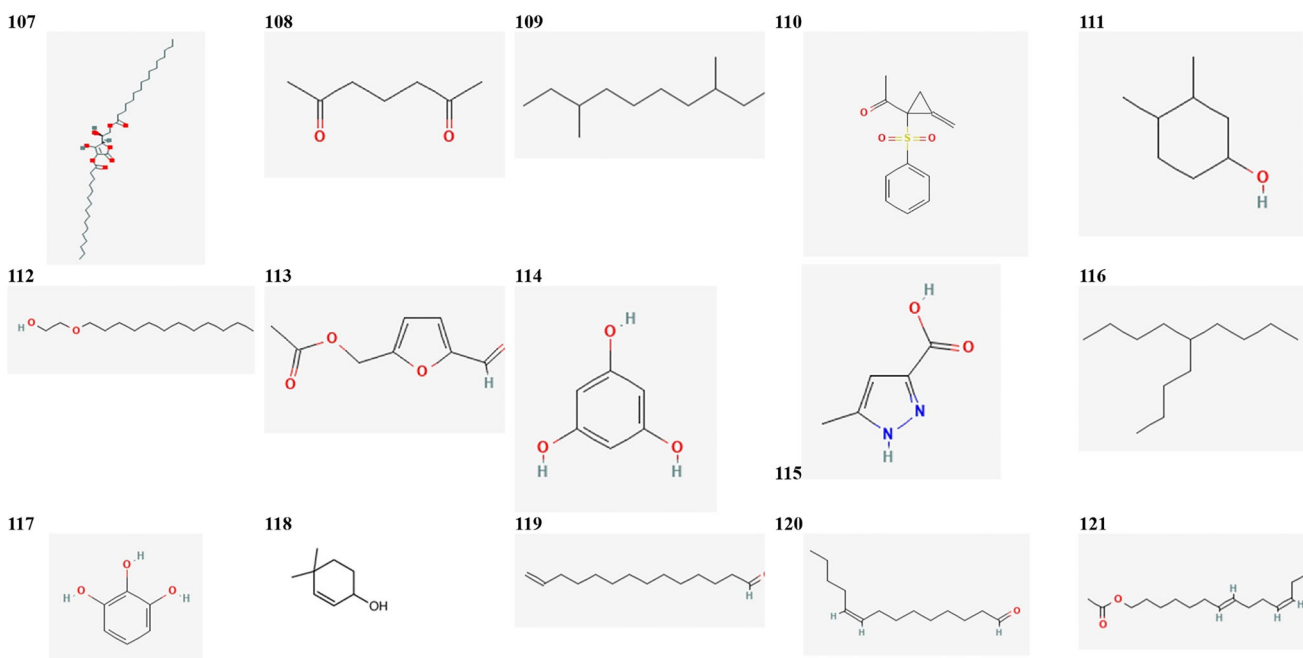


FIGURE 11 | Chemical structure of other compounds from *Ximenia americana* (107–121).

Fe^{2+} , which can trigger the Fenton reaction with hydrogen peroxide (H_2O_2), resulting in the production of highly reactive OH radicals ($^{\bullet}\text{OH}$) (Shahidi and Zhong 2015). The aqueous and hydroethanolic extracts of *X. americana* showed a relevant effect on the capture of hydrogen peroxide (H_2O_2) (Ballo et al. 2023). Furthermore, *X. americana* showed antioxidant activity through total antioxidant capacity (TAC), metal chelating activity, and the 2,2'-azodiisobutyramidine dihydrochloride (APPH) test. These

assays highlight the chelating and antiradical properties of the extract, which can inhibit the formation of free radicals, interact directly with them as scavengers, or chelate metals involved in free radical production, such as copper, iron, and zinc (Togbossi et al. 2020). These data, taken together, reinforce the ability of *X. americana* to neutralize reactive species, known for their prooxidant role, resist oxidative damage, and combat diseases associated with oxidative stress (Munteanu and Apetrei 2021).

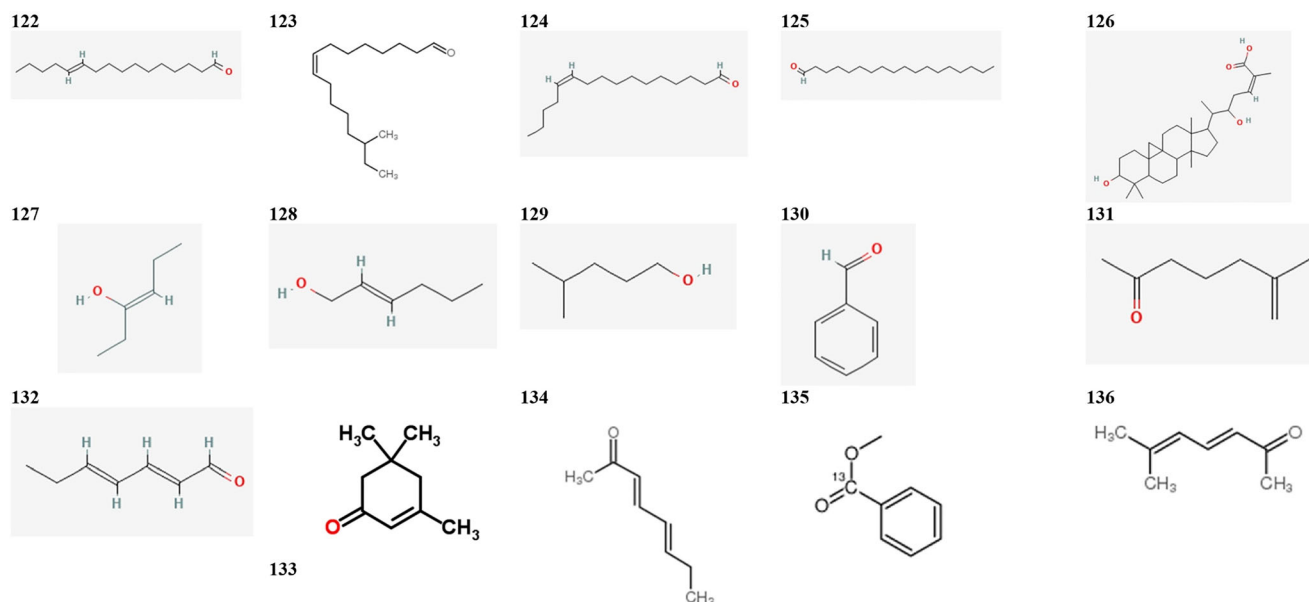


FIGURE 12 | Chemical structure of other compounds from *Ximenia americana* (122–136).

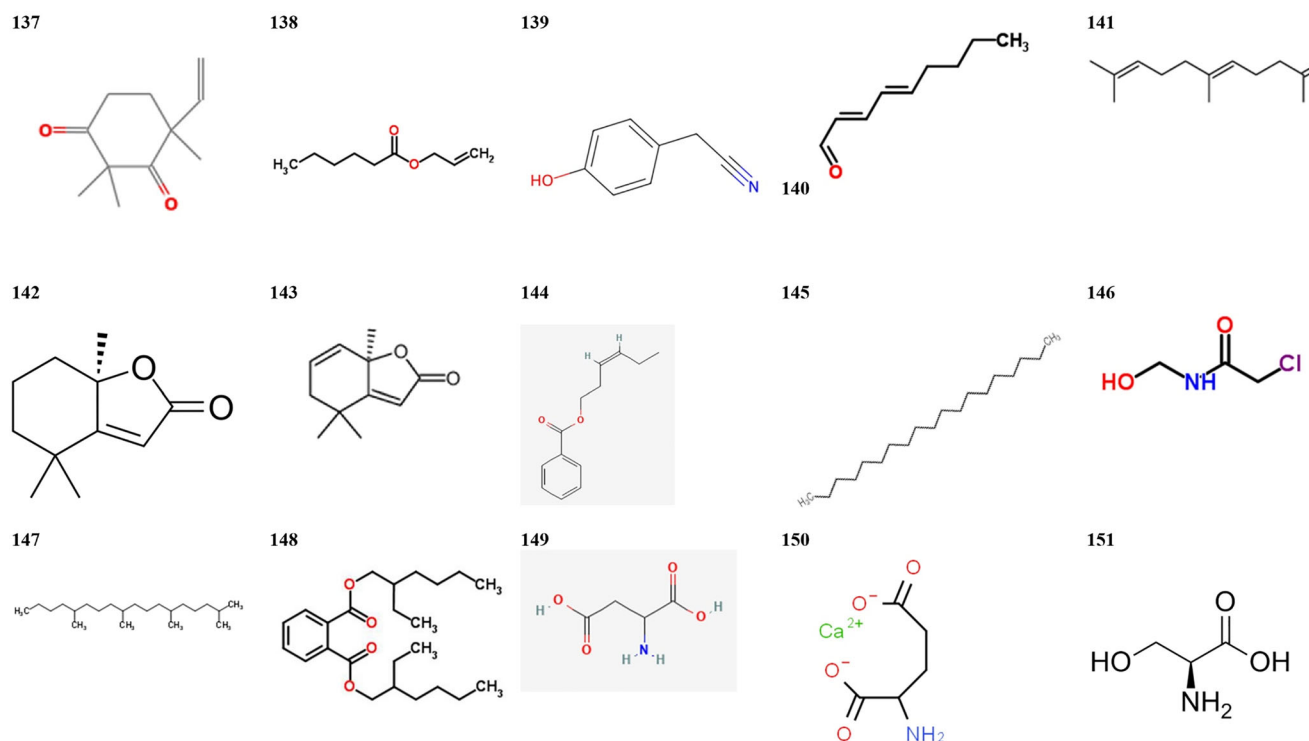


FIGURE 13 | Chemical structure of other compounds from *Ximenia americana* (137–151).

The antioxidant properties of *X. americana* were evidenced by the reduction of xanthine oxidase (XO) activity (Le et al. 2012) and the increase of ascorbate peroxidase, CAT, and SOD enzymes (Almeida et al. 2016). XO donates electrons directly to molecular oxygen (O_2), resulting in the formation of reactive oxygen species (ROS), such as superoxide anion (O_2^-) and hydrogen peroxide (H_2O_2), through one- and two-electron reductions, respectively. In the presence of iron, this can lead to the formation of

the OH radical (HO) through the Haber-Weiss and Fenton reactions (Battelli et al. 2016). During oxidative stress, ROS, such as superoxide radicals and hydrogen peroxide, are known to cause cellular damage. SOD converts superoxide radicals into oxygen and hydrogen peroxide (H_2O_2), whereas CAT transforms hydrogen peroxide (H_2O_2) into water and oxygen, helping to neutralize these reactive species and reduce oxidative stress (Chidambaram et al. 2024; Tolmacheva et al. 2023).

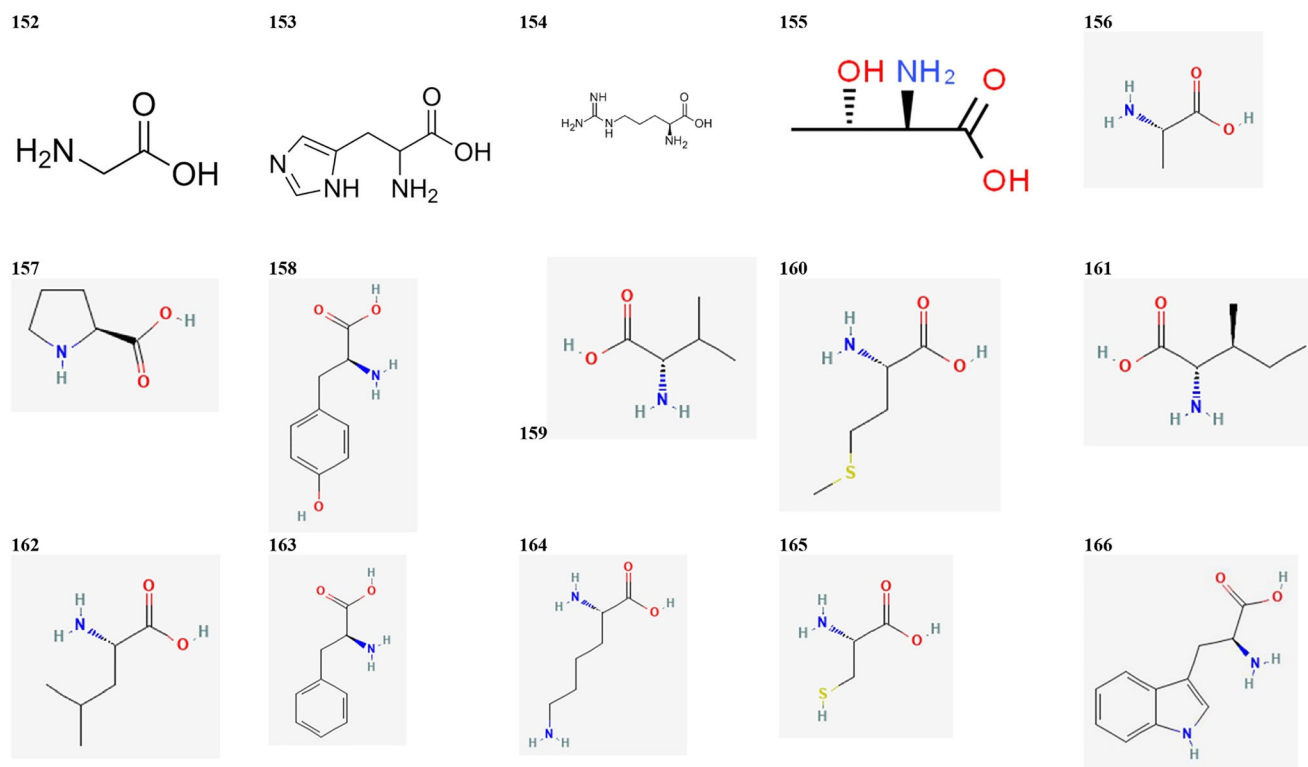


FIGURE 14 | Chemical structure of other compounds from *Ximenia americana* (152–166).

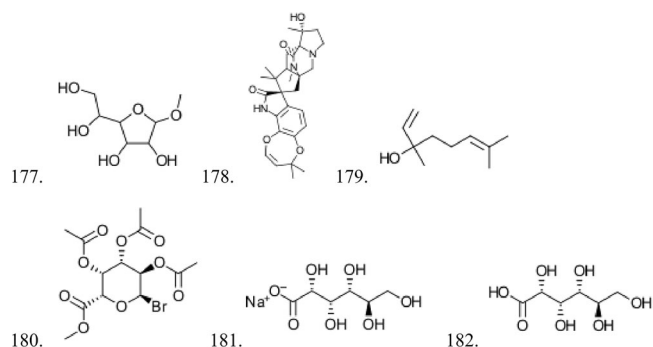


FIGURE 15 | Chemical structure of other compounds from *Ximenia americana* (177–182).

Another relevant process associated with oxidative stress is the damage to cell membrane lipids and lipoproteins caused by free radicals, which results in the formation of peroxidation products such as aldehydes and hydroperoxides (Borović Šunjić et al. 2024). In this context, *X. americana* has been shown to be effective in preventing lipoperoxidation, as evidenced by the TBARS test (Marques et al. 2020) (see Table 6).

3.7 | Anti-Inflammatory, Anti-Edematogenic, and Inflammation-Associated Activities In Vitro and In Vivo

Natural products from medicinal plants are widely used in the treatment of various inflammatory diseases, which has aroused the interest of researchers in recent years to understand the pharmacological properties of these products, based on

ethnopharmacological studies (da Silva et al. 2018). The anti-inflammatory activities of natural products can be confirmed by several in vitro assays and in vivo experimental models, with the aim of clarifying the possible mechanisms of action in the inflammatory pathways, as has already been demonstrated for *X. americana* (Koko et al. 2008; Al-Fattah Olabissi et al. 2011; Le et al. 2012; Shettar et al. 2015; Da Silva-Leite et al. 2017; Gaichu et al. 2017; Dias et al. 2018; Aragão et al. 2018; da Silva Pantoja et al. 2018; da Silva et al. 2018; da Silva-Leite et al. 2018; Sousa Carvalho et al. 2020; Aliyu et al. 2022; da Silva et al. 2023) due to the interest of the scientific community in searching for characteristic substances that have fewer side effects than non-steroidal anti-inflammatory drugs (NSAIDs), the current first-choice drugs for the treatment of inflammation and pain (Dutra et al. 2016).

Different types of *X. americana* extract preparations have been used to treat inflammation in rodents. Aqueous, hydroethanolic, and ethanolic extracts, butanol, methanol, hexane, dichloromethane-methanolic, ethyl acetate, and the ethanolic fraction of the stem and root barks, roots, and leaves were tested in rats and mice in the following models: (1) in vitro LPS-induced RAW264.7 cells, 15-lipoxygenase (LOX) inhibition, protein denaturation method with egg albumin, cytokines measurement, myeloperoxidase (MPO) activity, cyclooxygenase (COX) inhibition, quantification of total protein, and malondialdehyde-MDA (TBARS), (2) paw edema induced by carrageenan, zymosan, dextran, arachidonic acid (AA), serotonin, histamine, prostaglandin E₂ (PGE₂), and CFA, (3) peritonitis induced by intraperitoneal injection of carrageenan, (4) abdominal writhing model using intraperitoneal injection of acetic acid, (5) formalin, (6) vascular permeability, (7) turpentine pyrexia induced in rats, (8) carrageenan-induced pleurisy, (9)

TABLE 6 | (Continued)

Author (year), country	Part of the plant/Extraction method	Model	Concentration	Experimental methods for testing IC ₅₀ /EC ₅₀ values/control	Results/IC ₅₀ /EC ₅₀ /PI	Conclusion
Delma et al. (2023), Burkina Faso	Roots bark Aqueous ethanolic extract	DPPH FRAP	Extract: 30, 10, 3, 1, 0.3, and 0.1 µg/mL DPPH: 0.004% FRAP: no related Quercetin: no related Ascorbic acid: no related	DPPH NC: DPPH PC: quercetin FRAP NC: no related PC: ascorbic acid	DPPH Extract: IC ₅₀ —5.01 µg/mL Quercetin: IC ₅₀ —1.04 µg/mL FRAP Extract: 77.69 ± 2.06 mg EAA/100 mg Ascorbic acid: $y = 0.027x - 0.114$; $R^2 = 0.973$	<i>X. americana</i> extract has antioxidant activity

Abbreviations: DPPH, 2,2'-azodiisobutyramidine dihydrochloride; ABTS, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid); DPPH, 2,2-diphenyl-1-picrylhydrazyl; FRAP, ferric reducing/antioxidant power; PI, percentage of inhibition; PM, Mo-phosphate; SOD, superoxide dismutase; TAC, total antioxidant capacity.

ear edema induced by croton oil, AA, capsaicin, phenol, and histamine, (10) acute pancreatitis model, (11) spontaneous contractions of isolated rabbit ileum, histamine-induced contraction of isolated guinea pig ileum, and histamine-induced contraction of isolated guinea pig tracheal chain, (12) ethanol-induced mucosal lesions in rat, activity against ethanol-induced ulcers, induction of gastric lesions by absolute ethanol, gastric lesions by acidified ethanol, induction of gastric lesions by indomethacin, participation of sulfhydryl groups (–SH) and NO in gastroprotection and possible mechanisms (see Table 7).

The aqueous extract of *X. americana* roots demonstrated NO inhibitory capacity at a concentration of 0.25 g/L in RAW 264.7 cells exposed to 10 µg/mL of LPS after 24 h, expressed as mean values ($n = 12$) of 13.7% ($p < 0.001$). Furthermore, the aqueous extract demonstrated low cytotoxic capacity, increasing cell viability ($p < 0.01$) (Kumar-Roiné et al. 2009).

According to Le et al. (2012), the aqueous, ethanolic, and butanol extracts of *X. americana* leaves demonstrated a strong inhibitory effect on the enzyme 15-LOX, demonstrating IC₅₀ ± SD equal to 80.2 ± 5.5, 32.4 ± 0.5, and 102.7 ± 6.7 µg/mL, respectively. Fifteen-LOX inhibitors may be beneficial for ischemic conditions, inflammatory diseases, and cardiovascular diseases (Ackermann et al. 2017).

The aqueous ethanolic extract of *X. americana* root bark, when administered intraperitoneally at doses of 1, 10, and 100 mg/kg, showed antiedematogenic effects with a reduction of 40% ($p < 0.05$), 56% ($p < 0.01$), and 73% ($p < 0.001$), respectively, after 3 h of the carrageenan-induced paw edema test in mice. Furthermore, the extracts at doses of 10, 30, and 100 mg/kg were effective in decreasing the influx of leukocytes with inhibition of 33.96%, 39.90%, and 66.34%, respectively, and polymorphonuclear neutrophils with inhibitions of 34.42%, 39.49%, and 72.23%, respectively, for the peritoneal cavity induced by carrageenan-induced peritonitis. Vascular permeability was also reduced at these doses, demonstrating inhibition of 32.85% ($p < 0.05$), 39.34% ($p < 0.05$), and 57.36% ($p < 0.001$) (Al-Fattah Olabissi et al. 2011). The in vitro anti-inflammatory activity of the aqueous and methanolic extract of *X. americana* leaves was evaluated by the protein denaturation method. Concentrations of 100 µg/mL of the extracts were able to inhibit protein denaturation by 28.48% ± 2.11% and 77.51% ± 2.25%, respectively (Shettar et al. 2015).

It was demonstrated by Nyangacha et al. (2016) that the aqueous and methanolic extracts of *X. americana* stem bark, administered at a dose of 200 mg/kg (i.p.), are effective in reducing paw licking in both phases of the formalin test, with a greater reduction in the inflammatory phase (2nd phase) ($p < 0.05$). According to Da Silva-Leite et al. (2017), the methanolic fractions of the barks at doses of 0.1, 1.0, and 10 mg/kg (i.v.) also reduce inflammatory pain in the second phase of the formalin test. In corroboration, *X. americana* fractions significantly reduce abdominal contortions. This model evaluates different nociceptive mechanisms, including the release of inflammatory mediators such as histamine, serotonin, bradykinin (BK), and PGE₂ (Da Silva-Leite et al. 2017). According to these data, the fractions decreased the hypernociceptive response caused by carrageenan. In mice, injection of carrageenan into the animals' paws causes hypernociception,

TABLE 7 | General characteristics of the in vitro and in vivo studies related to the anti-inflammatory properties of *Ximenia americana* included in this review.

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Results/Targets/Outros			Conclusion
					Dose/ concentration and route/time of administration	Increase	Decrease	
Kumar-Roiné et al. (2009), France	In vitro anti- inflammatory	NO inhibition in RAW264.7 cells in vitro induced by LPS NC: no related PC: no related	Roots Aqueous extract	RAW264.7 cells; <i>n</i> = 12	0.0025, 0.025, 0.25, and 2.5 g/L; T: 24 h after induction with LPS	↑ cell viability	↓ NO production ↓ cytotoxicity	Aqueous extracts of <i>X. americana</i> have revealed to be effective NO inhibitors without showing cytotoxic or NO inductive effects
Olabissi et al. (2011), Burkina Faso	Systemic anti- inflammatory	Carrageenan- induced edema NC: saline solution PC: indomethacin and betamethasone Leukocyte and polymorphonu- clear neutrophil influx in carrageenan induced peritonitis NC: saline solution PC: indomethacin Vascular permeability: NC: saline solution PC: indomethacin	Root bark Aqueous ethanol extract	Male Swiss mice; weight: 25–35 g; <i>n</i> = 6 per group	Extract: 1, 10, 30, and 100 mg/kg (i.p.); indomethacin: 10 mg/kg (i.p.); Betamethasone: 2 mg/kg (i.p.)/T: 30 min before induction	—	↓ paw edema ↓ leukocyte influx to peritoneal cavities ↓ vascular permeability	Aqueous extract of <i>X. americana</i> has an anti- inflammatory effect

(Continues)

TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Results/Targets/Outros			Conclusion
					Dose/ concentration and route/time of administration	Increase	Decrease	
Le et al. (2012), Mali	In vitro anti- inflammatory	Inhibition of 15-lipoxygenase (15-LO) NC: water PC: quercetin	Leaves Ethanol, aqueous and butanol extract	15-Lipoxygenase (15-LO)	Extract: no related Quercetin: no related; T: no related	—	↓ of 15-LOX activity	<i>X. americana</i> extracts inhibit/modulate the activity of the inflammatory enzyme 15-LOX
Shettar et al. (2015), India	Anti- inflammatory	Protein denaturation method with egg albumin NC: phosphate buffered saline PC: diclofenac sodium	Leaves Aqueous extract Methanol extract	Egg albumin (from fresh hen's egg)	Extract: 100–500 µg/mL Diclofenac sodium: 100 and 200 µg/mL; T: 15 min before denaturation	—	↓ of protein denaturation	<i>X. americana</i> extract exhibits anti- inflammatory activity
Nyangacha et al. (2016), Kenya	Systemic anti- inflammatory	Formalin test 5% NC: saline PC: ASA	Stem-bark Aqueous extract Methanol extract	Male Swiss mice; weight: 25–30 g; <i>n</i> = 6 per group	Extract: 200 mg/kg (i.p.); ASA: 100 mg/kg (i.p.); T: 30 min before induction	—	↓ paw licking or biting time (2 ^a phase of formalin test)	<i>X. americana</i> extracts exhibit systemic anti- inflammatory activity related to inhibition of the 2 ^a phase of the formalin test
Silva-Leite et al. (2017), Brazil	Peripheral inflammatory nociception	Formalin test 2.5% NC: sterile saline PC: morphine and indomethacin Writhing test 0.8% NC: sterile saline	Barks Methanolic fractions	Mice Swiss; <i>n</i> = 6–8 per group	Methanolic fractions: 0.1, 1, 10 mg/kg (i.v.) or 100 mg/kg (v.o.); Indomethacin 10 mg/kg (i.p.) Morphine morphine 5 mg/kg (s.c.)	—	↓ Peripheral inflammatory nociception ↓ paw licking or biting time (2 ^a phase of formalin test)	Polysaccharides rich fractions of <i>X. americana</i> barks inhibit peripheral inflammatory nociception, being well tolerated by

(Continues)

TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		Conclusion
						Increase	Decrease	
Gaichu et al. (2017), Kenya	Systemic anti- inflammatory	PC: indomethacin Carrageenan- induced paw hypernocicep- tion NC: sterile saline PC: morphine	Leaf and Stem-bark Dichloromethane- methanolic extracts	Mice Swiss of either sex; weight: 15–35 g; <i>n</i> = 5 per group	Extract: 50, 100, and 150 mg/kg (route of administration no related) Diclofenac: 15 mg/kg (route of administration no related/ <i>T</i> : 1 h before induction)	—	↓ paw edema	The present study confirms the anti- inflammatory potential of the leaf and stem bark extracts of <i>X. americana</i> in experimental animals
		Carrageenan- induced paw edema NC: DMSO PC: diclofenac						
Gaichu et al. (2017), Kenya	Antipyretic activity	Turpentine induced pyrexia in rats NC: turpentine PC: aspirin	Leaf and stem-bark Dichloromethane- methanolic extract	Male Wistar rats, <i>Rattus norvegicus</i> /weight: 140–180 g/ <i>n</i> = 30 per group	Extract: 50, 100, and 150 mg/kg (i.p.) Aspirin: 100 mg/kg (i.p.)/ <i>T</i> : 1 h before induction	—	↓ pyrexia	The present study confirms the antipyretic potential of the leaf and stem bark extracts of <i>X. americana</i> in experimental animals

(Continues)

TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		Conclusion
						Increase	Decrease	
Agyira et al. (2017), Nigeria	Gastroprotective effect	Ethanol-induced mucosal lesions in rat NC: saline PC: misoprostol Activity against ethanol-induced ulcers NC: saline PC: cimetidine	Stem-bark Methanolic extract	Male Wistar rats/weight: 150–200 g/ <i>n</i> = 5 per group	Extract: 250, 500, and 1000 mg/kg (v.o.) Cimetidine: 100 mg/kg (v.o.) Misoprostol: 100 mg/kg (v.o.)/T: 1 h before induction	—	↓ lesion gastric ↓ indomethacin- induced injury	The extract of <i>X. americana</i> has a gastroprotective effect related to its anti-inflammatory effects
Aragão et al. (2018), Brazil	Gastroprotective effect	Induction of Gastric Lesions by Absolute Ethanol NC: 0.9% NaCl solution PC: pantoprazole Induction of Gastric Lesions by Acidified Ethanol NC: 0.9% NaCl solution PC: pantoprazole Induction of gastric lesions by indomethacin NC: 0.9% NaCl solution	Stem-bark Aqueous extract	Wistar rats and Swiss mice, both sexes; <i>n</i> = 6–7 per group	Extract: 100, 200, and 400 mg/kg (v.o.) Pantoprazole: 40 mg/kg (v.o.) Carbenoxolone: 100 mg/kg (v.o.)/T: 1 h before induction	↑ -SH and ON	↓ ethanol injury ↓ acidified ethanol injury ↓ indomethacin- induced injury	The extract of <i>X. americana</i> has a gastroprotective effect related to its anti-inflammatory effects

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros	
						Increase	Decrease
Da Silva et al. (2018), Brazil	Topical antiedematogenic activity	PC: pantoprazole Evaluation of the participation of sulphydryl groups (–SH) and nitric oxide (ON) in gastroprotection NC: 0.9% NaCl solution	Stem-bark Hydroethanolic extract	Female Swiss mice/weight: 20–30 g/ <i>n</i> = 6 per group	Extract: 100, 200, or 500 µg/ear (topic); Dexamethasone: 4 mg/mL (topic); Indomethacin: 25 mg/mL (topic)	—	The hydroethanolic extract of <i>X. americana</i> bark has a topical anti-edematogenic effect
		PC: carbenoxolone					
		Ear edema induced by single application of the croton oil NC: distilled water PC: dexamethasone Ear edema induced multiple applications of the croton oil NC: distilled water PC: dexamethasone					
						↓ of croton oil-induced edema (agude inflammation) ↓ of edema induced by multiple application of croton oil (chronic inflammation) ↓ of AA-induced edema ↓ of capsaicin-induced edema ↓ of	

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros	
						Increase	Decrease
		Ear edema induced by arachidonic acid, capsaicin, or phenol NC: distilled water PC: dexametha- sone/indomethacin					phenol-induced edema ↓ of histamine- induced edema
Da Silva-Pantoja et al. (2018), Brazil	Gastroprotective effect	Gastric lesions by indomethacin NC: 0.9% NaCl solution PC: no related Cytokines measurement NC: 0.9% NaCl solution PC: no related Assessment of leukocyte rolling and adhesion NC: 0.9% NaCl solution PC: no related	Barks Methanolic fractions and aqueous extract	Female Swiss mice/weight: 20–25 g/ <i>n</i> = 5–7 per group Cytokine IL-4 #171-I50001 Cytokine IL-8 #12007919 MPO: o-dianisidinedihy- drochloride and 1% hydrogen peroxide	Extract: 3, 10, 30, and 90 mg/kg (v.o.)	↑ gastric protection after indomethacin- induced injury ↑ IL-4 levels	↓ lesion gastric ↓ IL-8 levels ↓ rolling and adhesion in the indomethacin- induced gastric tissue injury ↓ rolling and adhesion in the indomethacin- induced gastric tissue injury
							<i>X. americana</i> extract ameliorates indomethacin- induced gastric injury, an effect that was associated with reduced neutrophil infiltration

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		
						Increase	Decrease	Conclusion
Dias et al. (2018), Brazil	Systemic and in vitro anti- inflammatory	Myeloperoxidase activity	Stem-bark Ethanolic extract and fractions	Swiss mice both sexes/weight: 20–30 g/ <i>n</i> = 7–8 per group COX-1: P22437 COX-2: Q05769	Extract and fractions: 100 mg/kg (i.p.) Dipyrrone: 10 mg/kg body weight (i.p.) Indomethacin 100 µmol/kg (i.p.)/ <i>T</i> : 40 min before for induction	—	↓ Peripheral inflammatory nociception ↓ paw licking or biting time (2 ^a phase of formalin test) ↓ of the activities of the enzymes COX-1 and COX-2 ↓ cell migration	<i>X. americana</i> extract exhibits systemic and in vitro anti- inflammatory effects
		NC: 0.9% NaCl solution						
		PC: no related						
		Acetic acid-induced writhing in mice						
		NC: vehicle						
		PC: dipyrrone						
		Formalin test						
		NC: vehicle						
		PC: indomethacin						
		In vitro cyclooxygenase inhibition						
		Assay						
		NC: vehicle						
		PC: indomethacin						
		Zymosan- induced peritonitis						
		NC: vehicle						
		PC: indomethacin						

(Continues)

TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		Conclusion
						Increase	Decrease	
Silva-Leite et al. (2018), Brazil	Systemic and in vitro anti- inflammatory	Acute pancreatitis model NC: saline PC: no related Pancreatic myeloperoxidase activity NC: saline PC: no related	Bark Methanolic fractions	Male Swiss mice/weight: 20–25 g/ <i>n</i> = 8 per group MPO: o-dianisidinedihy- drochloride and 1% hydrogen peroxide	Extract: 10 mg/kg (i.v.); 30 min before the first and 30 min after the 10th dose of caerulein	—	↓ Inflammatory infiltration ↓ edema ↓ MPO activity	<i>X. americana</i> bark fraction has anti- inflammatory effects on experimental acute pancreatitis of caerulein
Daniel Muthée et al. (2018), Kenya	Systemic antipyretic and anti- inflammatory	Turpentine induced pyrexia in rats NC: turpen- tine + DMSO PC: turpen- tine + DMSO + aspirin Carrageenan- induced inflammation in mice NC: car- rageenan + DMSO PC: Car- rageenan + DMSO + Diclofenac	Leaves and barks Dichloromethane- methanolic extracts	Male and female Wistar rats/weight: 140–180 g Both sexes of Swiss albino mice/weight: 15–35 g/ <i>n</i> = 5 per group	Extract: 50, 100, and 150 mg/kg (i.p.); Aspirin: 100 mg/kg (i.p.); Diclofenac: 15 mg/kg (i.p.)	—	↓ pyrexia ↓ paw edema	<i>X. americana</i> extract has powerful antipyretic and anti- inflammatory properties

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		Conclusion
						Increase	Decrease	
Kimondo et al. (2020), Kenya	Systemic anti-inflammatory	Carrageenan-induced rat paw edema assay NC: distilled water PC: diclofenac	Bark and leaves Methanol extracts	Adult Wistar rats/weight: 190–250 g/ <i>n</i> = 5 per group	Extract: 400 mg/kg (v.o.) Diclofenac 20 mg/kg (v.o.)/T: 1 h before the carrageenan injection	—	↓ paw edema	The present study confirms the anti-inflammatory potential of the leaf and stem bark extracts of <i>X. americana</i> in experimental animals
Marques et al. (2020), Brazil	Systemic anti-inflammatory	Paw Edema Model NC: saline PC: no related Peritonitis Model NC: saline PC: no related Differential leukocyte count NC: saline PC: no related Quantification of total protein NC: saline PC: no related Malondialdehyde-MDA (TBARS) NC: saline PC: no related	Barks Decoction	Swiss mice/weight: 25–35 g/ <i>n</i> = 8 per group	Extract: 50,100, and 150 mg/kg (v.o.)/T: 1 h before induction Total protein Ref. 99.1 MDA MAK568-IKT	—	↓ paw edema ↓ neutrophils ↓ total protein ↓ MDA	<i>X. americana</i> barks possess Anti-inflammatory effect in mice models of acute inflammation induced by zymosan

(Continues)

TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		
						Increase	Decrease	Conclusion
Aliyu et al. (2022), Nigeria	Anti-asthmatic	Spontaneous contractions of isolated rabbit ileum	Leaves Ethanol extract	Guinea pigs, rabbits, and rats of either sex/weight: 300–350 g, 1.3 kg, and 180–200 g respectively/ <i>n</i> = 5 per group	Extract: 0.4, 0.8, 1.6, and 3.2 mg/mL (in organ bath)	↑ relaxation of the ileum	↓ contraction of the ileum by histamine- induced contraction of isolated trachea	The leaves of <i>X. americana</i> have broncho- relaxant activity
		NC: no related						
		PC: no related						
		Histamine- induced			Ketotifen fumarate: 10 µg/mL (in organ bath)			
		contraction of isolated guinea pig ileum						
Ballo et al. (2023), Mali	In vitro anti- inflammatory	NC: no related						Hydroethanolic extracts of <i>X. americana</i> significant anti- inflammatory activity
		PC: no related						
		Cyclooxygenase (COX-1 and COX-2)	Roots Aqueous and hydroethanolic extract	COX 760111 Albumin serum (BSA) 11021029	Extract: 100, 250, and 500 µg/mL Diclofenac: 100, 250, and 500 µg/mL	—	↓ of the activities of the enzymes COX-1 and COX-2 ↓ of protein denaturation	
		inhibition test						
		NC: no related						
		PC: diclofenac/celecoxib						
		Inhibition of protein denaturation						
		NC: no related						
		PC: diclofenac						

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros	
						Increase	Decrease
Da Silva et al. (2023), Brazil	Antiedematogenic and anti- inflammatory properties	Carrageenan, zymosan, and dextran-induced paw edema NC: saline PC: no related Histamine, serotonin, AA, and PGE ₂ -induced paw edema NC: saline PC: no related Complete Freund's Adjuvant (CFA)-induced subchronic paw edema NC: saline PC: no related Carrageenan- induced pleurisy NC: saline PC: no related	Stem-bark Hydroethanolic extract	Female and male mice Swiss/weight: 20–30 g/ <i>n</i> = 6 per group TNF- α : #BMS607-3 IL-1 β : #BMS6002	Extract: 50, 100, and 250 mg/kg (v.o.)/T: 1 h before induction	—	↓ acute paw edema ↓ subchronic paw edema ↓ leukocytes ↓ IL-1 β and TNF- α levels
							<i>X. americana</i> bark extract has anti- edematogenic and anti- inflammatory activity

(Continues)

TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		
						Increase	Decrease	Conclusion
Delma et al. (2023), Burkina Faso	Antiulcer effect	HCl/Ethanol- induced peptic ulcer	Roots bark	Female mice/weight: 30–35 g/ <i>n</i> = 6 per group	Extract: 1, 10, and 30 mg/kg (v.o.)	↑cytoprotective effect	↓ ulcer formation	<i>X. americana</i> extract is protective in induced gastric ulcers
		NC: distilled water	Aqueous ethanolic extract		Lansoprazole 20 mg/kg (v.o.)/T: 1 h before induction		↓ ulceration	
		PC: lansoprazole						
		Hypothermic restraint-stress- induced peptic ulcer						
Pessoa et al. (2023), Brazil	Gastroprotective effect	Acidified ethanol-induced gastric injury	Stem-bark	Swiss mice (<i>Mus musculus</i>) of both sexes/weight: 20–30 g/ <i>n</i> = 6 per group	Extract: 50, 100, and 200 mg/kg (v.o.)	↑cytoprotective effect	↓ ulcer formation	<i>X. americana</i> extract has cytoprotective and gastroprotective effects
		NC: water for injection	Hydroethanolic extract		Omeprazole: 30 mg/kg (v.o.)	↑ -SH and ON	↓ ulceration	
		PC: omeprazole		MPO: o-dianisidinedihy- drochloride and 1% hydrogen peroxide	Misoprostol: 0.016 mg/kg (v.o.)		↓ MPO activity	
		Absolute ethanol-induced gastric injury			Ranitidine: 40 mg/kg (v.o.)			
		NC: water for injection			Carbenoxolone: 100 mg/kg (v.o.)			
		PC: omeprazole			L-arginine: 600 mg/kg (i.p.)			
		Indomethacin- induced gastric injury			Clonidine 0.05 mg/kg (v.o.)			
		NC: water for injection			Indomethacin 10 mg/kg (v.o.)/T: 1 h before induction			
		PC: omeprazole						
		The physical barrier test						

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Results/Targets/Outros		
					Dose/ concentration and route/time of administration	Increase	Decrease
		NC: water for injection PC: no related Involvement of the prostaglandin E ₂ pathway NC: water for injection PC: misoprostol Determination of gastric mucosal mucus NC: water for injection PC: misoprostol Involvement of H ₂ histamine receptors NC: water for injection PC: ranitidine Involvement of sulphydryl (SH) groups NC: water for injection PC: carbenoxolone Involvement of α_2 adrenergic receptors NC: water for					

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		
						Increase	Decrease	Conclusion
Meleh Umar et al. (2023), Nigeria	In vitro anti- inflammatory	injection PC: clonidine	Stem-bark <i>n</i> -Hexane, ethyl acetate, and methanol, and water extracts	Cells from unwitting humans	Extracts: 10, 25, 50, 100, 125, 250, 300, and 500 µg/mL Diclofenac sodium: 100 µg/mL	↑ RBC protection	↓ red blood cell hemolysis ↓ heat-induced red blood cell hemolysis	<i>X. americana</i> extract has anti- inflammatory effects
		Involvement of the nitric oxide pathway						
		NC: water for injection						
		PC: L-arginine						
		Myeloperoxidase (MPO) activity						
		NC: water for injection						
		PC: indomethacin						
		Membrane stabilization method						
		NC: no related PC: no related						
		Preparation of red blood cells (RBC's) suspension						
		NC: hyposaline						
		PC: diclofenac						
		Heat induced hemolysis						
		NC: saline						
		PC: diclofenac sodium						
		Hypotonic solution induced						

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		
						Increase	Decrease	Conclusion
Pessoa et al. (2024), Brazil	Antinociceptive potential	hemolysis NC: saline PC: diclofenac sodium	Stem-bark Hydroethanolic extract	Swiss mice (<i>M. musculus</i>) of both sexes/weight: 20–30 g/ <i>n</i> = 6 per group	Extract: 50, 100, and 200 mg/kg (v.o.)/T: 1 h before induction	—	↓ paw licking or biting time (2 ^a phase of formalin test) ↓ abdominal contortions	<i>X. americana</i> extract has an antinociceptive effect on inflammatory pain
		Acetic acid-induced abdominal contortions NC: water PC: no related The formalin test NC: water PC: no related				—	↓ CFA-induced inflammation ↓ myeloperoxidase (MPO) ↓ mechanical hyperalgesia	This study indicates that HEXA can modulate the inflammatory and hyperalgesic responses triggered by CFA in a murine RA model without evident hepatotoxicity
da Silva et al. (2025), Brazil	Anti- inflammatory and anti-hyperalgesic	Complete Freund's adjuvant (CFA)-induced arthritis model Mechanical hyperalgesia NC: water PC: no related	Stem-bark Hydroethanolic extract	Swiss mice (<i>M. musculus</i>) of both sexes/weight: 20–30 g/ <i>n</i> = 6 per group	Extract: 50 mg/kg	—	—	—

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TABLE 7 | (Continued)

Author (year), country	Activity/Effect evaluated	Experimental model/Test/ control	Part of the plant and extraction method	Animal characteristics species/weight/ <i>n</i> per group/cell lines/enzymes/ cytokines	Dose/ concentration and route/time of administration	Results/Targets/Outros		
						Increase	Decrease	Conclusion
Adehouni et al. (2025), Brazil	Analgesic and anti- inflammatory	Formaldehyde- induced paw irritation test in rats Carrageenan- induced paw irritation test in rats	Bark powder from <i>X. americana</i>	Swiss strain <i>M. musculus</i> mice, weighing between 20 g and 30 g Wistar strain <i>Rattus norvegicus</i> rats, weighing between 150 and 200 g	<i>X. americana</i> decoction: 0.25, 1, 2, 5, 10, 25, 50, 75, 100, and 150 mg/kg Hydroethanolic extract of <i>X. americana</i> : 0.25, 1, 2, 5, 10, 25, 50, 75, 100, and 150 mg/kg	—	↓inflammatory pain ↓inflammatory edema	The analysis of the tests utilized to evaluate the analgesic and anti- inflammatory activity of the decoction and the hydroethanol extract of <i>X. americana</i> demonstrated that they exhibited significant analgesic activity

Abbreviations: IL-1 β , interleukin-1 β ; LOX, lipoxygenase; MPO, myeloperoxidase; NO, nitric oxide; TNF- α , tumor necrosis factor-alpha.

which is marked by the release of inflammatory cytokines, such as tumor necrosis factor- α (TNF- α) and KC (keratinocyte-derived chemokine), which activate the release of interleukin-1 β (IL-1 β) (Cunha et al. 2005) and prostanoids, which play a role in the sympathetic component of pain (Nakamura and Ferreira 1987; Da Silva-Leite et al. 2017).

Dichloromethane extracts of *X. americana* leaves and stem bark at doses of 50, 100, and 150 mg/kg were effective in reducing carrageenan-induced paw edema at all time points evaluated, similarly to diclofenac. NSAIDs, such as diclofenac, ibuprofen, and indomethacin, are frequently indicated in the treatment of inflammatory processes. The action of these drugs occurs through the inhibition of prostaglandin biosynthesis, blocking COX. Thus, the anti-inflammatory properties of *X. americana* leaf and stem bark extracts in the treatment of inflammation can be attributed to the inhibition of PGs production (Gaichu et al. 2017).

Musyoki et al. (2017) investigated the effect of dichloromethanolic extracts of *X. americana* leaves and stem bark at doses of 50, 100, and 150 mg/kg (i.p.) on turpentine-induced pyrexia in rats. NSAIDs act by inhibiting COX-2 expression, which in turn reduces PGE₂ biosynthesis, resulting in decreased fever. The antipyretic action of several antipyretic drugs occurs by inhibiting COX-2 and reducing PGE₂ levels in the hypothalamus. COX-2 inhibitors are potent antipyretics, preventing the conversion of AA to PGE₂. In this context, it is believed that the *X. americana* extracts used by Musyoki et al. (2017) present antipyretic activity by inhibiting COX-2, which leads to a reduction in PGE₂ concentration.

Oral administration (v.o.) of the methanolic extract of *X. americana* bark at a dose of 1000 mg/kg ($p < 0.05$) was effective in reducing indomethacin-induced lesions in rats. Ethanol-induced lesions were also reduced by the extract at doses of 500 and 1000 mg/kg (v.o.) ($p < 0.05$) (Agyigra et al. 2017). Aragão et al. (2018) revealed that the aqueous extracts of *X. americana* bark at doses of 100, 200, and 400 mg/kg (v.o.) were effective in reducing ethanol-induced lesions in rats. The percentage of lesion inhibition was 76.08% ($p < 0.001$), 77.48% ($p < 0.01$), and 100% ($p < 0.0001$). However, the extracts were effective in reducing lesions induced by acidified ethanol and indomethacin. These results suggest that the anti-inflammatory actions of the extract confer a gastroprotective effect.

Topical administration of the hydroethanolic extract of *X. americana* stem bark at doses of 100, 200, or 500 μ g/ear was effective in reducing ear edema induced by single and multiple applications of croton oil in mice. The extract demonstrated antiedematogenic effects at the respective doses. The lowest doses ($p < 0.0001$) and for the dose of 500 μ g/ear ($p < 0.001$); in multiple applications the extract revealed $p < 0.0001$ at all doses. In addition, the extract at doses of 100 and 200 reduced ear edema induced by AA ($p < 0.001$ and $p < 0.0001$), capsaicin ($p < 0.0001$), phenol ($p < 0.0001$), and histamine ($p < 0.0001$ and $p < 0.001$) (da Silva et al. 2018).

The gastroprotective effect of the methanolic fractions and aqueous extract was also determined by da Silva Pantoja et al. (2018). The dose of 30 mg/kg of the methanolic fraction was effective in reducing indomethacin-induced gastric injury ($p < 0.05$) as well as reducing indomethacin-induced MPO enzyme activity

($p < 0.05$). In addition, the fraction was effective in increasing IL-4 ($p < 0.05$) and consequently decreasing inflammatory cell infiltrate and epithelial cell loss, as well as decreasing IL-8 ($p < 0.05$) and leukocyte rolling by 86% and adhesion by 84%. The aqueous extract reduced lesions and MPO activity ($p < 0.05$).

The administration of ethanolic extract and fractions of the stem bark of *X. americana* at a dose of 100 mg/kg (i.p.) demonstrated significant inhibition of acetic acid-induced abdominal contortions in mice ($p < 0.01$). In the second phase (inflammatory phase) of the formalin test, the ethanolic extract and hydromethanol fraction reduced paw licking ($p < 0.01$). NSAIDs and steroidal anti-inflammatory drugs inhibited only the late phase in the formalin test. In addition, the extract and fractions were effective in reducing cells in zymosan-induced peritonitis, as well as in inhibiting COX-1 and COX2 enzymes, key enzymes in the AA inflammatory pathway (Dias et al. 2018). da Silva-Leite et al. (2018) demonstrated that methanolic fractions of *X. americana* bark extract (10 mg/kg; i.v.) were effective in reducing edema, inflammatory infiltration, acinar cell necrosis, total scores, and reduced MPO activity in the caerulein-induced pancreatitis model at 11 h but caused no change at 24 h. Furthermore, activation of receptors involving cannabinoid type 2 (CB2) receptors may exert anti-inflammatory effects through a reduction in NF- κ B (da Silva-Leite et al. 2018).

The dichloromethane-methanolic extracts of the leaves and bark of *X. americana* when administered at doses of 50, 100, and 150 mg/kg (i.p.) show antipyretic effect in the turpentine-induced pyrexia model in rats ($p < 0.05$), as well as antiedematogenic effect in the carrageenan-induced paw model in rats ($p < 0.05$) (Daniel Muthee et al. 2018). Kimondo et al. (2020) demonstrated that the methanolic extracts of the bark and leaves at a dose of 400 mg/kg (v.o.) reduce paw edema from the 1st to the 4th evaluation in the carrageenan-induced paw edema model in rats.

The decoction of *X. americana* bark at doses of 50, 100, and 150 mg/kg (v.o.) was effective in reducing zymosan-induced paw edema ($p < 0.05$), as well as in inhibiting inflammatory and oxidative stress-causing parameters in zymosan-induced peritonitis (decrease in leukocytes [$p < 0.05$], decrease in total proteins [$p < 0.05$], and MDA-TBARS [$p < 0.05$]) (Marques et al. 2020).

According to Aliyu et al. (2022), the ethanolic extract of *X. americana* leaves at concentrations of 0.4, 0.8, 1.6, and 3.2 mg/mL increases the relaxation of the ileum of rabbits, also reducing the contraction of the ileum and trachea of guinea pigs induced by histamine ($p < 0.05$), demonstrating that the leaf extracts have bronchorelaxant activity. Concentrations of 100, 250, and 500 μ g/mL of the aqueous and ethanolic extract of *X. americana* roots are shown to be effective in in vitro anti-inflammatory activity, reducing the actions of COX-1 ($p < 0.001$), COX-2 ($p < 0.001$), and protein denaturation ($p < 0.001$) (Ballo et al. 2023).

The hydroethanolic extract of *X. americana* stem bark administered at doses of 50, 100, and 250 mg/kg (v.o.) demonstrated antiedematogenic effects in paw edema models induced by carrageenan, dextran, and zymosan at all times evaluated ($p < 0.0001$), as well as in the subchronic paw edema model

induced by CFA injection into the paw of mice ($p < 0.0001$). In addition, the extract at a dose of 50 mg/kg was shown to be effective in reducing paw edema models induced by AA ($p < 0.0001$), histamine ($p < 0.0001$), serotonin ($p < 0.0001$), and PGE₂ ($p < 0.0001$), as well as reducing the infiltration of total leukocytes into the pleural cavity in the pleurisy model induced by carrageenan ($p < 0.0001$) and levels of IL-1 β and TNF- α (da Silva et al. 2023).

According to Delma et al. (2023), the aqueous and ethanolic extract of *X. americana* roots at doses of 1, 10, and 30 mg/kg (v.o.) increases the cytoprotective effect and decreases ulceration in mice ($p < 0.05$, $p < 0.01$). Pessoa et al. (2023) demonstrated that the hydroethanolic extract of *X. americana* bark at doses of 50, 100, and 200 mg/kg (p.o.) is also effective in gastric cytoprotection, decreasing ulcer formation ($p < 0.01$, $p < 0.0001$) and reducing the action of MPO activity (< 0.0001). In addition, the gastroprotective effect is associated with the ability of the extract to stimulate mucus production and reduce intestinal motility through -SH groups, NO production, and activation of α_2 adrenergic receptors.

Extracts of stem bark, *n*-hexane, ethyl acetate, methanol, and water of *X. americana* at concentrations of 10, 25, 50, 100, 125, 250, 300, and 500 μ g/mL were evaluated for their in vitro anti-inflammatory capacity, demonstrating that the extracts demonstrate increased RBC protection and decreased red blood cell hemolysis in hypotonic solution and under heat (Meleh Umar et al. 2023). Pessoa et al. (2024) demonstrated that oral administration of the hydroethanolic extract of *X. americana* bark at doses of 50, 100, and 200 mg/kg was effective in reducing inflammatory nociception induced by acetic acid in mice ($p < 0.0001$) and in reducing paw licking in the formalin test in the second phase ($p < 0.0001$, $p < 0.001$, and $p < 0.0001$), respectively.

4 | Discussion

The use of plant extracts and herbal medicines has increased due to their low cost, easy availability, and almost nonexistent side effects. Medicinal plants, used in traditional medicine to treat several acute and chronic inflammatory disorders, contain important chemical compounds that act on multiple signaling pathways (Maione et al. 2016). Although the anti-inflammatory functions of these natural extracts were initially described, it was the subsequent phytochemical and pharmacological studies that allowed the identification and characterization of several natural active compounds. Furthermore, the molecular mechanisms observed in animal models also provided a basis for the possible clinical application of these compounds (Mózsik et al. 2009; Patrignani and Patrono 2015).

Research into the roots, bark, trunk bark, leaves, fruits, and seeds of the species *X. americana* has resulted in the production of various plant extracts and polyphytotherapeutic formulations, widely used in the treatment of various inflammatory disorders, such as toothache, gingivitis, stomatitis, inflammation of the uterus and ovaries, gastritis, vaginitis, arthritis, and dermatitis, diseases associated with inflammatory processes (James et al. 2008; Maikai et al. 2008, 2010; Le et al. 2012; de Carvalho Nilo Bitu et al. 2015; Aliyu et al. 2022), led to an increasing number of studies on the pharmacological and phytochemical potential of *X.*

americana, and it has been demonstrated in nonclinical in vitro and in vivo conditions, especially those involving oxidative stress, that it has potential for the treatment of inflammatory diseases.

Through numerous investigations, multiple classes of phytochemicals have been identified, quantified, and isolated, including saponins, flavonoids, glycosides, tannins, phenolic compounds, alkaloids, quinones, terpenoids, and sterols (Eromosele et al. 1994; Freiberger et al. 1998; Almeida et al. 2016; M. M. Dahiru et al. 2022; Aliyu et al. 2022; Barrera-Vázquez et al. 2023). In this context, this systematic review revealed a wide range of chemical substances, including terpenes, fatty acids, flavonoids, phenolic acids, polyphenols, and a range of other compounds identified in phytochemical analyses (Regina et al. 2008; Shantha et al. 2012). These chemical substances are studied and shown to have a strong effect on the signaling pathways of the inflammatory process, inhibiting/modulating the AA, COX-1, COX-2, PGE₂, IL-1 β , and TNF- α pathway or increasing the levels of anti-inflammatory cytokines such as IL-4 and IL-10 (Eslick et al. 2022; del Prado-Audelo et al. 2021; Sridhar et al. 2021; Bai et al. 2021; Chiorcea-Paquim 2023; Xie et al. 2024).

Regarding the antioxidant effect, in vitro studies have shown that *X. americana* is a potent antioxidant, capable of neutralizing free radicals, decreasing lipid peroxidation, reducing NO production, and regulating the enzymes XO, SOD, CAT, and ascorbate peroxidase (Lamien-Meda et al. 2008; Kumar-Roiné et al. 2009; Le et al. 2012; Shettar et al. 2015; Darcio and Sarmiento 2015; Almeida et al. 2016; Sidonie Beatrice et al. 2021; Ballo et al. 2023) (Figure 16). This impact on oxidative stress and resistance to free radical damage, often associated with a prooxidant effect, may play an important role in combating inflammatory responses (Munteanu and Apetrei 2021). In this context, medicinal plants, which contain a wide variety of phytochemicals with redox-modulating properties, have a significant capacity to regulate the inflammatory response. These compounds, considered “health-promoting” due to their radical-scavenging activity and/or direct antioxidant effects on cellular biomolecules, interfere with cellular functions by blocking reactive species in critical cellular signaling pathways. In addition, interactions of these compounds with enzymes, receptors, and transcription factors have also been reported (Allegra 2019; Munteanu and Apetrei 2021; Gonfa et al. 2023).

Inflammation is a complex biological response of vascular tissues to harmful stimuli. Acute inflammation is associated with increased leukocyte migration, capillary damage, and increased vascular permeability. Chronic inflammation is a persistent and debilitating immune-mediated condition influenced by genetic and environmental factors. The main signs of inflammation include redness, swelling, pain, heat, and loss of function (Kumar et al. 2013; Khumalo et al. 2022). In this context, the analysis of antipyretic, analgesic, anti-inflammatory, gastroprotective/antiulcerogenic, antiedematogenic, and anti-inflammatory activities demonstrates the effects of *X. americana* on the signs of the inflammatory process in experimental models.

In this context, fever results from the interaction between the peripheral immune system and the brain. When there is contact with a pathogen or an inflammatory stimulus, macrophages and other immune cells are activated to release cytokines.

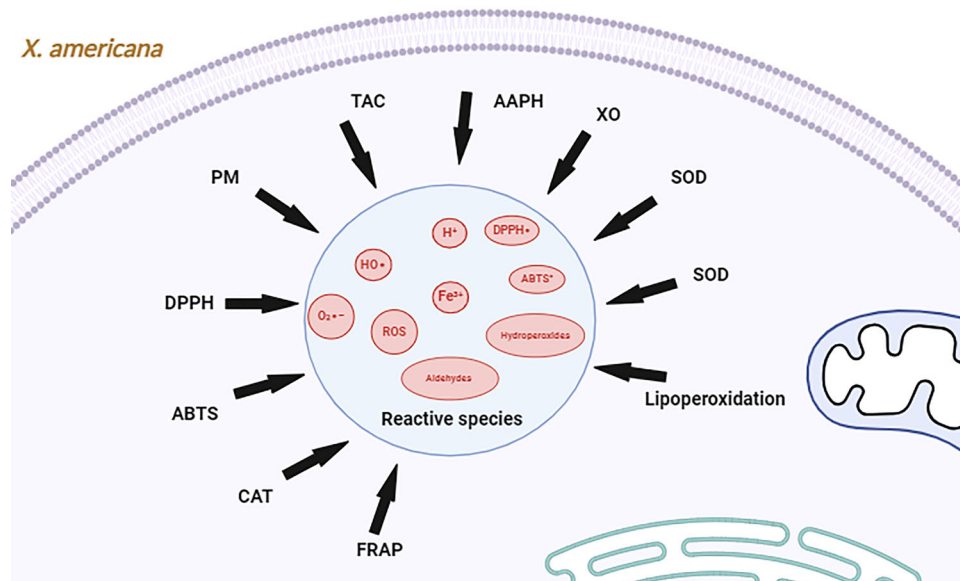


FIGURE 16 | Possible antioxidant mechanism of action of *Ximenia americana*. AAPH, 2,2'-Azodiisobutyramidine dihydrochloride; CAT, catalase; DPPH, 2,2-diphenyl-1-picrylhydrazyl; FRAP, ferric reducing/antioxidant power; PM, Mo-phosphate; SOD, superoxide dismutase; TAC, total antioxidant capacity; XO, xanthine oxidase.

There are two main types of cytokines involved in the induction of fever. Endogenous pyrogens, such as IL-1 β , IL-6, IL-8, macrophage inflammatory protein-1 β (MIP-1 γ), interferon- γ , and PGE₂, are responsible for this process. Traditionally, pharmacological approaches have been employed to understand the role of medicinal plants in the regulation of fever (such as turpentine and LPS) (Leon 2002; Kang et al. 2023). Thus, the antipyretic activity of *X. americana* strengthens the evidence of its benefits in the treatment of fever and pyrexia in mice and rats (Musyoki et al. 2017; Daniel Muthee et al. 2018). Furthermore, in other research, *X. americana* showed efficacy in reducing or modulating PGE₂, IL-1 β , IL-8, and COX-2, which suggests a possible mechanism of inhibition or modulation of pyrexia in the extracts in experimental studies (Da Silva et al. 2018; Da Silva-Pantoja et al. 2018; Da Silva et al. 2023).

Inflammatory disorders and pain-related conditions continue to be significant global health challenges, affecting people worldwide. Pain, especially back pain and headaches, is one of the most common conditions. Although there are several classes of medications to treat these conditions, NSAIDs are widely used. However, the use of these drugs in clinical practice is often associated with adverse and toxic effects. Therefore, the search for herbal alternatives becomes essential (Khumalo et al. 2022).

In this context, *X. americana* exhibits effects on inflammatory pain induced by (1) formalin test, (2) acetic acid-induced abdominal writhing, and (3) carrageenan-induced paw hypernociception (Nyangacha et al. 2016; Silva-Leite et al. 2017; Dias et al. 2018; Pessoa et al. 2024). Through a precise analysis of the studies, we suggest that the antinociceptive effect of *X. americana* on inflammatory pain occurs with the participation of different targets, related to the modulation/inhibition of COX-2 and inflammatory mediators such as BK and PGE₂ (Nyangacha et al. 2016; Silva-Leite et al. 2017; Dias et al. 2018; Da Silva et al. 2018; Da Silva et al. 2023; Ballo et al. 2023; Pessoa et al. 2024).

Inhibition/modulation of PGE₂ in inflammatory pain can directly alter the function of ion channels by acting on EP receptors, especially EP1 and EP4. This modulation or inactivation would lead to the deactivation of protein kinase C (PKC) and PKA, the closure of transient receptor potential vanilloid-1 (TRPV-1), and the opening of K_{ATP} channels. In addition, inhibition or modulation of PGE₂ would result in a decrease in indirect effects, such as the reduction in the sensitivity of peripheral neurons to BK, which acts on B2 receptors, resulting in the antinociceptive effect of *X. americana* in inflammatory pain (Chen et al. 2013; Machairiotis et al. 2021) (Figure 17). Another proposed mechanism for the antinociceptive activity of *X. americana* in inflammatory pain is the increased expression of cannabinoid type 2 (CB2) receptors. Agonists of these receptors have significant antinociceptive actions in models of neuropathic, chronic, and inflammatory pain. Furthermore, activation of CB2 receptors may exert anti-inflammatory effects through reduction of NF- κ B (Silva-Leite et al. 2018).

The pathogenesis of gastric diseases is a complex process, influenced by several factors, such as genetic, environmental, and lifestyle aspects. Among the most common gastrointestinal diseases, gastric inflammation stands out, characterized by increased acid secretion, oxidative stress, and alterations in the functioning of the immune system (Filippis et al. 2020). When analyzing the studies, *X. americana* demonstrates its gastroprotective effects associated with several pathways, which include increased levels of -SH, NO, activation of α_2 adrenergic receptors, elevated levels of the cytokine IL-4, and decreased levels of IL-8 and MPO (Aragão et al. 2018; Da Silva-Pantoja et al. 2018; Pessoa et al. 2023).

The main function of inflammation is to mobilize the body's cells to combat harmful agents and repair damaged tissues, promoting healing of affected areas. The inflammatory response is effective due to the release of several mediators that play essential roles in the initiation, progression, maintenance, regulation, and reso-

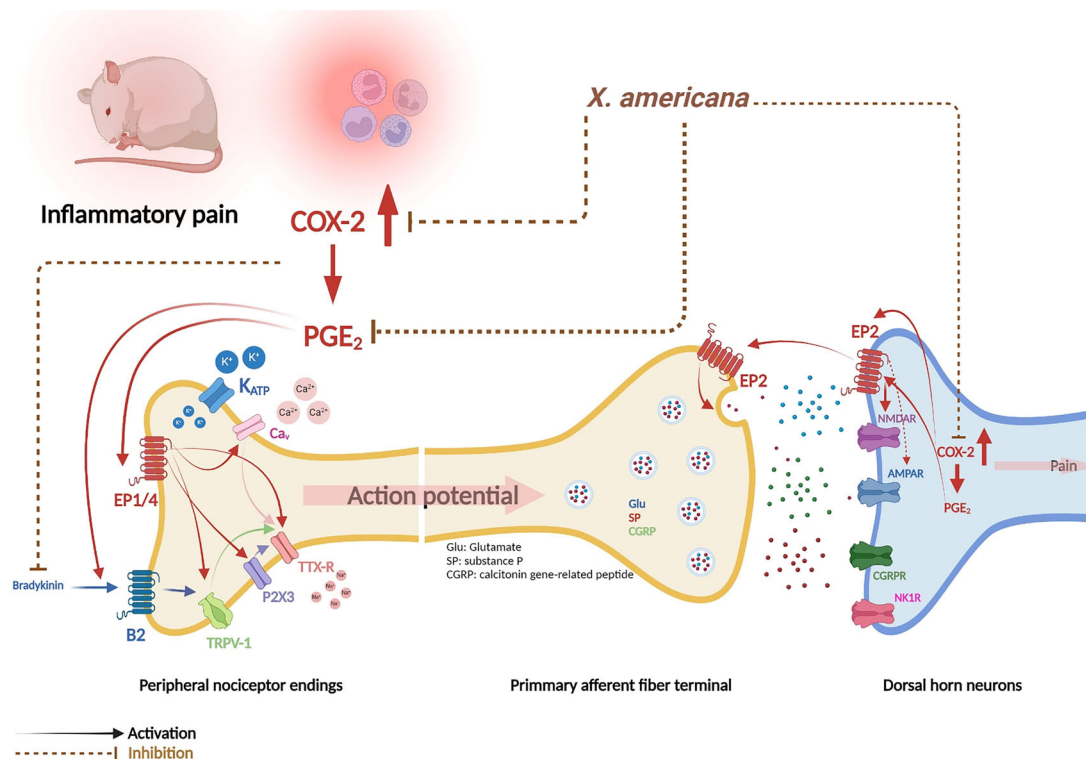


FIGURE 17 | Possible mechanism in inflammatory pain of *Ximenia americana*. COX, cyclooxygenase; PGE₂, prostaglandin E₂; TRPV-1, transient receptor potential vanilloid-1.

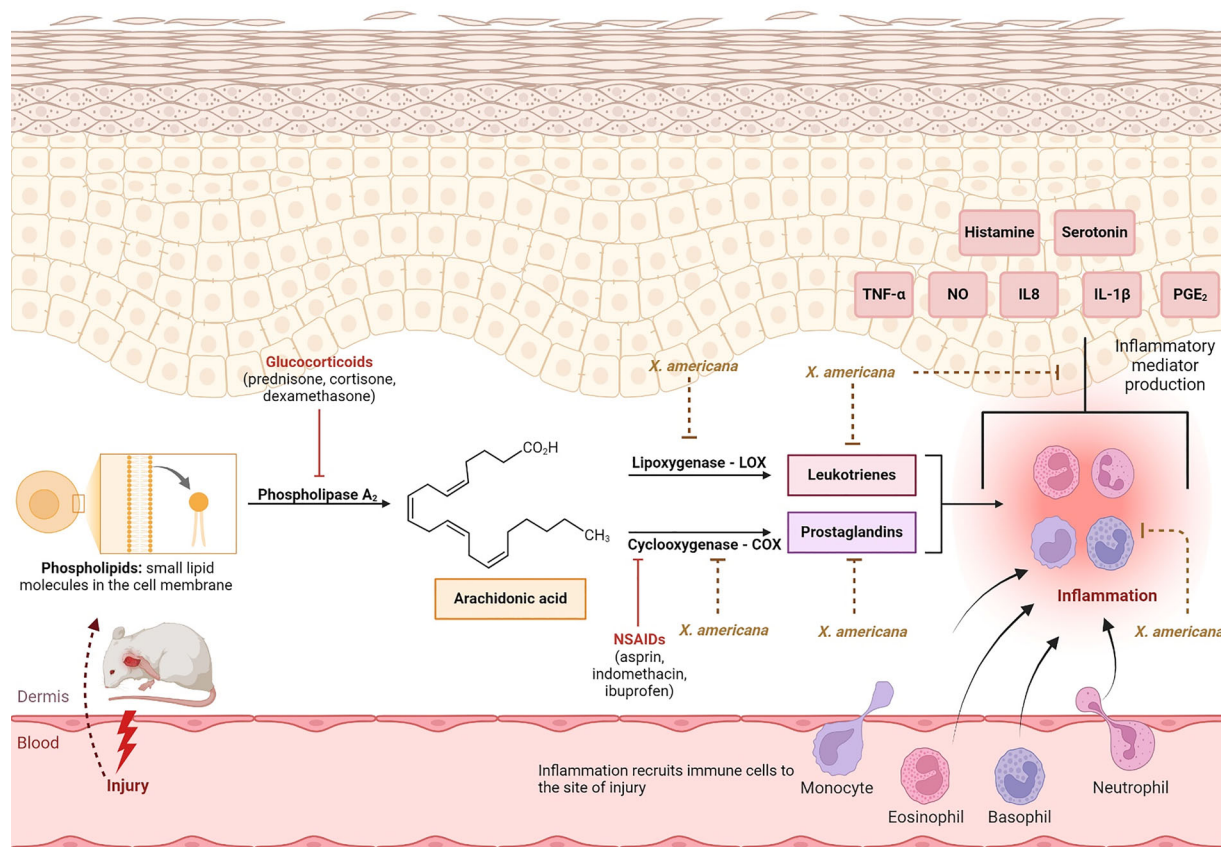


FIGURE 18 | Possible anti-inflammatory mechanism of action of *Ximenia americana*. COX, cyclooxygenase; IL-1β, interleukin-1β; IL-8, interleukin-8; LOX, lipoygenase; NO, nitric oxide; TNF-α, tumor necrosis factor-alpha.

lution of inflammation. During this process, there is an elevated production of ROS, reactive nitrogen species (RNS), TNF- α , ILs, COX-1, and COX-2, which act as inflammatory bioindicators in host cells (Chen et al. 2013; Gonfa et al. 2023).

Protein denaturation, which occurs when a protein loses its natural structure and biological function, is strongly related to several inflammatory factors and plays an important role in inflammatory responses. This process may be crucial for inflammation, a normal and complex immune response to damage or infection, involving a series of molecular events. Protein denaturation is one of the main factors involved in the induction of inflammation (Gonfa et al. 2023). Lipid peroxidation, generated by free radicals, is responsible for causing this damage. Stabilization of cell membranes can prevent the leakage of serum proteins and fluids into tissues. Increased membrane permeability acts as an intermediate step in this inflammatory process (Yesmin et al. 2020). Furthermore, *X. americana* has an inhibitory effect on protein denaturation, corroborating its anti-inflammatory properties and benefits in reducing lipid peroxidation (Shettar et al. 2015; Marques et al. 2020; Ballo et al. 2023; Meleh Umar et al. 2023).

In this context, *X. americana* showed antiedematogenic and anti-inflammatory effects, reducing leukocyte migration, as well as the activity of the enzymes 15-LOX, COX-1, and COX-2. In addition, there was a decrease in the levels of inflammatory mediators, such as vasoactive amines (histamine and serotonin), IL-1 β , IL-8, NO, PGE₂, and TNF- α . Its administration was effective in reducing edema, inflammatory infiltration, acinar cell necrosis, and total scores and decreasing MPO activity in pancreatitis models. On the basis of the analysis of the studies, we suggest that *X. americana* exerts its anti-inflammatory effect through the regulation of COXs and LOX, reduction of lipid peroxidation and, mainly, by decreasing inflammatory mediators that impact the recruitment of leukocytes to the site of inflammation (Figure 18).

It is important to highlight that *X. americana* is a medicinal plant widely used in the treatment of gastrointestinal and respiratory disorders, general inflammation, and painful conditions, with some of these applications being scientifically validated, as described in this systematic review. However, it is essential to note that many studies present evidence of limited methodological quality, predominantly based on in vitro and in vivo models.

Additionally, there is a scarcity of clinical trials in humans, which restricts the extrapolation of preclinical findings and limits the consolidation of the species' translational applicability. Therefore, there is a clear need for well-designed clinical investigations to robustly evaluate the efficacy and safety of *X. americana* for therapeutic use in humans.

A limitation of this systematic review was the impossibility of performing a comparative analysis through meta-analysis due to the heterogeneity of the protocols employed in the studies analyzed. Nevertheless, this work contributes by identifying gaps in the current scientific knowledge and suggesting directions for future research, including the conduction of controlled clinical trials to validate the existing preclinical evidence.

5 | Conclusion

X. americana is a plant widely used in folk medicine for the treatment of several inflammatory disorders. It has antinociceptive activity in inflammatory pain involving the inhibition/modulation of PGE₂, TRPV-1 receptor, and K_{ATP} channels via EP1 and EP2 receptors, as well as by increasing the expression of cannabinoid type 2 receptors (CB2). It also has anti-inflammatory activity through the modulation of inflammatory mediators, including vasoactive amines (histamine and serotonin), IL-4, IL-8, NO, PGE₂, IL-1 β , TNF- α , and reduction of lipid peroxidation. Other activities demonstrated by this plant include its potent antioxidant effects. It is concluded that *X. americana* is an important plant species that may become promising in the pharmaceutical industry for the elucidation of new bioactive molecules for the treatment of inflammatory conditions.

Author Contributions

Bruno Anderson F. Silva, Eduardo S. Silva, Lucas Yure S. Silva, Renata Torres Pessoa, Maria Gabriely de Lima Silva contributed to the systematic literature review, data collection, and writing of the manuscript. Laurent Picot, Silvio C. Alves-Júnior, Jullyana S. S. Quintans performed the phytochemical and pharmacological data analysis and contributed to the critical discussion of findings. Irwin Rose A. Menezes, Lucindo J. Quintans-Júnior coordinated the research project, contributed to conceptualizing the study, and revised the manuscript for intellectual content and final approval.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

No data were used for the research described in the article.

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