Advances in Traditional Medicine
https://doi.org/10.1007/s13596-024-00764-z

REVIEW

Maclura tinctoria (L.) D. Don ex Steud. (Moraceae): a review of the advances in ethnobotanical knowledge, phytochemical composition, and pharmacological potential

Patricia Quintero-Rincón[1,2] · **Yina Pájaro-González**[1,3] · **Fredyc Diaz-Castillo**[1]

Received: 11 March 2024 / Accepted: 26 May 2024

Abstract

Maclura tinctoria (Moraceae), commonly known as dinde, is a lactescent tree of significant economic importance with extensive ethnomedicinal and ethnobotanical applications. Among native populations in the Neotropics, dinde is used to address diverse forms of inflammatory arthritis, along with ailments stemming from viral, bacterial, or fungal origins. Its efficacy stands out notably in the treatment of conditions affecting the buccal cavity, respiratory tract, and venereal infections. These medicinal attributes have spurred investigations into their potential for developing nutraceuticals and pharmacological agents. Also, dinde has a commercial appeal intertwined with the remarkable qualities of its wood, which include the resistance to moisture and termites. This review consolidates information encompassing peer-reviewed articles from major scientific databases such as Science Direct, Scopus, Springer, PubMed, and Google Scholar. The review spans fifty-four phytocompounds, characterized by remarkable structural complexity and identified from the year 2000 onward. These compounds are categorized into flavones, isoflavones, flavonols, flavanols, flavanones, chalcones, and xanthones, where a significant portion exhibiting glycosylation or prenylation. Additionally, phenolic acids and condensed tannins contribute to the chemical diversity of this species. This comprehensive review offers updated insights into the potential bioactivity of chemical constituents identified in this plant, elucidating findings derived from different studies employing both in vitro and in vivo assays.

✉ Patricia Quintero-Rincón
patriciaquintero@gmail.com;
patricia.quintero1@udea.edu.co

✉ Fredyc Diaz-Castillo
fdiazc1@unicartagena.edu.co

Yina Pájaro-González
yinapajaro@uniatlantico.edu.co

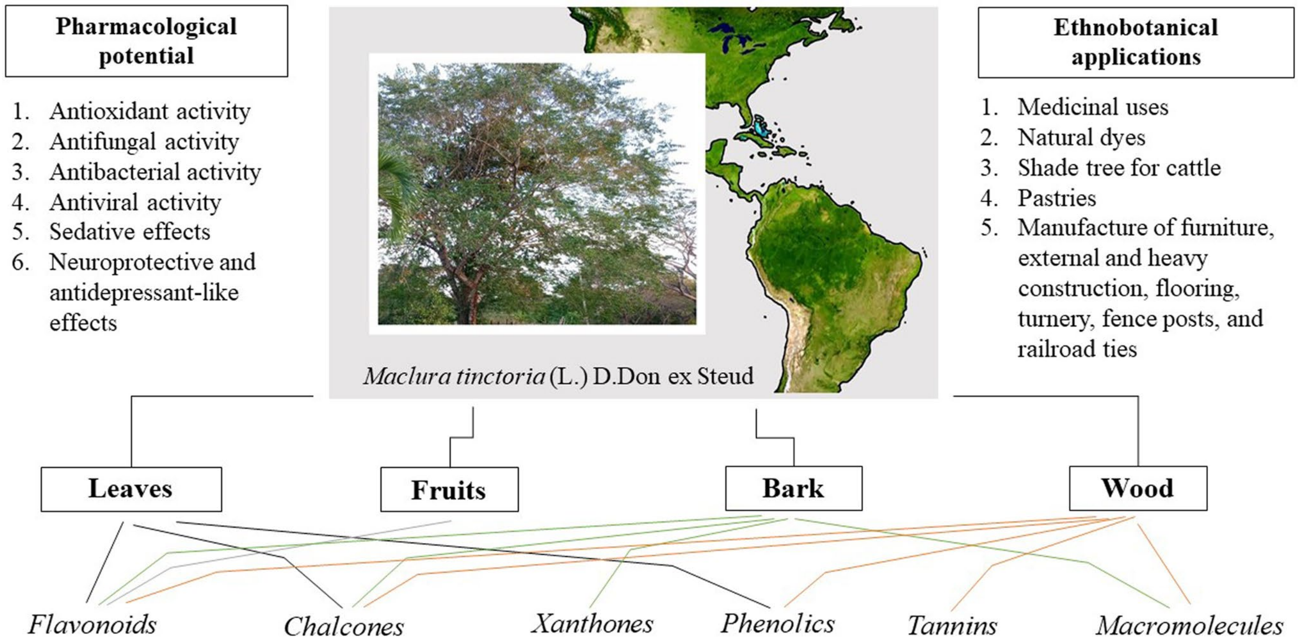
1 Phytochemical and Pharmacological Research Laboratory of the Universidad de Cartagena (LIFFUC), Faculty of Pharmaceutical Sciences, Universidad de Cartagena, Cartagena 130001, Colombia

2 Research Group Design and Formulation of Medicines, Cosmetics, and Related, Faculty of Pharmaceutical and Food Sciences, Universidad de Antioquia, Medellín 050010, Colombia

3 Research Group in Healthcare Pharmacy and Pharmacology, Faculty of Chemistry and Pharmacy, Universidad del Atlántico, Barranquilla 080001, Colombia

Published online: 20 June 2024

Graphical abstract



Keywords Sustainable uses · Moraceae · *Maclura tinctoria* · Phytochemistry · Ethnobotanical approach · Pharmacologic potential

Introduction

Maclura is a genus of the Moraceae family, which is represented by plant species of economic importance due to producing valuable wood and medicinal properties (Oyama and Souza 2011; Yang et al. 2022a, b). The Moraceae family is predominantly tropical and presents approximately 1500 species grouped into 63 genera (Oyama and Souza 2011; Lamounier et al. 2012). The genus *Maclura* is composed of 10–12 species of trees and woody climbers distributed on all continents, except Antarctica (Gardner et al. 2017). In America, three species have been reported, *M. pomifera*, *M. tinctoria*, and *M. brasiliensis* (Lamounier et al. 2012; Pájaro-González 2023). *Maclura tinctoria* (L.) D. Don. Steud. (syn. Morus, Broussonetia, Fusticus, or *Chlorophora tinctoria*), commonly known as dinde, moral, palo de mora, palo amarillo (Lachance et al. 2001), mulberry, taíuva (Battilani et al. 2006), amoreira, amarelinho (Lamounier et al. 2012), and tajuva (Coldebella et al. 2021), is a native tree with a wide Neotropical distribution (Amais et al. 2021) and is considered an important economic and cultural resource throughout Latin America since it offers multiple ecosystem services, mainly provision, regulation, and cultural services (Montes-Londoño et al. 2018).

It has been reported that the fruits of *M. tinctoria* are edible and have high nutritional value (Oyama et al. 2013). The leaves, sap, bark, and wood, including fruits, are important natural sources of molecules with therapeutic properties, including flavonoids, chalcones, xanthones, phenolics, and tannins, which support their use in traditional medicine for treating colds, oral infections, relief of toothaches, as a purgative and diuretic, venereal diseases, gout, and rheumatism (Lamounier et al. 2012; Camargo et al. 2022). Santos-Buelga et al. reported that the chemical properties of the organic extracts obtained from *M. tinctoria* are affected by temperature, light, and environmental conditions (Santos-Buelga et al. 2019); however, the microencapsulation technique has been recommended as a viable alternative to preserve the properties of its extracts (Diaz et al. 2021).

This species has been recognized as a natural source of morin **1**, a flavonol with antioxidant, anti-inflammatory, antiarthritic, antifertility, antiplasmodial, and anticancer properties (Mbaveng et al. 2014; Jangid et al. 2018). One of the most important attractions of the dinde is its wood, which is durable and resistant to rot and termites. However, due to low germination rates (~30%) and indiscriminate use of its wood, *M. tinctoria* is considered endangered (Gomes et al. 2010).

The economic, cultural, and medicinal significance of *M. tinctoria* has driven the ethnobotanical, phytochemical, and biological studies focused on this species. This review aims to present up-to-date information to guide future research on the potential advantages of this plant.

Methodology

Information presented was collected using electronic searchers for articles published in peer-reviewed journals (Science Direct, Scopus, Springer, PubMed, and Google Scholar). The search terms were "*Maclura tinctoria*" and "phytochemistry" or "ethnobotanical" or "ethnopharmacology" or "biological activities" from 2000. Relevant original articles, scientific research in the area of interest, and crucial reference articles were used as inclusion criteria. Some botanical aspects of the plant were taken from "The World Flora Online (WFO)". Duplicate publications and irrelevant articles were excluded.

Botanical description, habitat, and global distribution

Description. Tree species are 10–20 m tall and 40–60 cm in diameter, dioecious, thorny, lactescent, and semideciduous (Battilani et al. 2006). *Leaves*: the leaves are ovate, elliptic, or obovate, measuring 6–13 cm in length and 2–6 cm in width. They have a pointed to attenuate apex and a mostly asymmetric base, which can be obtuse to truncate, rounded, or slightly cordate. The margins are serrated or toothed, especially on the distal part. The upper surface of the leaves is either glabrous or slightly scabrous, while the veins on the lower surface are visible. *Petioles and stipules*: the petioles are 5–11 mm long, connecting the leaves to the stem. The stipules are paired, deciduous, and measure 3–6.2 mm in length. *Inflorescences*: the flowers of *M. tinctoria* are arranged in solitary inflorescences (WFO 2022). *Fruits*: the fruit originates from the subglobose female inflorescence, oblong and formed by compressed nutlets, with a sweet, fleshy pericarp; indehiscent, and greenish-yellow when mature (Battilani et al. 2006). The ovule is anacampylotropous, suspended, bitegmic, and crassinucellate. Mature seed flattened, slightly ovated, cream-colored, with unspecialized membrane coat with thin-walled cells more or less crushed. Seeds: the seed has a parenchymatic endosperm with lipophilic content. The embryo is straight, with two cotyledons of the same size. Ontogenetic studies have revealed that fruits are infructescences (Oyama and Souza 2011). *Habitat*: Humid and dry tropical forest (Lachance et al. 2001; Cioffi et al. 2003), common in the Pacific and north-central zones with an altitudinal elevation range of 0–1500 m.a.s.l. (Bernal et al. 2019). *Distribution*. From México to Central America, and South America (even Argentina), including the Antilles (WFO 2022).

Some botanical and phytochemical aspects of *M. tinctoria* are shown in Fig. 1.

Ethnobotanical applications

The tree of *M. tinctoria* is leafy and serves as a shade tree for cattle (Gomes et al. 2003). Peel, leaves, and stem segments produce a milky liquid that has been used in folk medicine for the treatment of different pathologies (Gomes et al. 2010). The tree produces edible and juicy fruit, with a very nice and sweet flavor, which is consumed either alone or in juices mixed with wine and in pastries (Lamounier et al. 2012). The fruit is attractive to local fauna (Coldebella et al. 2021) and contains a large number of seeds that quickly become nonviable (Gomes et al. 2003).

The wood of *M. tinctoria* is characterized by being moderately heavy, flexible, and very durable (Lamounier et al. 2012). This species resists adverse conditions related to humidity and climate and is highly resistant to xylophagous organisms (Oyama and Souza 2011; Lamounier et al. 2012). These characteristics make wood an appropriate resource for the manufacture of furniture, external and heavy construction, flooring, turnery, fence posts, and railroad ties. It has been introduced for production, conservation, and restoration purposes in agricultural landscapes and is recommended for shipbuilding (Lamounier et al. 2012). Furthermore, the wood has a beautiful golden sheen due to a yellow dye called fustic (from which morin **1** is extracted), historically used to dye brown, yellow, khaki, and green textiles (Montes-Londoño et al. 2018). Currently, *M. tinctoria* syncarps (accessory fruits ~ 2 cm in diameter) are frequently used to produce yellow dye for dyeing fabrics (Gardner et al. 2017). Morin **1** is also used to perform spot tests for certain metal ions (Oyama et al. 2013) and plays a role in preventing fungal attacks (Lachance et al. 2001).

Maclura tinctoria has been used to explore the creation of various combinations and alternatives for the incorporation of fibers (low-density polyethylene) and natural substrates within a polymeric matrix to determine its potential use as reinforcement or filler material and to evaluate its potential as an agent that promotes the biodegradation of the material (Nikolaeva et al. 2015).

Uses in traditional medicine

Native populations of the Neotropics use stem resin, leaves, stem segments, and bark infusion from *M. tinctoria* for the treatment of several illnesses. The leaves are used as a dressing after tooth extractions to prevent pain and swelling, and it has been reported that the extract acts as a natural biocide against bacteria in the oral cavity

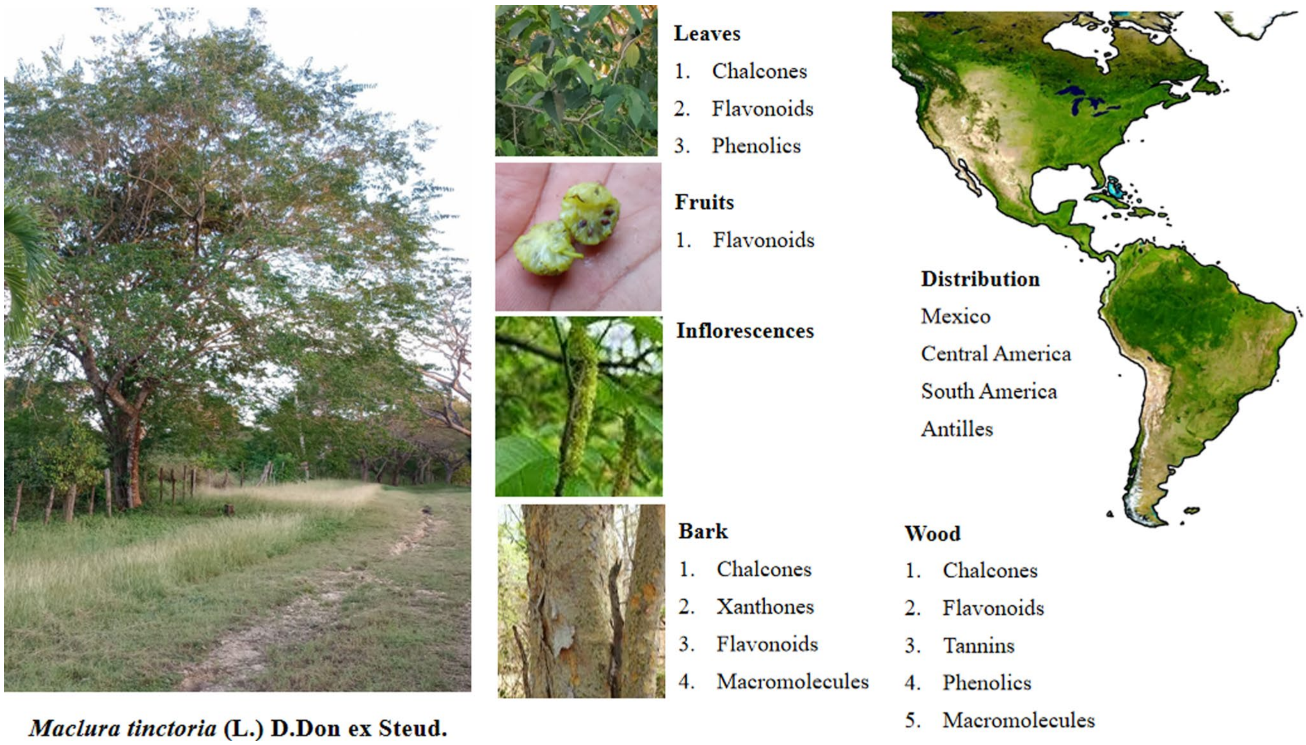


Fig. 1 Botanical and phytochemical aspects of *M. tinctoria*

(Coldebella et al. 2021). These anti-inflammatory properties have also been approached by Guarani-Kaiowá indigenous people in Brazil and the Amazonian indigenous community in Bolivia, who use infusions of the bark against toothache (Gomes et al. 2003; Bueno et al. 2005; Oyama et al. 2013). The use of this species extends to wound management due to its healing properties. It is also useful for the treatment of hernias (Gomes et al. 2010). In Latin America, *M. tinctoria* is used to treat urinary tract infections, coughs, gout, pharyngitis, rheumatism, sore throat, and syphilis (Oyama et al. 2013).

Phytochemical composition

To date, fifty-four phytocompounds isolated mainly from the leaves, fruits, bark, and wood of *M. tinctoria* collected in Bolivia, Brazil, Colombia, Mexico, Peru, and Venezuela have been identified. These phytocompounds are classified into different groups, including flavonoids (**1–33**), chalcones (**34–42**), xanthones (**43–46**), phenolic acids (**47–53**), and tannins (**54**).

Table 1 summarizes the country where the plant material was collected, the specific part of the plant used, and the extraction solvent used.

Flavonoids

Flavonoids are the most abundant, ubiquitous, and structurally diverse secondary metabolites of the plant kingdom (Mathesius 2018; Ateba et al. 2019). Currently, these are some of the most studied compounds due to their versatile biological properties, making them attractive for studying new therapeutic agents in both the pharmaceutical and healthcare industries. In plants, flavonoids exert protective functions against many biotic and abiotic stressors (UV radiation, herbivores, heat, cold, salinity), serve as phytoalexins and exogenous antioxidants, and participate in the regulation of photosynthesis, morphogenesis, and growth factors, among others (Górniak et al. 2018). The ability of flavonoids to neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS) has led to a much deeper pharmacological investigation, and their potential has been demonstrated in multiple pathologies related to inflammatory processes, including cancer (Ullah et al. 2020), inflammatory bowel diseases (Pei et al. 2020), age-related neurodegenerative diseases such as dementia, Parkinson's and Alzheimer's disease (Ullah et al. 2020), and other medicinal benefits, such as the management of topical infections and wounds (Sychrová et al. 2022), as well as cardioprotective properties (Ciumărnean et al. 2020).

Table 1 Results of phytochemical studies of *M. tinctoria*

Country and date of collection	Part of the plant/solvent of extraction	Group of extracted compounds	References
Peru, Feb. 1988	Bark/dichloromethane: methanol (1:1)	Xanthones (prenylated), flavonoids	Groweiss et al. (2000)
Venezuela, Oct. 1994	Leaves/95% ethanol	Chalcones, flavonoids (prenylated)	ElSohly et al. (2001)
Bolivia, Sept. 1998	Stem bark/methanol	Chalcone (glycosides), flavonoids	Cioffi et al. (2003)
Brazil, Feb. 2007	Wood and bark/cyclohexane: ethanol (1:2, v/v), 95% ethanol and water	Macromolecules	Lamounier et al. (2012)
Brazil, Dec. 2008	Fruits/methanol	Flavonoids (prenylated)	Oyama et al. (2013)
Brazil, not date	Leaves/dichloromethane and metha-nol, 1:1	Flavonoids (prenylated)	das Chagas Almeida et al. (2019)
Mexico, not date	Fruit/50% ethanol	Phenolics, flavonoids (glycosides)	Diaz et al. (2021)
Brazil, not date	Leaves/ethanol	Phenolics, flavonoids (glycosides)	Pires et al. (2021)
Brazil, not date	Bark/ethanol	Phenolics, flavonoids (glycosides)	Pires et al. (2021)
Brazil, not date	Heartwood/ethanol	Phenolics, flavonoids (glycosides)	Pires et al. (2021)
Brazil, not date	Sapwood/ethanol	Chalcones, phenolics, flavonoids, phenylpropanoids	Pires et al. (2021)
Brazil, not date	Leaves/water	Phenolics, flavonoids, aromatic aldehydes	Camargo et al. (2022)
Colombia, not date	Leaves/ethanol	Flavonoids (prenylated)	Pájaro-González (2023)

In general, flavonoids are synthesized from phenylalanine. These are composed of two benzene rings (A and B) linked by a heterocyclic ring containing oxygen (C). As shown in Fig. 2, depending on the connection between the B and C rings, the structure of the B ring, the level of unsaturation, and patterns of hydroxylation, methylation, glycosylation, and prenylation of the three rings, flavonoids can be grouped into different subclasses, which include flavones, flavonols, flavanols, flavanones, flavanonols (2-phenylchromen subclasses), and isoflavones (3-phenylchromen subclasses), among others (Górniak et al. 2018; Maleki et al. 2019; Ciumărnean et al. 2020). These diverse patterns afford complexity and diversity in flavonoid structures and influence solubility, stability, bioavailability, and biological activities (Maleki et al. 2019). For example, glycosylation patterns include both O-glycoside and C-glycoside (Ji et al. 2020). The type of sugar (mainly glucose, rhamnose, and apiose), number, and location of substitution exert unique properties in flavonoid glycosides (increase in water solubility, toxicity decreased, improved specific targeting, rapid absorption,

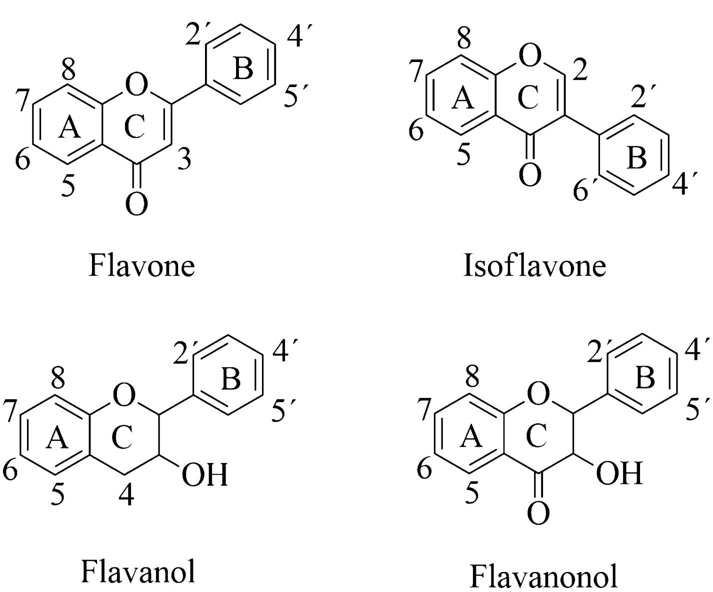


Fig. 2 Different subclass backbones of flavonoids

and easy metabolism: glucuronidation, methylation, and others) in contrast to their corresponding aglycones (Yang et al. 2018; Al-Maharik 2019; Ciumărnean et al. 2020; Ji et al. 2020). Other molecules with enormous biological potential are prenylated flavonoids. These flavonoids combine a subclass of backbone and prenyl side chain(s), which increases lipophilicity and membrane permeability (Ateba et al. 2019). Prenylated compounds of this type, exhibit anticancer, anti-inflammatory, neuroprotective nutraceutical, antifungal, antibacterial, antiviral, antioxidant, antidiabetic, estrogenic, and vasorelaxant properties (Kushwaha et al. 2020; Osorio et al. 2021; Wen et al. 2022).

Phytochemistry studies of *M. tinctoria* have (tentatively) identified flavonols: morin **1**, quercetin **2**; flavones: apigenin **3**, luteolin **4**; flavone glycosides: isoorientin **5**; isovitexin **6**, kaempferol-3-O-rutinoside **7**; prenylated flavones: dinklagin B **8**, dinklagin C **9**; di-prenylated flavones: cudraflavone C **10**, dihydrocudraflavone B **11**, ulexone B **12**; isoflavone: genistein **13**; prenylated isoflavones: alpinum isoflavone **14**, derrone **15**, isoderrone **16**, licoflavonol **17**, luteone **18**, wighteone **19**, isowighteone **20**; di-prenylated isoflavones: 6,8-diprenylorobol **21**, isocyclomulberrin **22**, ulexin D **23**; flavonol glycoside: quercetin-3-O-galactoside **24**; flavanols: catechin **25**, epicatechin **26**; flavanone: naringenin **27**; flavanone glycosides: eridictyol 7-O-beta-D-glucopyranoside **28**, naringenin 4´-O-beta-D-glucopiranoside **29**; prenylated flavanone: sigmoidin C **30**; di-prenylated flavanones: cudraflavanone A **31**, Euchrestaflavanone **32**, and flavanonol: taxifolin **33** (Fig. 3).

Many of these compounds are currently being investigated. A brief review of research articles on the biological effects of these compounds (in vitro and in vivo) is mentioned in Table 2.

Chalcones

Chalcones are natural precursors of flavonoids (chalcone subclass backbone) and isoflavonoids (dihydrochalcone subclass backbone) (Fig. 4). In brief, these are aromatic ketone and enone characterized by their ability to activate the nuclear factor erythroid 2-related factor (2NRF2) pathway (Wang et al. 2019). The chalcone family acts as a defensive system participating in plant–insect interactions, i.e., they are allelochemicals for plants (Batovska and Todorova 2010; Górniak et al. 2018). In vitro and in vivo studies have demonstrated that chalcones exert anticancer activity via multiple mechanisms (Ouyang et al. 2021) and exert antinociceptive (Mohamad et al. 2010), antiangiogenic (Mirossay et al. 2017), osteogenic (Ortolan et al. 2017), anti-inflammatory, antioxidant, and antimicrobial activities (Katsori and Hadjipavlou-Litina 2011). Natural chalcone-O-glycosides have demonstrated antimicrobial potential (Çelik 2020), while natural prenylated chalcones exhibit antioxidant, anti-inflammatory, and antiproliferation properties (Venturelli et al. 2016). Some synthetic prenylated chalcones have shown antileishmanial and antitrypanosomal potential (Passalacqua et al. 2015).

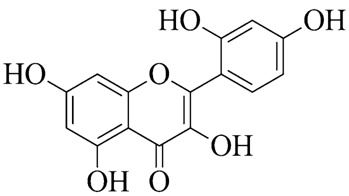
Phytochemistry analysis of *M. tinctoria* has identified eight chalcones grouped into prenylated chalcones: 2′,4′,4,2″-tetrahydroxy-3′-(3″-methylbut-3″-enyl)-chalcone **34**, bakuchalcone **35**, bavachromanol **36**, and isobavachalcone **37**; chalcone glycosides: phloridzin **38**, 4′-O-β-D-(2″-*p*-coumaroyl)glucopyranosyl-4,2′,3′-trihydroxychalcone **39**, 4′-O-β-D-(2″-*p*-coumaroyl-6″-acetyl) glucopyranosyl-4,2′,3′-trihydroxychalcone **40**, and 4′-O-β-D-(2″-acetyl-6″-cinnamoyl)glucopyranosyl-4,2′,3′-trihydroxychalcone **41**, and a prenylated chalcone glycoside: 3′-(3-methyl-2-butenyl)-4′-O-β-D-glucopyranosyl-4,2′-dihydroxychalcone **42**. The chemical structures of chalcones identified in *M. tinctoria* are shown in Fig. 5.

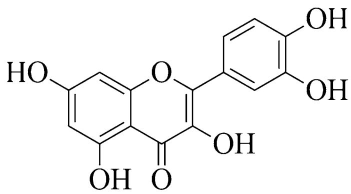
It is well known that some of these chalcones are bioactive and have been studied to deepen the knowledge about their biological activities (Table 3).

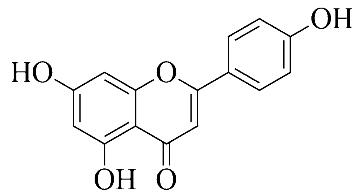
Xanthones

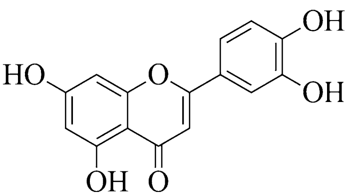
Xanthones are polyphenols synthesized from the shikimate and acetate pathways. Their structures and chromatographic behavior are related to those of flavonoids. Structurally, xanthones are composed of a tricyclic scaffold (Fig. 6), which can be modified by the addition of isoprene, sugar, methoxyl, and hydroxyl groups in the A and B rings (Gutierrez-Orozco and Failla 2013).

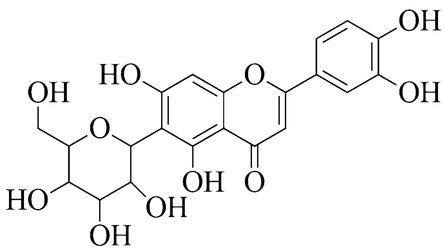
The study of the dichloromethane: methanol (1:1) extract of dinde bark has allowed the identification of diprenylated xanthones: macluraxanthone B **43**, macluraxanthone C **44**, gartanin **45**, and 8-desoxygartanin **46** (Groweiss et al. 2000). In general, some compounds of this type, exhibit anti-inflammatory effects (Xue et al. 2020), antiproliferative activity against breast, colon, and lung cancer cells (Gunter et al. 2022), protective potential of intestinal barrier integrity in HT-29 cells (Tocmo et al. 2021), and act as inhibitors of lipopolysaccharide-stimulated nitric oxide production in RAW 264.7 cells (Jo et al. 2017). A review of articles (PubChem) discussing the relationship between diprenylated xanthones identified in dinde and their biological effects indicates that macluraxanthone B **43** and macluraxanthone C **44** exhibit moderate in vitro antiviral activity against HIV (Pham et al. 2020), while gartanin **45** inhibits the growth of prostate cancer lines via autophagy initiation (Kim et al. 2015; Luo et al. 2017), exhibits an antiproliferative effect in T98G cells (Gao et al. 2016), and exerts neuroprotective effects (Dai and Mumper 2010), among other bioactivities. The chemical structures of chalcones identified in *M. tinctoria* are shown in Fig. 7.

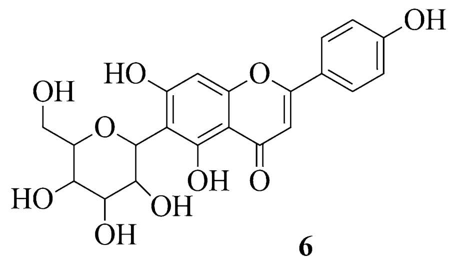

1

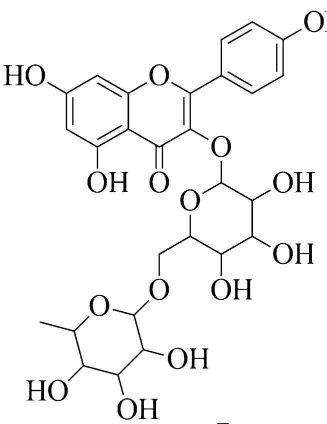

2

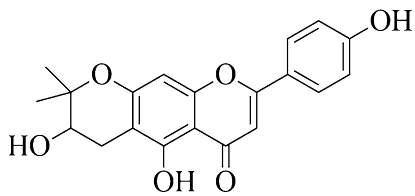

3

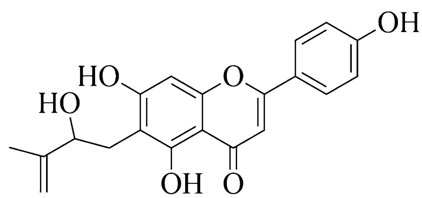

4

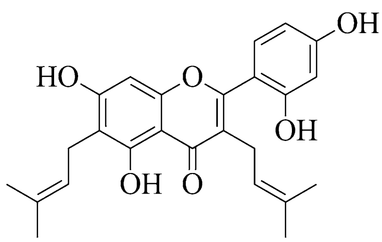

5

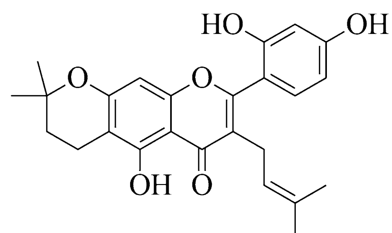

6

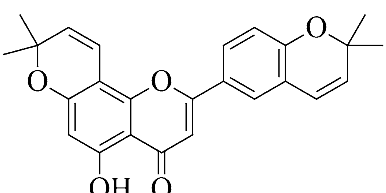

7

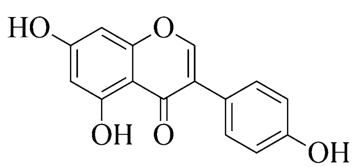

8

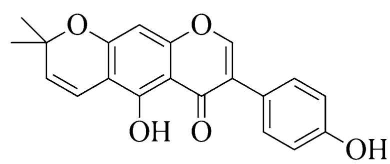

9

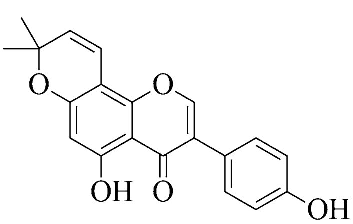

10

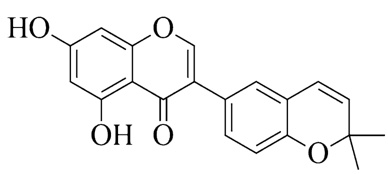

11


12


13


14


15


16

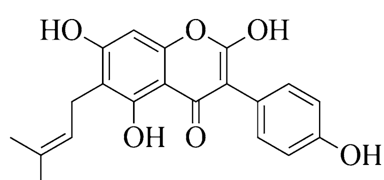
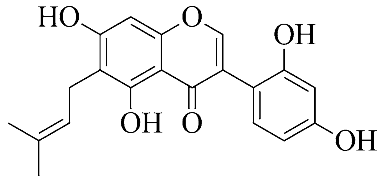
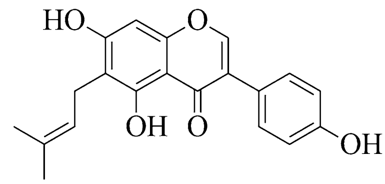

17

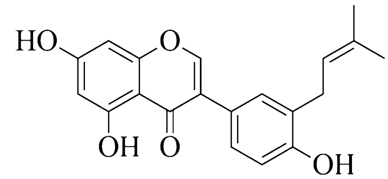
Fig. 3 Structures of flavonoids (**1–33**)



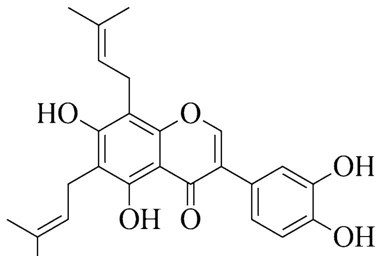
18



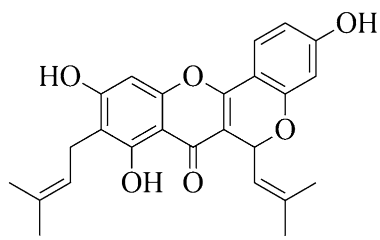
19



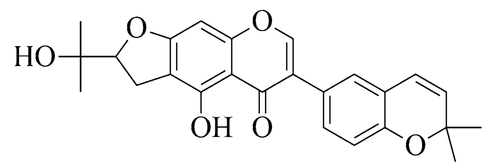
20



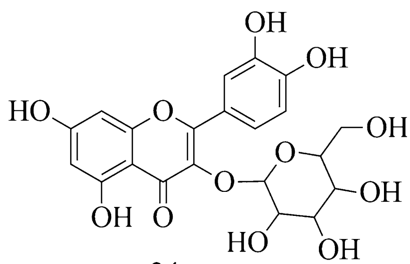
21



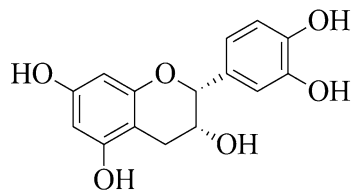
22



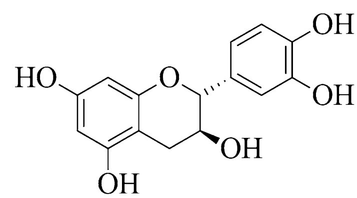
23



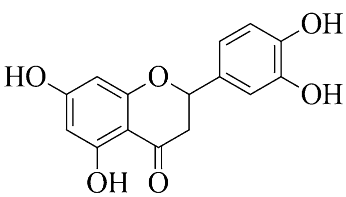
24



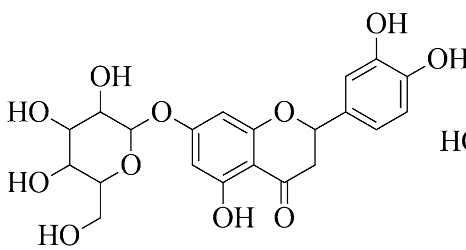
25



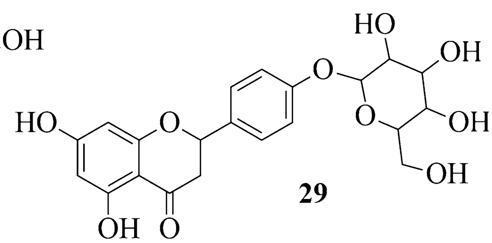
26



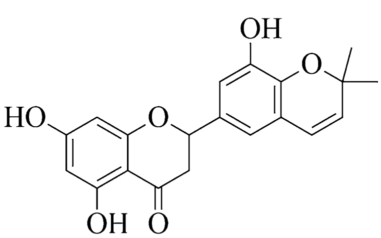
27



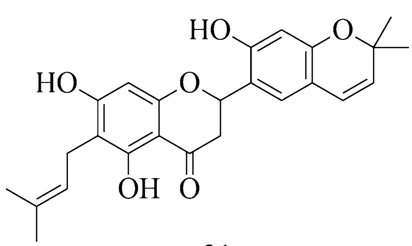
28



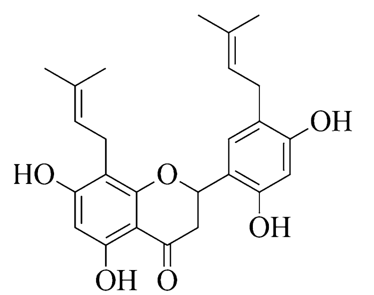
29



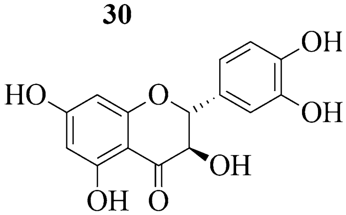
30



31



32



33

Fig. 3 (continued)

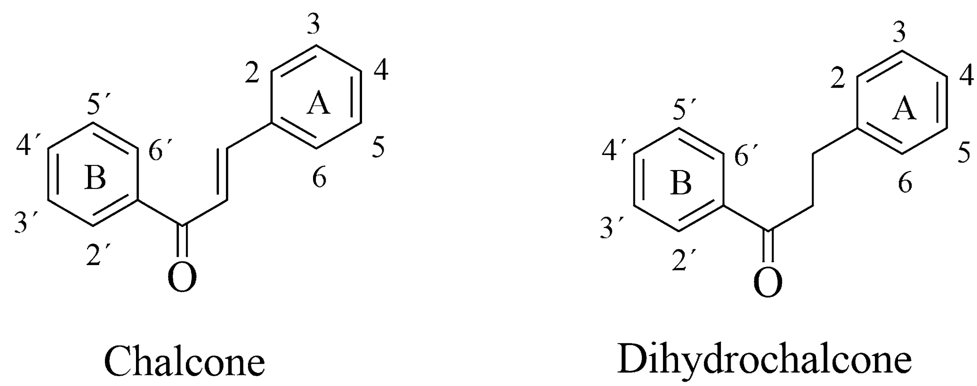
Table 2 Research articles (PubChem) discussing the relationship between some flavonoids identified in *M. tinctoria* and their biological effects

Flavonoids (subclass backbone)	Biological effects	References
Morin **1** (flavonol)	Exhibits vasorelaxant effects Ameliorates chronic restraint stress-induced biochemical disruption, neuronal, and behavioral dysfunctions in mice	Carullo et al. (2023) Akinluyi et al. (2022)
Quercetin **2** (flavonol)	Inhibits proliferation, migration, and invasion, blocks the cell cycle progression of lung squamous cell carcinoma (LUSC), and downregulates the expression of the LUSC target gene PLK1 at the protein level	Lu et al. (2022)
Apigenin **3** (flavone)	Ameliorates ulcerative colitis Antioxidant activity Protects against hepatorenal damage Ameliorates hyperuricemia and renal injury	Fu et al. (2022) Alghamdi et al. (2022) Fehaid et al. (2022) Liu et al. (2022a, b, c, d)
Luteolin **4** (flavone)	Alleviates neutrophilic asthma Inhibits the proliferation of NPC CNE2 cells and promoted cell apoptosis	Qiao et al. (2023) Xiong et al. (2022)
Isoorientin **5** (flavone glycoside)	Induces apoptosis and migration inhibition in gastric cancer AGS cells Ameliorates osteoporosis and oxidative stress in postmenopausal rats Ameliorates ovalbumin-induced asthma in a murine model of asthma	Sharma et al. (2022) Cao et al. (2022) Liang et al. (2022)
Isovitexin **6** (flavone glycoside)	Protects against lipopolysaccharide-induced renal injury and inflammation (protective autophagy) Regulates MAPK/NF-κB signal in mice with acute ulcerative colitis	Tseng et al. (2023) Liu et al. (2022a, b, c, d)
Kaempferol-3-O-rutinoside **7** (flavone glycoside)	Stimulates glucose uptake Exerts cardioprotective effects	Kashyap et al. (2023) Hua et al. (2022)
Cudraflavone C **10** (di-prenylated flavone)	Inhibits pathogenic, multidrug-resistant *S. aureus*, persisters, and biofilms Induces apoptosis of A375.S2 melanoma cells Induces tumor-specific apoptosis in colorectal cancer cells (KM12, Caco-2, HT29, HCC2998, HCT116, and SW48)	Meenu et al. (2021) Lee et al. (2017) Soo et al. (2017)
Dihydrocudraflavone B **11** (di-prenylated flavone)	HIV-inhibitory activity	Groweiss et al. (2000)
Genistein **13** (isoflavone)	Phytoestrogen actions on breast cancer Anti-inflammatory potential Inhibits the phosphoinositide 3-kinase (PI3K)-AKT pathway	Malik et al. (2023) Shete et al. (2023) Zhang et al. (2022)
Alpinum isoflavone **14** (prenylated isoflavone)	Antimicrobial activity	Akter et al. (2016)
Derrone **15** (prenylated isoflavone)	Inhibits platelet aggregation, granule secretion, thromboxane A2 generation, and clot retraction Induces autophagic cell death	Shin et al. (2021) Kang et al. (2019)
Isoderrone **16** (prenylated isoflavone)	α-Glucosidase inhibitory activity	Shi et al. (2022)
Licoflavonol **17** (prenylated isoflavone)	Reduces Aβ secretion (increases BACE1 phosphorylation to facilitate BACE1 degradation)	Gu et al. (2019)
Luteone **18** (prenylated isoflavone)	Antibacterial activity against sensitive (MSSA) and resistant strains (MRSA and MDRSA) of *S. aureus*	Akter et al. (2016)
Wighteone **19** (prenylated isoflavone)	Exhibits antitumor activity against EGFR L858R/T790M mutation non-small cell lung cancer	Sun et al. (2021)
6,8-Diprenylorobol **21** (di-prenylated isoflavone)	Inhibits strains of *S. aureus* sensitive (ATCC 29213) and resistant to methicillin (ATCC 33591) Inhibits endometriosis progression Induces apoptosis in LoVo and HCT15 cells Induces apoptosis in HepG2 and Huh-7	Pájaro-González 2023) Song et al. (2022) Choi et al. (2021) Lee et al. (2020)
Isocyclomulberrin **22** (di-prenylated isoflavone)	Exhibits cytotoxicity against hepatocellular carcinoma (SMMC-7721) and gastric carcinoma (BGC-823 and SGC-7901) cell lines	Ma et al. (2010)
Catechin **25** (flavanol)	Acts neutralizing SARS-CoV-2 Omicron variant Ameliorates hepatic encephalopathy Reduces blood pressure in hypertensive rats	Zhang et al. (2023a, b) Zhou et al. (2022) Elbarbry et al. (2022)

Table 2 (continued)

Flavonoids (subclass backbone)	Biological effects	References
Epicatechin **26** (flavanol)	Inhibits amyloid fibrillation of glaucoma-associated myocilin protein	Sharma et al. (2022)
Naringenin **27** (flavanone)	Reverses spinal sensitization and arthritic pain Exerts contradictory cytoprotective and cytotoxic effects on tamoxifen-induced apoptosis in HepG2 cells	Jiang et al. (2022) Xu et al. (2022)
Eridictyol 7-O-beta-D-glucopyranoside **28** (Flavanone glycoside)	Ameliorates lipid disorders Antioxidant properties	Liang et al. (2017) Cioffi et al. (2003)
Cudraflavanone A **31** (di-prenylated flavanone)	Anti-neuroinflammatory effects Inhibits vascular smooth muscle cell growth	Kim et al. (2018) Han et al. (2007)
Taxifolin **33** (flavanonol)	Ameliorates cigarette smoke-induced chronic obstructive pulmonary disease (inhibits inflammation and apoptosis) Reduces blood pressure in elderly hypertensive rats	Liu et al. (2023) Tukhovskaya et al. (2022)

Fig. 4 Different subclass backbones of chalcones



Phenolic acids

Phenolics are compounds possessing one or more aromatic rings with one or more hydroxyl groups. These compounds exert important functions in plants by acting as a defense mechanism against UV radiation or aggression by pathogens, predators, and parasites. Phenolic acids are considered the simplest molecules within the group of phenolic compounds (Działo et al. 2016). These molecules form a diverse group of phytocompounds that can be grouped into derivatives of hydroxybenzoic acid (e.g., gallic acid **47**) and derivatives of hydroxycinnamic acid (e.g., ferulic acid **48**). The wide biological properties of these compounds result from patterns and degrees of substitution in their basic structural skeletons (hydroxybenzoic and hydroxycinnamic acids) (Dong et al. 2022).

Phytochemical analysis of *M. tinctoria* has identified approximately eight phenolic compounds, including gallic acid **47**, ferulic acid **48**, *o*-coumaric acid **49**, *p*-hydroxybenzoic acid **50**, protocatechuic acid **51**, syringic acid **52**, and syringaldehyde **53** (Fig. 8) (Pires et al. 2021; Camargo et al. 2022). A brief review of articles that explore the pharmacological potential of the phenolic compounds identified in this plant indicates promising activities: neuroprotective activity (Cavichioli et al. 2022; Çelikezen et al. 2022; Sheikhpour et al. 2023), cytotoxic potential (Pinto et al. 2017), antidiabetic activity (Gan et al. 2023), and other interesting activities that make these compounds promising molecules for the development of therapeutic agents (Table 4).

Condensed tannins

Tannins are water-soluble secondary metabolites of variable chemical structures, characterized by their ability to precipitate proteins (Redondo et al. 2014). Their structural skeletons consist mainly of simple, oligomeric, and polymeric compounds. These can be hydrolyzable or condensed (Rauf et al. 2019). Condensed tannins are one of the most ubiquitous groups of all polyphenolics in the plant kingdom. These types of compounds confer astringency, a property that protects plants from pathogens and predators. Condensed tannins are oligomers or polymers of flavan-3-ol linked through an interflavan carbon bond, produced as an end product of the flavonoid biosynthetic pathway (Rauf et al. 2019). These compounds present structural diversity due mainly to variations in hydroxylation pattern, the stereochemistry at the three chiral centers, the degree of substitution (methoxylation, glycosylation, and galloylation), and the location and type of interflavan linkage (Koleckar et al. 2008; Shnawa et al. 2020). In *M. tinctoria*, A-type Procyanidin dimer **54**,

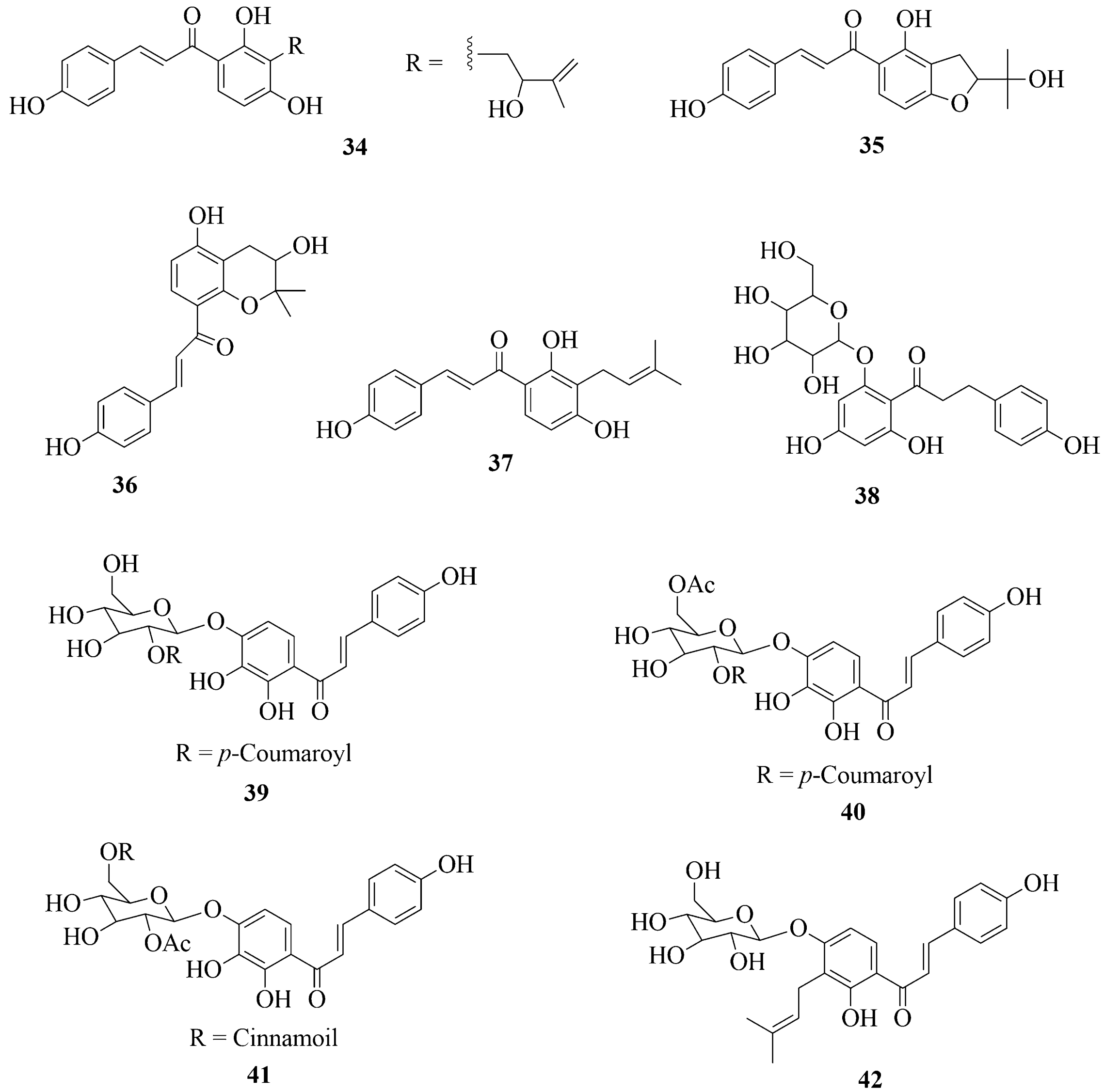


Fig. 5 Structures of chalcones (**34**–**42**)

a class of condensed tannins with strong anti-inflammatory and antiproliferative properties has been identified (Xie et al. 2023), which exerts protective effects against H_2O_2-induced oxidative stress in prostate cancer cells (Yan et al. 2021) (Fig. 9).

Pharmacological potential of extracts obtained from *M. tinctoria*

Antioxidant activity

ROS are byproducts of normal cellular metabolism produced by the electron transport chain. However, elevated ROS levels disrupt the homeostasis of the redox system and cause oxidative stress upon reacting with lipids, proteins, or nucleic acids (Nogueira and Hay 2013). Scientific evidence suggests that oxidative stress plays a pivotal role in both human health and disease. In this sense, lipid peroxidation by ROS causes cell membrane damage that is conducive to cell death (Ullah et al. 2020). Reactive oxygen species may lead to oxidation in both amino acid side chains and protein backbones that are associated with protein fragmentation or protein–protein cross-linkages (Zhang et al. 2013). Additionally, ROS may lead to the modification of cellular nucleic acids (Chao et al. 2013). In the search for new alternatives as antioxidant agents, the scavenging capacity of ROS, and the ability to decrease the production of ROS have been evaluated. Generally, sensitive techniques to identify antioxidant activity based on the ability to scavenge radical cations

Table 3 Research articles (PubChem) discussing the relationship between some chalcones identified in *M. tinctoria* and their biological effects

Chalcones (subclass backbone)	Biological effects	References
2′,4′,4,2″-tetrahydroxy-3′-(3″-methylbut-3″-enyl)-chalcone **34**, bakuchalcone **35**, and bavachromanol **36** (prenylated chalcones)	Antifungal against AIDS-related opportunistic pathogens (*Candida albicans* and *Cryptococcus neoformans*)	ElSohly et al. (2001)
Isobavachalcone **37** (prenylated chalcone)	Antifungal against AIDS-related opportunistic pathogens (*Candida albicans* and *Cryptococcus neoformans*) Activates antitumor immunity on orthotopic pancreatic cancer model Presents antibacterial activity against *Clostridium difficile* Exerts benefit effects for treating rheumatoid arthritis Ameliorates cognitive deficits Ameliorates diabetic nephropathy-Anti-neuroinflammatory effect Exerts anti-proliferative and pro-apoptotic effects	ElSohly et al. (2001) Liu et al. (2022a, b, c, d) Liu et al. (2022a, b, c, d) Wang et al. (2022) Zhang et al. (2021) Dong et al. (2020) Li et al. (2020) Li et al. (2019a, b)
Phloridzin **38** (dihydrochalcone glycoside)	Exerts antioxidant and anti-aging effects Exerts hepatoprotective effects Exerts beneficial effects against liver fibrosis Alleviates cholinergic memory impairment and regulates gut microbiota Exerts beneficial effects on blood glucose and key enzyme G-6-Pase of gluconeogenesis	Park and Park (2022) Yang et al. (2022a, b) Kang et al. (2019) Su et al. (2022) Wang et al. (2021)

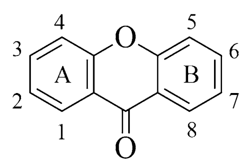
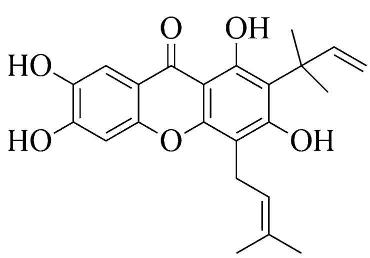


Fig. 6 Xanthone nucleus

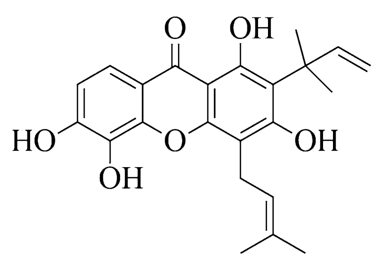
are used. In the evaluation of the antioxidant properties of extracts and phytocompounds isolated from *M. tinctoria*, DPPH and ABTS methods have been used. The DPPH assay determines the ability of antioxidants to scavenge the radical 1,1-Diphenyl-2-picrylhydrazyl, while the ABTS assay determines the ability of antioxidants to scavenge the radical cation [(2,2-azino-bis(3-etilbenzotiazolin)-6-sulfonic acid]. Oxidation of DPPH and ABTS results in the formation of a colored product, which can be determined spectrophotometrically in the range of 600–750 nm.

In this sense, Cioffi et al. evaluated the antioxidant activity of seven chalcones isolated from *M. tinctoria* stem

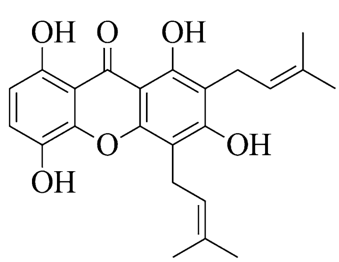
Fig. 7 Structures of xanthones (**43**–**46**)



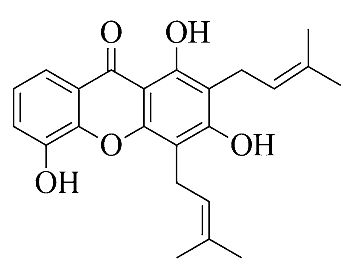
43



44



45



46

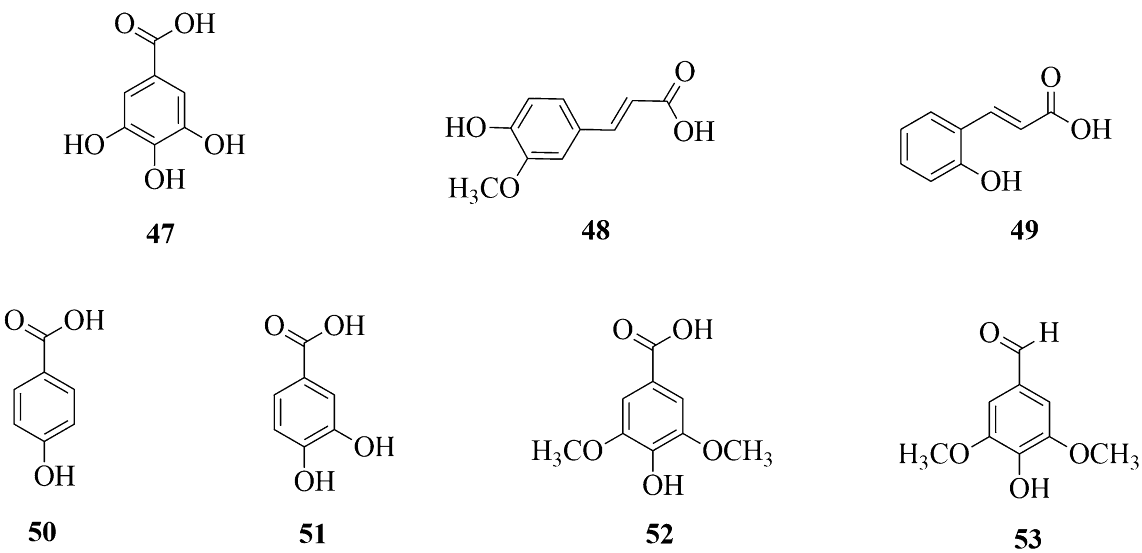
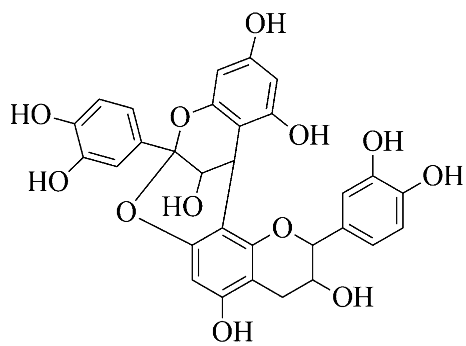


Fig. 8 Structures of phenolic acids (**47**–**53**)

Table 4 Research articles (PubChem) discussing the relationship between some phenolics (acids or aldehydes) identified in *M. tinctoria* and their biological effects

Phenolics	Biological effects	References
Gallic acid **47** (derivatives of hydroxybenzoic acid)	Inhibits neuroinflammation and reduces neonatal hypoxic-ischemic brain damage Improves symptoms of Parkinson's disease induced by rotenone Inhibits adipocyte differentiation Alleviates nonalcoholic fatty liver disease	Dong et al. (2022) Sheikhpour et al. (2023) Wu et al. (2023) Zhang et al. (2023a, b)
Ferulic acid **48** (derivatives of hydroxycinnamic acid)	Presents potential antiviral via activation of photosynthesis Exerts protective effects on metabolic syndrome Alleviates diabetes symptoms	Gan et al. (2023) Salau et al. (2022) Huang et al. (2018)
o-Coumaric acid **49** (derivatives of hydroxycinnamic acid)	Exerts antidepressant-like effect in mice, and antioxidant capacity in a plant extract (as a major component) Exerts selective cytotoxicity on neuroblastoma cells in a plant extract (as a major component) Exerts anti-ulcerogenic effects in a plant extract (as a major component)	Cavichioli et al. (2022) Çelikezen et al. (2022) Pinto et al. (2017)
p-Hydroxybenzoic acid **50** (derivatives of hydroxybenzoic acid)	Ameliorates colitis	Han et al. (2022)
Protocatechuic acid **51** (derivatives of hydroxybenzoic acid)	Attenuates the molecular, biochemical, and histological alterations associated with myocardial infarction development Ameliorates doxorubicin-induced cardiotoxicity	Li et al. (2023) Okpara et al. (2022)
Syringic acid **52** (derivatives of hydroxybenzoic acid)	Exerts anti-steatotic and anti-inflammatory effects Inhibits aldose reductase activity and prevents diabetic cataract pathogenesis Controls accumulation of inflammatory cells and markers, enhancements antioxidant markers, suppress reactive oxygen species, and controls airway hyperreactivity	Ham et al. (2016) Wei et al. (2012) Li et al. (2019a, b)
Syringaldehyde **53** (derivatives of hydroxybenzoic acid)	Effects on oxidative stress and inflammatory status in peripheral blood mononuclear cells	Shahzad et al. (2020)



54

Fig. 9 Structure of condensed tannin (**54**)

bark through the ABTS assay. The activity of the tested compounds was expressed as TEAC (Trolox Equivalent Antioxidant Capacity) values, which is defined as the concentration of standard 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox) with the same antioxidant capacity (1 mM concentration). Quercetin **2** was used as a reference compound. It was observed that the compound 3′-(3-methyl-2-butenyl)-4′-O-β-D-glucopyranosyl-4,2′-dihydroxychalcone **42** had a free-radical-scavenging activity of less potency with respect to quercetin **2**, 4′-O-β-D-(2″-*p*-coumaroyl-6″-acetyl) glucopyranosyl-4,2′,3′-trihydroxychalcone **40** and 4′-O-β-D-(2″-acetyl-6″-cinnamoyl)glucopyranosyl-4,2′,3′-trihydroxychalcone **41** had moderate activity, while naringenin **27** and naringenin 4´-O-β-d-glucopyranoside **29** were weakly active (Cioffi et al. 2003). The antioxidant activity of methanol extracts of wood and bark obtained from *M. tinctoria* was evaluated by DPPH assay. It was observed that the wood of dinde had a higher antioxidant activity than the bark, showing average effective concentration (IC_{50}) values of 18.7 ± 0.5 and 20.9 ± 0.6 µg/mL, respectively (Lamounier et al. 2012).

Antifungal activity

As previously mentioned, phytochemical and biological studies from *M. tinctoria* were conducted to evaluate the antifungal activity of 2′,4′,4,2″-tetrahydroxy-3′-(3″-methylbut-3″-enyl)-chalcone **34**, isobavachalcone **37**, bakuchalcone **35**, bavachromanol **36**, and 6,8-diprenylorobol **21** against AIDS-related opportunistic fungal pathogens (*Candida albicans* and *Cryptococcus neoformans*) using a modification of the protocol recommended by the National Committee on Clinical Laboratory Standards and amphotericin B as a positive control. The inhibitory activity of the sample was assessed as the minimum inhibitory concentration tested in which no growth was observed. Of all the compounds tested, isobavachalcone **37** was active against both yeasts (ElSohly et al. 2001).

Antibacterial activity

The antibacterial activity against the etiologic agents of dental caries of wood and bark extracts of *M. tinctoria* was tested by the broth microdilution method using *Streptococcus sanguinis* (ATCC 10556), *S. mitis* (ATCC 49456), *S. mutans* (ATCC 25175), *Prevotella nigrescens* (ATCC 33563), *Actinomyces naeslundii* (ATCC 19039), and *Porphyromonas gingivalis* (ATCC 33277). The most relevant results showed that the hydromethanolic extract of the bark has a minimal inhibitory concentration (MIC) of 80 µg/mL against the major etiologic agents. Furthermore, the cyclohexane: ethanol extract of the bark inhibited growth and showed some of the highest antibacterial activity with an MIC of 20 µg/mL for *P. nigrescens*, and 60 µg/mL for *A. naeslundii* and *P. gingivalis*, respectively. These results suggest that the bark of dinde is very promising for the development of protective agents against dental caries (Lamounier et al. 2012).

The antibacterial activity of ethanol extract obtained from *M. tinctoria* leaf was evaluated on *S. mutans* (ATCC25175) and *P. gingivalis* (ATCC33277) using broth dilution tests to determine the MIC and minimum bactericidal concentration (MBC). The bacteriostatic activity of the extract against *S. mutans* was observed at a concentration of 125 µg/mL, while the bactericidal activity was determined at higher concentrations (250 and 500 µg/mL). The ethanol extract was less active against *P. gingivalis*, and MIC and MBC values of 500 µg/mL were observed (Matson Robles et al. 2015).

das Chagas Almeida et al. (2019) demonstrated the antimicrobial activity of organic or aqueous extracts from dinde using *Galleria mellonella* larvae infected with *Staphylococcus aureus* by in vitro standard methods. An organic extract obtained from leaves showed the lowest MIC (0.08 mg/mL). Its fractionation led to fraction 11FO d (MIC of 0.04 mg/mL). This fraction showed strong activity against veterinary *S. aureus* isolates and contributed to the increased survival of *G. mellonella* larvae infected with *S. aureus* (ATCC 29213). The phytochemical study led to the identification of an enriched fraction in prenylated isoflavones and flavanones luteone **18**, wighteone **19**, euchrestaflavanone **32**, and cudraflavanone A **31** with possible antistaphylococcal properties.

The antibacterial activity of extracts obtained from leaves, bark, sapwood, and heartwood from dinde was evaluated against *Aeromonas hydrophila* (ATCC 7966), *A. hydrophila* (MF 372509), *A. hydrophila* (MF 372510), *A. hydrophila* (MH 397689), *A. veronii* (MH 397688), and *Escherichia coli* (ATCC 25922). The most important results indicated that the heartwood extract presented the lowest MIC and MBC against the six strains analyzed, compared to the evaluated extracts obtained from the other plant organs (leaves, bark, sapwood), where MIC values ranged from 400 to 1600 µg/mL, and MBC ranged from 800 to 6400 µg/mL (Pires et al. 2021).

Pájaro-González evaluated the antibacterial activity of crude ethanol extracts and toluene, chloroform, ethyl acetate, and methanol fractions obtained from *M. tinctoria* leaves against strains of *S. aureus* sensitive (ATCC 29213) and resistant to methicillin (ATCC 33591). It was observed that the dinde extract (FD-I-82H) inhibited growth with an MIC_{90} value of 64 µg/mL for all strains of *S. aureus*. Chloroform (82H-F02) and ethyl acetate (82H-F03) fractions were active, showing the same MIC_{90} range of 32 to 64 µg/mL), but the 82H-F03 fraction generated the most active subfraction (MIC_{90} range of 16 to 32 µg/mL), which was obtained with hexane: ethyl acetate 30% (82HF-13). From the 82HF-13 subfraction, an active compound against all strains tested (MIC_{90} of 8 µg/mL) with IC_{50} values > 10 µg/mL against MRC-5 fibroblasts was isolated. This active compound was identified as 6,8-diprenylorobol **21** (Pájaro-González 2023).

Antiviral activity

The organic extract of the bark from *M. tinctoria* exhibited moderate in vitro antiviral activity against HIV. Bioguided fractionation led to the isolation of diprenylated xanthones (macluraxanthone B **43**, macluraxanthone C **44**, gartanin **44**, and 8-desoxygartanin **45**), diprenylated flavones (cudraflavone C **9** and dihydrocudraflavone B **11**), and a diprenylated isoflavone (isocyclomulberrin **21**). Of these compounds, only macluraxanthone B **43** and macluraxanthone C **44** were identified as molecules responsible for this activity (Groweiss et al. 2000).

Sedative effects

The central depressant activity and long-term effects induced by ethanolic extracts of *M. tinctoria* (leaves, bark, sapwood, and heartwood) were evaluated in black catfish (*Rhamdia quelen*) to explore its possible sedative effects. In brief, the fish submitted to the extracts presented a light sedation induction profile (stage S2) characterized by the absence of reaction to external stimuli. The assay revealed that only the leaf extract at a concentration of 300 mg/L took the catfishes to the deep sedation stage (S3b). Exposure of black catfish to 30 mg/L heartwood extracts for 24 h mimicked a sedative profile previously detected, indicating a greater safety profile. Only the animals exposed to 100 mg/L of leaf extract presented a deepening of the sedation stages, with behavior similar to that observed for diazepam (DZP). The fish exposed to bark, sapwood, and heartwood at 30 mg/L presented a behavior similar to the vehicle control after 30 min, while those subjected to bark, sapwood, and heartwood at 100 mg/L only after 10 h of exposure. These results indicated that heartwood extract can be considered a promising sedative for catfish and its use can be evaluated in aquaculture (Pires et al. 2021).

Neuroprotective and antidepressant-like effects

The neuroprotective and antidepressant effects of *M. tinctoria* aqueous extract were evaluated by Camargo et al. against glutamate-induced toxicity and in a model of antidepressant-like effects in mice, respectively. It was demonstrated that repeated treatment with the aqueous extract at the lowest dose (1 mg/kg) was effective in abolishing the depressive-like phenotype, and this effect was comparable to fluoxetine administration (10 mg/kg). Furthermore, dinde aqueous extract (1 mg/kg) exhibited neuroprotective effects against glutamate-induced toxicity. These effects were attributed to flavonoids and phenolics identified in the extract, including quercetin **2**, catechin **25**, epicatechin **26** (major flavonoid), gallic acid **47**, ferulic acid **48**, syringic acid **52**, and syringaldehyde **53** (Camargo et al. 2022).

Conclusions

For centuries, the traditional use of medicinal plants has played a significant role in the therapeutic approach to various diseases. This property is associated with the wide range of phytocompounds identified in the different species, which confirms the folkloric uses of the plants. *Maclura tinctoria* is a tree of economic importance and culture for Latin America because it offers multiple ecosystem services. These services are attributed to the different applications since dinde serves as a shade tree for cattle. Its wood is an appropriate resource for the manufacture of furniture and external constructions. Additionally, the wood produces a yellow dye called fustic amply used to dye brown, yellow, khaki, and green textiles. The fruits are attractive to fauna and comestibles for humans and have applications in pastries. Phytochemical and pharmacologic studies in *M. tinctoria* have allowed the identification of a wide variety of complex structures isolated from leaves, fruits, bark, and wood. Of all identified compounds, flavonoids of type flavones, isoflavone, flavonols, flavanols, flavanone, flavanonol, and flavonoid precursors such as chalcones and related compounds such as xanthones, and polyphenols were remarkable. In vitro and in vivo studies have explored the antioxidant properties, antimicrobial potential, sedative effects, and neuroprotective effects of dinde extracts. Other findings are the anti-inflammatory, antibacterial, anticancer activities, and protective effects on the liver, kidneys, brain, and heart (including blood vessels) of both isolated phytocompounds and prenylated or glycoside derivatives. This spectrum of bioactivities observed in dinde indicates that this species is a natural source of molecules with the potential for drug agents and nutraceutical development.

Acknowledgements The authors wish to thank the Universidad de Cartagena, Universidad del Atlántico, Universidad Metropolitana, and Minciencias (Colciencias) for the financial support under Grant Agreement No 649-2018 (code 110777757752), and the Universidad de Cartagena Grant Agreement No 067-2019, 111-2019, 030-2021, 073-2021, 111-2021.

Funding Open Access funding provided by Colombia Consortium.

Data availability The authors confirm that the data supporting the findings of this study are available within the article.

Declarations

Ethical statement This article does not contain any studies involving animals performed by any of the authors. This article does not contain any studies involving human participants performed by any of the authors.

Conflict of interest Patricia Quintero-Rincón has no conflict of interest. Yina Pájaro-González has no conflict of interest. Fredyc Diaz-Castillo has no conflict of interest.

References

Akinluyi E, Aderibigbe A, Adeoluwa O, Adebesin A, Adeoluwa G (2022) Ameliorating effect of morin hydrate on chronic restraint stress-induced biochemical disruption, neuronal, and behavioral dysfunctions in BALB/c mice. Basic Clin Neurosci 13(3):393–406. https://doi.org/10.32598/bcn.2022.1059.2

Akter K, Barnes EC, Loa-Kum-Cheung WL, Yin P, Kichu M, Brophy JJ, Barrow RA, Imchen I, Vemulpad SR, Jamie JF (2016) Antimicrobial and antioxidant activity and chemical characterisation of *Erythrina stricta* Roxb. (Fabaceae). J Ethnopharmacol 185:171–181. https://doi.org/10.1016/j.jep.2016.03.011

Alghamdi A, Almuqbil M, Alrofaidi MA, Burzangi AS, Alshamrani AA, Alzahrani AR, Kamal M, Imran M, Alshehri S, Mannasaheb BA, Alomar NF, Asdaq SMB (2022) Potential antioxidant activity of apigenin in the obviating stress-mediated depressive symptoms of experimental mice. Molecules 27(24):9055. https://doi.org/10.3390/molecules27249055

Al-Maharik N (2019) Isolation of naturally occurring novel isoflavonoids: an update. Nat Prod Rep 36(8):1156–1195. https://doi.org/10.1039/c8np00069g

Amais RS, Moreau PS, Francischini DS, Magnusson R, Locosselli GM, Godoy-Veiga M, Ceccantini G, Ortega D, Tomazello-Filho M, Arruda MA (2021) Trace elements distribution in tropical tree rings through high-resolution imaging using LA-ICP-MS analysis. J Trace Elem Med Biol 68:126872. https://doi.org/10.1016/j.jtemb.2021.126872

Ateba SB, Mvondo MA, Djiogue S, Zingué S, Krenn L, Njamen D (2019) A pharmacological overview of alpinumisoflavone, a natural prenylated isoflavonoid. Front Pharmacol 10:952. https://doi.org/10.3389/fphar.2019.00952

Batovska DI, Todorova IT (2010) Trends in utilization of the pharmacological potential of chalcones. Curr Clin Pharmacol 5(1):1–29. https://doi.org/10.2174/157488410790410579

Battilani JL, Santiago EF, Souza ALTD (2006) Morfologia de frutos, sementes e desenvolvimento de plântulas e plantas jovens de *Maclura tinctoria* (L.) D. Don. ex Steud. (Moraceae). Acta Bot Bras 20:581–589

Bernal R, Gradstein SR, Celis M (eds) (2019) Catálogo de plantas y líquenes de Colombia. Instituto de Ciencias Naturales, Universidad Nacional de Colombia, Bogotá. Available online: http://catalogoplantasdecolombia.unal.edu.co (accessed on 25 Nov 2023)

Bueno NR, Castilho RO, Costa RBD, Pott A, Pott VJ, Scheidt GN, Batista MDS (2005) Medicinal plants used by the Kaiowá and Guarani indigenous populations in the Caarapó Reserve, Mato Grosso do Sul, Brazil. Acta Bot Bras 19:39–44

Camargo A, Dalmagro AP, Rebelo AM, Reinke CK, Zeni ALB (2022) Phenolic profile, antidepressant-like and neuroprotective effects of *Maclura tinctoria* leaves extract. Nat Prod Res 36(18):4692–4695. https://doi.org/10.1080/14786419.2021.2000407

Cao Z, Liu W, Bi B, Wu H, Cheng G, Zhao Z (2022) Isoorientin ameliorates osteoporosis and oxidative stress in postmenopausal rats. Pharm Biol 60(1):2219–2228. https://doi.org/10.1080/13880209.2022.2142614

Carullo G, Falbo F, Ahmed A, Trezza A, Gianibbi B, Nicolotti O, Campiani G, Aiello F, Saponara S, Fusi F (2023) Artificial intelligence-driven identification of morin analogues acting as CaV1.2 channel blockers: synthesis and biological evaluation. Bioorg Chem 131:106326. https://doi.org/10.1016/j.bioorg.2022.106326

Cavichioli N, Dalmagro AP, Sasse OR, Junges LH, Rebelo AM, Reinke CK, Zeni ALB (2022) Antidepressant-like effect and phenolic profile of Brazilian native and exotic species from *Psidium* genus. Chem Biodivers 19(11):e202200242. https://doi.org/10.1002/cbdv.202200242

Çelik G (2020) New chalcone-3-O-glycoside derivatives: synthesis and characterization. J Chem Res 44(9–10):598–601

Çelikezen FÇ, Türkez H, Firat M, Arslan ME, Öner S (2022) In vitro evaluation of selective cytotoxic activity of *Chaerophyllum macropodum* Boiss. on cultured human SH-SY5Y neuroblastoma cells. Neurotox Res 40(5):1360–1368. https://doi.org/10.1007/s12640-022-00537-z

Chao MR, Rossner P Jr, Haghdoost S, Jeng HA, Hu CW (2013) Nucleic acid oxidation in human health and disease. Oxid Med Cell Longev 2013:368651. https://doi.org/10.1155/2013/368651

Choi YJ, Lee J, Ha SH, Lee HK, Lim HM, Yu SH, Lee CM, Nam MJ, Yang YH, Park K, Choi YS, Jang KY, Park SH (2021) 6,8-Diprenylorobol induces apoptosis in human colon cancer cells via activation of intracellular reactive oxygen species and p53. Environ Toxicol 36(5):914–925. https://doi.org/10.1002/tox.23093

Cioffi G, Morales Escobar L, Braca A, De Tommasi N (2003) Antioxidant chalcone glycosides and flavanones from *Maclura*

(*Chlorophora*) *tinctoria*. J Nat Prod 66(8):1061–1064. https://doi.org/10.1021/np030127c

Ciumărnean L, Milaciu MV, Runcan O, Vesa ȘC, Răchișan AL, Negrean V, Perné MG, Donca VI, Alexescu TG, Para I, Dogaru G (2020) The effects of flavonoids in cardiovascular diseases. Molecules 25(18):4320. https://doi.org/10.3390/molecules25184320

Coldebella R, Gentil M, Berger C, Dalla Costa HW, Pedrazzi C, Labidi J, Delucis RA, Missio AL (2021) Nanofibrillated cellulose-based aerogels functionalized with Tajuva (*Maclura tinctoria*) heartwood extract. Polymers 13(6):908. https://doi.org/10.3390/polym13060908

Dai J, Mumper RJ (2010) Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. Molecules 15(10):7313–7352. https://doi.org/10.3390/molecules15107313

das Chagas Almeida A, Azevedo Rodrigues L, Dos Santos Paulino G et al (2019) Prenylated flavonoid-enriched fraction from *Maclura tinctoria* shows biological activity against *Staphylococcus aureus* and protects *Galleria mellonella* larvae from bacterial infection. BMC Complement Altern Med 19(1):189. https://doi.org/10.1186/s12906-019-2600-y

Diaz JS, Miranda MCF, Abarca NA, Coronado AF, González AL, Ulloa MG, Ocampo HAG (2021) Effect of microencapsulated phenolic compound extracts of *Maclura tinctoria* (L.) Steud on growth performance and humoral immunity markers of white leg shrimp (*Litopenaeus vannamei*, Boone, 1931) juveniles. Span J Agric Res 19(1):604

Dong WH, Chu QQ, Liu SQ, Deng DT, Xu Q (2020) Isobavachalcone ameliorates diabetic nephropathy in rats by inhibiting the NF-κB pathway. J Food Biochem 44(9):e13405. https://doi.org/10.1111/jfbc.13405

Dong X, Luo S, Hu D, Cao R, Wang Q, Meng Z, Feng Z, Zhou W, Song W (2022) Gallic acid inhibits neuroinflammation and reduces neonatal hypoxic-ischemic brain damages. Front Pediatr 10:973256. https://doi.org/10.3389/fped.2022.973256

Działo M, Mierziak J, Korzun U, Preisner M, Szopa J, Kulma A (2016) The potential of plant phenolics in prevention and therapy of skin disorders. Int J Mol Sci 17(2):160. https://doi.org/10.3390/ijms17020160

Elbarbry F, Jones G, Ung A (2022) Catechin reduces blood pressure in spontaneously hypertensive rats through modulation of arachidonic acid metabolism. Molecules 27(23):8432. https://doi.org/10.3390/molecules27238432

ElSohly HN, Joshi AS, Nimrod AC, Walker LA, Clark AM (2001) Antifungal chalcones from *Maclura tinctoria*. Planta Med 67(1):87–89. https://doi.org/10.1055/s-2001-10621

Fehaid A, Al-Ghamdi MS, Alzahrani KJ, Theyab A, Al-Amer OM, Al-Shehri SS, Algahtani MA, Oyouni AA, Alnfiai MM, Aly MH, Alsharif KF, Albrakati A, Kassab RB, Althagafi HA, Alharthi F, Abdel Moneim AE, Lokman MS (2022) Apigenin protects from hepatorenal damage caused by lead acetate in rats. J Biochem Mol Toxicol 37:e23275. https://doi.org/10.1002/jbt.23275

Fu R, Wang L, Meng Y, Xue W, Liang J, Peng Z, Meng J, Zhang M (2022) Apigenin remodels the gut microbiota to ameliorate ulcerative colitis. Front Nutr 9:1062961. https://doi.org/10.3389/fnut.2022.1062961

Gan X, Zhang W, Lan S, Hu D (2023) el Cyclized derivatives of ferulic acid as potential antiviral agents through activation of photosynthesis. J Agric Food Chem 71(3):1369–1380. https://doi.org/10.1021/acs.jafc.2c06422

Gao XY, Wang SN, Yang XH, Lan WJ, Chen ZW, Chen JK, Xie JH, Han YF, Pi RB, Yang XB (2016) Gartanin protects neurons against glutamate-induced cell death in HT22 cells: independence of Nrf-2 but involvement of HO-1 and AMPK. Neurochem Res 41(9):2267–2277. https://doi.org/10.1007/s11064-016-1941-x

Gardner EM, Sarraf P, Williams EW, Zerega NJC (2017) Phylogeny and biogeography of *Maclura* (Moraceae) and the origin of an anachronistic fruit. Mol Phylogenet Evol 117:49–59. https://doi.org/10.1016/j.ympev.2017.06.021

Gomes GAC, Paiva R, Paiva PDDO, De Santiago EJA (2003) Plant regeneration from callus cultures of *Maclura tinctoria*, an endangered woody species. In Vitro Cell Dev Biol Plant 39(3):293–295

Gomes GAC, Paiva R, Herrera RC, Paiva PDDO (2010) Micropropagation of *Maclura tinctoria* L.: an endangered woody species. Rev Árvore 34:25–30

Górniak I, Bartoszewski R, Króliczewski J (2018) Comprehensive review of antimicrobial activities of plant flavonoids. Phytochem Rev. https://doi.org/10.1007/s11101-018-9591-z

Groweiss A, Cardellina JH, Boyd MR (2000) HIV-Inhibitory prenylated xanthones and flavones from *Maclura tinctoria*. J Nat Prod 63(11):1537–1539. https://doi.org/10.1021/np000175m

Gu MY, Chun YS, Yong RS, Yang HO (2019) Licoflavonol reduces Aβ secretion by increasing BACE1 phosphorylation to facilitate BACE1 degradation. Mol Nutr Food Res 63(3):e1800474. https://doi.org/10.1002/mnfr.201800474

Gunter NV, Teh SS, Jantan I, Cespedes-Acuña CL, Mah SH (2022) The mechanisms of action of prenylated xanthones against breast, colon, and lung cancers, and their potential application against drug resistance. Phytochem Rev 22:467–503. https://doi.org/10.1007/s11101-022-09846-9

Gutierrez-Orozco F, Failla ML (2013) Biological activities and bioavailability of mangosteen xanthones: a critical review of the current evidence. Nutrients 5(8):3163–3183. https://doi.org/10.3390/nu5083163

Ham JR, Lee HI, Choi RY, Sim MO, Seo KI, Lee MK (2016) Anti-steatotic and anti-inflammatory roles of syringic acid in high-fat diet-induced obese mice. Food Funct 7(2):689–697. https://doi.org/10.1039/c5fo01329a

Han HJ, Kim TJ, Jin YR, Hong SS, Hwang JH, Hwang BY, Lee KH, Park TK, Yun YP (2007) Cudraflavanone A, a flavonoid isolated from the root bark of *Cudrania tricuspidata*, inhibits vascular smooth muscle cell growth via an Akt-dependent pathway. Planta Med 73(11):1163–1168. https://doi.org/10.1055/s-2007-981584

Han X, Li M, Sun L, Liu X, Yin Y, Hao J, Zhang W (2022) *p*-Hydroxybenzoic acid ameliorates colitis by improving the mucosal barrier in a gut microbiota-dependent manner. Nutrients 14(24):5383. https://doi.org/10.3390/nu14245383

Hua F, Li JY, Zhang M, Zhou P, Wang L, Ling TJ, Bao GH (2022) Kaempferol-3-O-rutinoside exerts cardioprotective effects through NF-κB/NLRP3/Caspase-1 pathway in ventricular remodeling after acute myocardial infarction. J Food Biochem 46(10):e14305. https://doi.org/10.1111/jfbc.14305

Huang J, Wang X, Tao G, Song Y, Ho C, Zheng J, Ou S (2018) Feruloylated oligosaccharides from maize bran alleviate the symptoms of diabetes in streptozotocin-induced type 2 diabetic rats. Food Funct 9(3):1779–1789. https://doi.org/10.1039/c7fo01825h

Jangid AK, Pooja D, Kulhari H (2018) Determination of solubility, stability and degradation kinetics of morin hydrate in physiological solutions. RSC Adv 8(50):28836–28842. https://doi.org/10.1039/c8ra04139c

Ji Y, Li B, Qiao M, Li J, Xu H, Zhang L, Zhang X (2020) Advances on the in vivo and in vitro glycosylations of flavonoids. Appl Microbiol Biotechnol 104(15):6587–6600. https://doi.org/10.1007/s00253-020-10667-z

Jiang YP, Wang S, Lai WD, Wu XQ, Jin Y, Xu ZH, Moutal A, Khanna R, Park KD, Shan ZM, Wen CP, Yu J (2022) Neuronal CRMP2 phosphorylation inhibition by the flavonoid, naringenin, contributes to the reversal of spinal sensitization and arthritic pain improvement. Arthritis Res Ther 24(1):277. https://doi.org/10.1186/s13075-022-02975-8

Jo YH, Kim SB, Liu Q, Hwang BY, Lee MK (2017) Prenylated xanthones from the roots of *Cudrania tricuspidata* as inhibitors of lipopolysaccharide-stimulated nitric oxide production. Arch Pharm 350(1):e1600263. https://doi.org/10.1002/ardp.201600263.10.1002/ardp.201600263

Kang MJ, Kim SY, Kwon EB, Jo YH, Lee MK, Lee HS, Moon DO, Kim MO (2019) Derrone induces autophagic cell death through induction of ROS and ERK in A549 cells. PLoS ONE 14(6):e0218659. https://doi.org/10.1371/journal.pone.0218659

Kashyap B, Saikia K, Samanta SK, Thakur D, Banerjee SK, Borah JC, Talukdar NC (2023) Kaempferol 3-O-rutinoside from *Antidesma acidum* Retz. Stimulates glucose uptake through SIRT1 induction followed by GLUT4 translocation in skeletal muscle L6 cells. J Ethnopharmacol 301:115788. https://doi.org/10.1016/j.jep.2022.115788

Katsori AM, Hadjipavlou-Litina D (2011) Recent progress in therapeutic applications of chalcones. Expert Opin Ther Pat 21(10):1575–1596. https://doi.org/10.1517/13543776.2011.596529

Kim MO, Lee HS, Chin YW, Moon DO, Ahn JS (2015) Gartanin induces autophagy through JNK activation which extenuates caspase-dependent apoptosis. Oncol Rep 34(1):139–146. https://doi.org/10.3892/or.2015.3948

Kim KW, Quang TH, Ko W, Kim DC, Yoon CS, Oh H, Kim YC (2018) Anti-neuroinflammatory effects of cudraflavanone A isolated from the chloroform fraction of *Cudrania tricuspidata* root bark. Pharm Biol 56(1):192–200. https://doi.org/10.1080/13880209.2018.1447972

Koleckar V, Kubikova K, Rehakova Z, Kuca K, Jun D, Jahodar L, Opletal L (2008) Condensed and hydrolysable tannins as antioxidants influencing the health. Mini Rev Med Chem 8(5):436–447. https://doi.org/10.2174/138955708784223486

Kushwaha PP, Prajapati SK, Pothabathula SV, Singh AK, Shuaib M, Joshi K, Kumar S (2020) Prenylated flavonoids as a promising drug discovery candidate: a pharmacological update. In: Egbuna C, Kumar S, Ifemeje JC, Ezzat SM, Kaliyaperumal S (eds) Phytochemicals as lead compounds for new drug discovery, pp 347–355. https://doi.org/10.1016/b978-0-12-817890-4.00023-8

Lachance MA, Klemens JA, Bowles JM, Janzen DH (2001) The yeast community of sap fluxes of Costa Rican *Maclura* (*Chlorophora*) *tinctoria* and description of two new yeast species, *Candida galis* and *Candida ortonii*. FEMS Yeast Res 1(2):87–92. https://doi.org/10.1111/j.1567-1364.2001.tb00019.x

Lamounier KC, Cunha LC, de Morais SA, de Aquino FJ, Chang R, do Nascimento EA, de Souza MG, Martins CH, Cunha WR (2012) Chemical analysis and study of phenolics, antioxidant activity, and antibacterial effect of the wood and bark of *Maclura tinctoria* (L.) D. Don ex Steud. Evid Based Complement Altern Med 2012:451039. https://doi.org/10.1155/2012/451039

Lee CW, Yen FL, Ko HH, Li SY, Chiang YC, Lee MH, Tsai MH, Hsu LF (2017) Cudraflavone C induces apoptosis of A375.S2 melanoma cells through mitochondrial ROS production and MAPK activation. Int J Mol Sci 18(7):1508. https://doi.org/10.3390/ijms18071508

Lee CM, Lee J, Jang SN, Shon JC, Wu Z, Park K, Liu KH, Park SH (2020) 6,8-Diprenylorobol induces apoptosis in human hepatocellular carcinoma cells via activation of FOXO3 and inhibition of CYP2J2. Oxid Med Cell Longev 2020:8887251. https://doi.org/10.1155/2020/8887251

Li B, Xu N, Wan Z, Li B, Xu N, Wan Z, Ma L, Li H, Cai W, Chen X, Huang Z, He Z et al (2019a) Isobavachalcone exerts antiproliferative and pro-apoptotic effects on human liver cancer cells by targeting the ERKs/RSK2 signaling pathway. Oncol Rep 41(6):3355–3366. https://doi.org/10.3892/or.2019.7090

Li Y, Zhang L, Wang X, Wu W, Qin R (2019b) Effect of syringic acid on antioxidant biomarkers and associated inflammatory markers in mice model of asthma. Drug Dev Res 80(2):253–261. https://doi.org/10.1002/ddr.21487

Li Z, Wang Q, Luan H, Yang M, Li Y, Tian G, He W (2020) A novel target TAX1BP1 and P38/Nrf2 pathway independently involved in the anti-neuroinflammatory effect of isobavachalcone. Free Radic Biol Med 153:132–139. https://doi.org/10.1016/j.freeradbiomed.2020.04.011

Li L, Ma H, Zhang Y, Jiang H, Xia B, Sberi HA, Elhefny MA, Lokman MS, Kassab RB (2023) Protocatechuic acid reverses myocardial infarction mediated by β-adrenergic agonist via regulation of Nrf2/HO-1 pathway, inflammatory, apoptotic, and fibrotic events. J Biochem Mol Toxicol 37:e23270. https://doi.org/10.1002/jbt.23270

Liang Y, Niu H, Ma L, Du D, Wen L, Xia Q, Huang W (2017) Eriodictyol 7-O-β-D glucopyranoside from *Coreopsis tinctoria* Nutt. ameliorates lipid disorders via protecting mitochondrial function and suppressing lipogenesis. Mol Med Rep 16(2):1298–1306. https://doi.org/10.3892/mmr.2017.6743

Liang S, Zhao Y, Chen G, Wang C (2022) Isoorientin ameliorates OVA-induced asthma in a murine model of asthma. Exp Biol Med (maywood) 247(16):1479–1488. https://doi.org/10.1177/15353702221094505

Liu T, Gao H, Zhang Y, Wang S, Lu M, Dai X, Liu Y, Shi H, Xu T, Yin J, Gao S, Wang L, Zhang D (2022a) Apigenin ameliorates hyperuricemia and renal injury through regulation of uric acid metabolism and JAK2/STAT3 signaling pathway. Pharmaceuticals (basel) 15(11):1442. https://doi.org/10.3390/ph15111442

Liu MX, Li T, Wang WG, Guo J, Wang RR, He HP, Li SQ, Li YP (2022b) Regulatory effect of isovitexin on MAPK/NF-κB signal in mice with acute ulcerative colitis. J Asian Nat Prod Res 25(8):765–782. https://doi.org/10.1080/10286020.2022.2142121

Liu X, Zhang H, Cao J, Zhuo Y, Jin J, Gao Q, Yuan X, Yang L, Li D, Wang Y (2022c) Isobavachalcone activates antitumor immunity on orthotopic pancreatic cancer model: a screening and validation. Front Pharmacol 13:919035. https://doi.org/10.3389/fphar.2022.919035

Liu XW, Yang YJ, Qin Z, Li SH, Bai LX, Ge WB, Li JY (2022d) Isobavachalcone from *Cullen corylifolium* presents significant antibacterial activity against clostridium difficile through disruption of the cell membrane. Front Pharmacol 13:914188. https://doi.org/10.3389/fphar.2022.914188

Liu X, Ma Y, Luo L, Zeng Z, Zong D, Chen Y (2023) Taxifolin ameliorates cigarette smoke-induced chronic obstructive pulmonary disease via inhibiting inflammation and apoptosis. Int Immunopharmacol 115:109577. https://doi.org/10.1016/j.intimp.2022.109577

Lu Y, Zhang W, Li H, Liu C, Gao D, Zhuang J, Liu R, Wu J, Sun C (2022) The mechanism of quercetin in the treatment of lung squamous cell carcinoma based on a protein-protein interaction network. Evid Based Complement Altern Med 2022:9985160. https://doi.org/10.1155/2022/9985160

Luo M, Liu Q, He M, Yu Z, Pi R, Li M, Yang X, Wang S, Liu A (2017) Gartanin induces cell cycle arrest and autophagy and suppresses migration involving PI3K/Akt/mTOR and MAPK signalling pathway in human glioma cells. J Cell Mol Med 21(1):46–57. https://doi.org/10.1111/jcmm.12937

Ma JP, Qiao X, Pan S, Shen H, Zhu GF, Hou AJ (2010) New isoprenylated flavonoids and cytotoxic constituents from *Artocarpus tonkinensis*. J Asian Nat Prod Res 12(7):586–592. https://doi.org/10.1080/10286020.2010.485932

Maleki SJ, Crespo JF, Cabanillas B (2019) Anti-inflammatory effects of flavonoids. Food Chem 299:125124. https://doi.org/10.1016/j.foodchem.2019.12512

Malik P, Singh R, Kumar M, Malik A, Mukherjee TK (2023) Understanding the phytoestrogen genistein actions on breast cancer: insights on estrogen receptor equivalence, pleiotropic essence and emerging paradigms in bioavailability modulation. Curr Top Med Chem. https://doi.org/10.2174/1568026623666230103163023

Mathesius U (2018) Flavonoid functions in plants and their interactions with other organisms. Plants 7(2):30. https://doi.org/10.3390/plants7020030

Matson Robles A, Herrera Herrera A, Diaz A (2015) In vitro antibacterial activity of *Maclura tinctoria* and *Azadirachta indica* against *Streptococcus mutans* and *Porphyromonas gingivalis*. Br J Pharm Res 7:291–298. https://doi.org/10.9734/BJPR/2015/18308

Mbaveng AT, Zhao Q, Kuete V (2014) Harmful and protective effects of phenolic compounds from African medicinal plants. In: Kuete V (ed) Toxicological survey of African medicinal plants, pp 577–609. https://doi.org/10.1016/b978-0-12-800018-2.00020-0

Meenu MT, Kaul G, Shukla M, Radhakrishnan KV, Chopra S (2021) Cudraflavone C from *Artocarpus hirsutus* as a promising inhibitor of pathogenic, multidrug-resistant *S. aureus*, persisters, and biofilms: a new insight into a rational explanation of traditional wisdom. J Nat Prod 84(10):2700–2708. https://doi.org/10.1021/acs.jnatprod.1c00578

Mirossay L, Varinská L, Mojžiš J (2017) antiangiogenic effect of flavonoids and chalcones: an update. Int J Mol Sci 19(1):27. https://doi.org/10.3390/ijms19010027

Mohamad AS, Akhtar MN, Zakaria ZA, Perimal EK, Khalid S, Mohd PA, Khalid MH, Israf DA, Lajis NH, Sulaiman MR (2010) Antinociceptive activity of a synthetic chalcone, flavokawin B on chemical and thermal models of nociception in mice. Eur J Pharmacol 647(1–3):103–109. https://doi.org/10.1016/j.ejphar.2010.08.030

Montes-Londoño I, Montagnini F, Ashton MS (2018) Allometric relationships and reforestation guidelines for *Maclura tinctoria*, an important multi-purpose timber tree of Latin America. New for 49:249–263. https://doi.org/10.1007/s11056-017-9617-1

Nikolaeva S, Saavedra-Arias JJ, Saenz-Maple G, Salas R, Baudrit JV, Rodriguez G, Pantyukhov P, Popov A (2015) Materiales poliméricos compuestos por polietileno (PEBD) y fibras del árbol *Maclura tinctoria* (Moraceae). Cuad Inv UNED 7(2):209–216

Nogueira V, Hay N (2013) Molecular pathways: reactive oxygen species homeostasis in cancer cells and implications for cancer therapy. Clin Cancer Res 19(16):4309–4314. https://doi.org/10.1158/1078-0432.CCR-12-1424

Okpara ES, Adedara IA, Guo X, Klos ML, Farombi EO, Han S (2022) Molecular mechanisms associated with the chemoprotective role of protocatechuic acid and its potential benefits in the amelioration of doxorubicin-induced cardiotoxicity: a review. Toxicol Rep 9:1713–1724. https://doi.org/10.1016/j.toxrep.2022.09.001

Ortolan XR, Mezadri TJ, Tames DR, Braga RC, Buzzi FC (2017) Osteogenic potential of different chalcones in an in vivo model: a preliminary study. J Oral Res 6(8):209–215

Osorio M, Carvajal M, Vergara A, Butassi E, Zacchino S, Mascayano C, Montoya M, Mejías S, Martín MC, Vásquez-Martínez Y (2021) Prenylated flavonoids with potential antimicrobial activity: synthesis, biological activity, and in silico study. Int J Mol Sci 22(11):5472. https://doi.org/10.3390/ijms22115472

Ouyang Y, Li J, Chen X, Fu X, Sun S, Wu Q (2021) Chalcone derivatives: role in anticancer therapy. Biomolecules 11(6):894. https://doi.org/10.3390/biom11060894

Oyama SDO, Souza LAD (2011) Morphology and anatomy of the developing fruit of *Maclura tinctoria*, Moraceae. Rev Bras Bot 34:187–195

Oyama SDO, Souza LAD, Baldoqui DC, Sarragiotto MH, Silva AA (2013) Prenylated flavonoids from *Maclura tinctoria* fruits. Quim Nova 36:800–802

Pájaro-González Y (2023) Evaluación de la actividad frente a bacterias del grupo ESKAPE-E de extractos etanólicos y compuestos de plantas nativas de la región Caribe colombiana. (Doctoral dissertation, Universidad de Cartagena)

Park S, Park SK (2022) Anti-oxidant and anti-aging effects of phlorizin are mediated by DAF-16-induced stress response and autophagy in *Caenorhabditis elegans*. Antioxidants 11(10):1996. https://doi.org/10.3390/antiox11101996

Passalacqua TG, Dutra LA, de Almeida L, Velásquez AM, Torres FA, Yamasaki PR, dos Santos MB, Regasini LO, Michels PA, VdaS B, Graminha MA (2015) Synthesis and evaluation of novel prenylated chalcone derivatives as anti-leishmanial and anti-trypanosomal compounds. Bioorg Med Chem Lett 25(16):3342–3345. https://doi.org/10.1016/j.bmcl.2015.05.072

Pei R, Liu X, Bolling B (2020) Flavonoids and gut health. Curr Opin Biotechnol 61:153–159. https://doi.org/10.1016/j.copbio.2019.12.018

Pham V, Rendon R, Le VX, Tippin M, Fu DJ, Le TH, Miller M, Agredano E, Cedano J, Zi X (2020) Gartanin is a novel NEDDylation inhibitor for induction of Skp2 degradation, FBXW2 expression, and autophagy. Mol Carcinog 59(2):193–201. https://doi.org/10.1002/mc.23140

Pinto MV, Oliveira EM, Martins JL, Pinto MV, Oliveira EM, Martins JL, de Paula JR, Costa EA, da Conceição EC, Bara MT et al (2017) Obtaining a dry extract from the *Mikania laevigata* leaves with potential for antiulcer activity. Pharmacogn Mag 13(49):76–80. https://doi.org/10.4103/0973-1296.197640

Pires LDC, Rodrigues P, Garlet QI, Barbosa LB, da Silveira BP, Bandeira Junior G, Lima L, Gindri A, Coldebella R, Pedrazzi C, Castagna A, Baldisserotto B, Heinzmann BM (2021) *Maclura tinctoria* extracts: in vitro antibacterial activity against *Aeromonas hydrophila* and sedative effect in *Rhamdia quelen*. Fishes 6(3):25. https://doi.org/10.3390/fishes6030025

Qiao XR, Feng T, Zhang D, Zhi LL, Zhang JT, Liu XF, Pan Y, Xu JW, Cui WJ, Dong L (2023) Luteolin alleviated neutrophilic asthma by inhibiting IL-36γ secretion-mediated MAPK pathways. Pharm Biol 61(1):165–176. https://doi.org/10.1080/13880209.2022.2160770

Rauf A, Imran M, Abu-Izneid T, Patel S, Pan X, Naz S, Sanches A, Saeed F, Ansar H, Suleria HAR (2019) Proanthocyanidins: a comprehensive review. Biomed Pharmacother 116:108999. https://doi.org/10.1016/j.biopha.2019.108999

Redondo LM, Chacana PA, Dominguez J, Yan FE, Fernandez Miyakawa ME (2014) Perspectives in the use of tannins as alternative to antimicrobial growth promoter factors in poultry. Front Microbiol 5:118. https://doi.org/10.3389/fmicb.2014.00118

Salau VF, Erukainure OL, Koorbanally NA, Islam MS (2022) Ferulic acid promotes muscle glucose uptake and modulate dysregulated redox balance and metabolic pathways in ferric-induced pancreatic oxidative injury. J Food Biochem 46(4):e13641. https://doi.org/10.1111/jfbc.13641

Santos-Buelga C, González-Paramás AM, Oludemi T, Ayuda-Durán B, González-Manzano S (2019) Plant phenolics as functional food ingredients. Adv Food Nutr Res 90:183–257. https://doi.org/10.1016/bs.afnr.2019.02.012

Shahzad S, Mateen S, Kausar T, Naeem SS, Hasan A, Abidi M, Nayeem SM, Faizy AF, Moin S (2020) Effect of syringic acid and syringaldehyde on oxidative stress and inflammatory status in peripheral blood mononuclear cells from patients of myocardial infarction. Naunyn Schmiedebergs Arch Pharmacol 393(4):691–704. https://doi.org/10.1007/s00210-019-01768-2

Sharma R, Kumari A, Kundu B, Grover A (2022) Amyloid fibrillation of the glaucoma associated myocilin protein is inhibited by epicatechin gallate (ECG). RSC Adv 12(45):29469–29481. https://doi.org/10.1039/d2ra05061g

Sheikhpour E, Mard SA, Farbood Y, Bavarsad K, Sarkaki A (2023) The effects of gallic acid and vagotomy on motor function, intestinal transit, brain electrophysiology and oxidative stress alterations in a rat model of Parkinson's disease induced by rotenone. Life Sci 315:121356. https://doi.org/10.1016/j.lfs.2022.121356

Shete VS, Telange DR, Mahajan NM, Pethe AM, Mahapatra DK (2023) Development of phospholipon®90H complex nanocarrier with enhanced oral bioavailability and anti-inflammatory potential of genistein. Drug Deliv 30(1):2162158. https://doi.org/10.1080/10717544.2022.2162158

Shi Y, Yan T, Lu X, Li K, Nie Y, Jiao C, Sun H, Li T, Li X, Han D (2022) Phloridzin reveals new treatment strategies for liver fibrosis. Pharmaceuticals 15(7):896. https://doi.org/10.3390/ph15070896

Shin JH, Irfan M, Rhee MH, Kwon HW (2021) Derrone inhibits platelet aggregation, granule secretion, thromboxane A2 generation, and clot retraction: an in vitro study. Evid Based Complement Altern Med 2021:8855980. https://doi.org/10.1155/2021/8855980

Shnawa HA, Khalaf MN, Taobi AAH, Panampilly B, Thomas S (2020) General and chemical perspectives and studies on tannins as natural phenolic compounds for some ecoefficient applications. In: Volova TG, Mahapatra DK, Khanna S, Haghi AK (eds) Natural products chemistry. Apple Academic Press, New Jersey, pp 115–137

Song J, Song G, Park S, Lim W (2022) Inhibitory effects of 6,8-diprenylorobol on endometriosis progression in humans by disrupting calcium homeostasis and mitochondrial function. Antioxidants 11(1):171. https://doi.org/10.3390/antiox11010171

Soo HC, Chung FF, Lim KH, Yap VA, Bradshaw TD, Hii LW, Tan SH, See SJ, Tan YF, Leong CO, Mai CW (2017) Cudraflavone C induces tumor-specific apoptosis in colorectal cancer cells through inhibition of the phosphoinositide 3-kinase (PI3K)-AKT pathway. PLoS ONE 12(1):e0170551. https://doi.org/10.1371/journal.pone.0170551

Su YL, Liu D, Liu YJ, Ji YL, Liu GS, Wang JL, Wang B, Wang H (2022) Phlorizin alleviates cholinergic memory impairment and regulates gut microbiota in d-galactose induced mice. Exp Gerontol 165:111863. https://doi.org/10.1016/j.exger.2022.111863

Sun P, Qu Y, Wang Y, Wang J, Wang X, Sheng J (2021) Wighteone exhibits an antitumor effect against EGFR L858R/T790M mutation non-small cell lung cancer. J Cancer 12(13):3900–3908. https://doi.org/10.7150/jca.54574

Sychrová A, Škovranová G, Čulenová M, Bittner Fialová S (2022) Prenylated flavonoids in topical infections and wound healing. Molecules 27(14):4491. https://doi.org/10.3390/molecules27144491

Tocmo R, Le B, Heun A, van Pijkeren JP, Parkin K, Johnson JJ (2021) Prenylated xanthones from mangosteen (*Garcinia mangostana*) activate the AhR and Nrf2 pathways and protect intestinal barrier integrity in HT-29 cells. Free Radic Biol Med 163:102–115. https://doi.org/10.1016/j.freeradbiomed.2020.11.018

Tseng CY, Yu PR, Hsu CC, Lin HH, Chen JH (2023) The effect of isovitexin on lipopolysaccharide-induced renal injury and inflammation by induction of protective autophagy. Food Chem Toxicol 172:113581. https://doi.org/10.1016/j.fct.2022.113581

Tukhovskaya EA, Slashcheva GA, Shaykhutdinova ER, Ismailova AM, Palikova YA, Palikov VA, Rasskazova EA, Semushina SG, Perepechenova NA, Sadovnikova ES, Kravchenko IN, Dyachenko IA, Murashev AN (2022) Taxifolin reduces blood pressure in elderly hypertensive male Wistar rats. Bull Exp Biol Med 174(1):29–32. https://doi.org/10.1007/s10517-022-05642-9

Ullah A, Munir S, Badshah SL, Khan N, Ghani L, Poulson BG, Emwas AH, Jaremko M (2020) Important flavonoids and their role as a therapeutic agent. Molecules 25(22):5243. https://doi.org/10.3390/molecules25225243

Venturelli S, Burkard M, Biendl M, Lauer UM, Frank J, Busch C (2016) Prenylated chalcones and flavonoids for the prevention and treatment of cancer. Nutrition 32(11–12):1171–1178. https://doi.org/10.1016/j.nut.2016.03.020

Wang J, Huang L, Cheng C, Li G, Xie J, Shen M, Chen Q, Li W, He W, Qiu P, Wu J (2019) Design, synthesis and biological evaluation of chalcone analogues with novel dual antioxidant mechanisms as potential anti-ischemic stroke agents. Acta Pharm Sin b 9(2):335–350. https://doi.org/10.1016/j.apsb.2019.01.003

Wang JZ, Bian Y, Deng GG, Wang Y, Yan HL, Zhang XL, Huang YM, Li A, Liao XY, Feng TY (2021) Effects of phloridzin on blood glucose and key enzyme G-6-Pase of gluconeogenesis in mice. J Food Biochem 45(11):e13956. https://doi.org/10.1111/jfbc.13956

Wang S, Du Q, Sun J, Geng S, Zhang Y (2022) Investigation of the mechanism of Isobavachalcone in treating rheumatoid arthritis through a combination strategy of network pharmacology and experimental verification. J Ethnopharmacol 294:115342. https://doi.org/10.1016/j.jep.2022.115342

Wei X, Chen D, Yi Y, Qi H, Gao X, Fang H, Gu Q, Wang L, Gu L (2012) Syringic acid extracted from herba dendrobii prevents diabetic cataract pathogenesis by inhibiting aldose reductase activity. Evid Based Complement Altern Med 2012:426537. https://doi.org/10.1155/2012/426537

Wen L, Zhou T, Jiang Y, Chang SK, Yang B (2022) Prenylated flavonoids in foods and their applications on cancer prevention. Crit Rev Food Sci Nutr 62(18):5067–5080. https://doi.org/10.1080/10408398.2021.1881437

WFO (2022) *Maclura tinctoria* (L.) D. Don ex Steud. Available online: http://www.worldfloraonline.org/taxon/wfo-0000447821 (accessed on 25 Nov 2022)

Wu Z, Yu W, Ni W, Teng C, Ye W, Yu C, Zeng Y (2023) Improvement of obesity by Liupao tea is through the IRS-1/PI3K/AKT/GLUT4 signaling pathway according to network pharmacology and experimental verification. Phytomedicine 110:154633. https://doi.org/10.1016/j.phymed.2022.154633

Xie C, Wang K, Liu X, Liu G, Hu Z, Zhao L (2023) Characterization and bioactivity of A-type procyanidins from litchi fruitlets at different degrees of development. Food Chem 405(Pt A):134855. https://doi.org/10.1016/j.foodchem.2022.134855

Xiong Y, Zhong W, Liu J, Cheng B, Fan J, Zhou F, He L, Tian D, He Y (2022) Luteolin isolated from *Polygonum cuspidatum* is a potential compound against nasopharyngeal carcinoma. Biomed Res Int 2022:9740066. https://doi.org/10.1155/2022/9740066

Xu Z, Jia Y, Liu J, Ren X, Yang X, Xia X, Pan X (2022) Naringenin and quercetin exert contradictory cytoprotective and cytotoxic effects on tamoxifen-induced apoptosis in HepG2 cells. Nutrients 14(24):5394. https://doi.org/10.3390/nu14245394

Xue Q, Chen Y, Yin H, Teng H, Qin R, Liu H, Li Q, Mei Z, Yang G (2020) Prenylated xanthones and benzophenones from the fruits of *Garcinia bracteata* and their potential antiproliferative and anti-inflammatory activities. Bioorg Chem 104:104339. https://doi.org/10.1016/j.bioorg.2020.104339

Yan F, Chen L, Chen W, Zhao L, Lu Q, Liu R (2021) Protective effect of procyanidin A-type dimers against H_2O_2-induced oxidative stress in prostate DU145 cells through the MAPKs signaling pathway. Life Sci 266:118908. https://doi.org/10.1016/j.lfs.2020.118908

Yang B, Liu H, Yang J, Gupta VK, Jiang Y (2018) New insights on bioactivities and biosynthesis of flavonoid glycosides. Trends Food Sci Technol 79:116–124. https://doi.org/10.1016/j.tifs.2018.07.006

Yang J, Chu Q, Meng G, Kong W (2022a) The complete chloroplast genome sequences of three *Broussonetia* species and comparative analysis within the Moraceae. PeerJ 10:e14293. https://doi.org/10.7717/peerj.14293

Yang J, Li G, Bao X, Suo Y, Xu H, Deng Y, Feng T, Deng G (2022b) Hepatoprotective effects of phloridzin against isoniazid-rifampicin induced liver injury by regulating CYP450 and Nrf2/HO-1 pathway in mice. Chem Pharm Bull 70(11):805–811. https://doi.org/10.1248/cpb.c22-00466

Zhang W, Xiao S, Ahn DU (2013) Protein oxidation: basic principles and implications for meat quality. Crit Rev Food Sci Nutr 53(11):1191–1201. https://doi.org/10.1080/10408398.2011.577540

Zhang M, Wu Q, Zhao R, Yao X, Du X, Liu Q, Lv G, Xiao S (2021) Isobavachalcone ameliorates cognitive deficits, and Aβ and tau pathologies in triple-transgenic mice with Alzheimer's disease. Food Funct 12(17):7749–7761. https://doi.org/10.1039/d1fo01306h

Zhang N, Zhang W, Guo X, Liu J, Li S, Zhang H, Fan B (2022) Genistein protects against hyperglycemia and fatty liver disease in diet-induced prediabetes mice via activating hepatic insulin signaling pathway. Front Nutr 9:1072044. https://doi.org/10.3389/fnut.2022.1072044

Zhang J, Zhang W, Yang L, Zhao W, Liu Z, Wang E, Wang J (2023a) Phytochemical gallic acid alleviates nonalcoholic fatty liver disease via AMPK-ACC-PPARa axis through dual regulation of lipid metabolism and mitochondrial function. Phytomedicine 109:154589. https://doi.org/10.1016/j.phymed.2022.154589

Zhang Z, Hao M, Zhang X, He Y, Chen X, Taylor EW, Zhang J (2023b) Potential of green tea EGCG in neutralizing SARS-CoV-2 Omicron variant with greater tropism toward the upper respiratory tract. Trends Food Sci Technol 132:40–53. https://doi.org/10.1016/j.tifs.2022.12.012

Zhou Z, Li K, Guo J, Wang Y, Wei Y, Duan J, Chen M, Shi L, Hu W (2022) Green tea catechin EGCG ameliorates thioacetamide-induced hepatic encephalopathy in rats via modulation of the microbiota-gut-liver axis. Mol Nutr Food Res 67:e2200821. https://doi.org/10.1002/mnfr.202200821