



Erythrina velutina Willd.: A review of its traditional uses, phytochemistry, pharmacology, and toxicology

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ABSTRACT

Ethnopharmacological relevance: *Erythrina velutina* Willd., commonly known as “mulungu” in Brazil, is a leguminous tree with various traditional medicinal uses. These uses include treating insomnia, central nervous system disorders, convulsions, nervous cough, and inflammation.

Aim of the review: This review aims to comprehensively summarize the ethnomedicinal uses, chemical constituents, pharmacology, and toxicology of *E. velutina* to explore its potential as a source for new therapeutic agents. **Materials and methods:** Information was collected from scientific databases, dissertations, and books. Chemical structures were generated using ChemDraw. To ensure the accuracy of the plant names, “World Flora Online” (www.worldfloraonline.org) was consulted for the accepted names of plants.

Results: *E. velutina* is indigenous to Brazil, Peru, Ecuador, Colombia, Venezuela, and Hispaniola. Approximately 244 compounds, mainly alkaloids and flavonoids, have been isolated from it. The plant and its extracts have exhibited various bioactivities, such as anti-inflammatory, anxiolytic, anticonvulsant, neuroprotective, analgesic, antimicrobial, and antioxidant effects, validating some of its traditional medicinal uses. *Erythrina velutina* shows promising therapeutic potential for conditions like convulsion, central nervous disorders, anxiety, insomnia, and inflammation, primarily due to its alkaloid and flavonoid content.

Conclusion: The traditional medicinal uses of the plant, combined with modern scientific research, underscore its pharmacological potential. This makes it a significant candidate for drug development. Further research should focus on conducting toxicological studies, clinical trials, and mechanistic investigations. These efforts will enable a comprehensive exploration of its pharmacological properties and potential applications in drug development.

1. Introduction

Medicinal plants, encompassing various forms such as herbs, trees, and shrubs, are naturally abundant in our surroundings. Throughout history, these plants have been harnessed by diverse cultures worldwide for maintaining health and combating illnesses (Rahman et al., 2022). The utilization of these accessible and culturally significant traditional medicines not only offers an affordable healthcare approach but also serves as a crucial source of livelihood for indigenous and rural communities (Weldegerima, 2009). Medicinal plants are known for their

abundance of bioactive compounds, including polyphenols, flavonoids, alkaloids, sterols, saponins, among others. These bioactive substances hold promising potential as a foundation for the development of novel pharmaceuticals with health benefits for humanity (Iftikhar et al., 2022). A compelling example is the isolation of artemisinin and its derivatives from *Artemisia annua*, which have been established as the recommended first-line antimalarial drugs for malaria treatment. This medicinal plant has been an integral part of traditional Chinese herbal medicine for over two centuries and utilized in the treatment of fever and malaria (Weldegerima, 2009; Xia et al., 2020). The realm of traditional medicine employs between 50,000 and 80,000 plant species

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Abbreviations

¹ H- and ¹³ C-NMR	¹ H- and ¹³ C-Nuclear Magnetic Resonance
(HR)-MS	High Resolution Mass Spectroscopy
AChE	Acetylcholinesterase
BuChE	Butyrylcholinesterase
CC	Column Chromatography
EVLAE	<i>Erythrina velutina</i> leaves aqueous extract
GABA	Gamma-aminobutyric acid
GC-MS	Gas Chromatography – Mass Spectroscopy
HEEVS	Hydroalcoholic extract of <i>Erythrina velutina</i> stem bark
HPLC	High Performance Liquid Chromatography
HPLC-PDA	High Performance Liquid Chromatography - Photodiode Array Detector
HR-LC-MS/MS	High Resolution – Liquid Chromatography – Tandem Mass Spectroscopy
LC-DAD-MS	Liquid Chromatography – Diode-Array Detection - Mass Spectroscopy
LC-MS/MS	Liquid Chromatography – Tandem Mass Spectroscopy
NMR	Nuclear Magnetic Resonance
NREM	Non-rapid eye movement
MS	Mass Spectroscopy
TRAIL	TNF- related apoptosis-inducing ligand
WAEVS	Water: alcohol extract of <i>Erythrina velutina</i> stem bark

globally (Rahman et al., 2022). However, for many medicinal plants, including some species in the genus *Erythrina*, there remains a significant lack of extensive exploration concerning the interrelationship between traditional uses, chemical constituents, and pharmacological activities. Hence, it is important to document the ethnopharmacological information on medicinal plants to provide rationale for their selection for scientific investigation.

Erythrina L. species, which encompass generally large trees (reaching up to 30 m) and occasionally small shrubs, belong to the Fabaceae family. They are primarily distributed across tropical and subtropical regions worldwide (Fahmy et al., 2020), with notable presence in South America, Africa, and Asia.

Their substantial medicinal properties have led to numerous scientific studies investigating the biological and chemical composition of various *Erythrina* species. These research efforts have not only validated the traditional uses of these plants but have also unveiled new potential pharmacological activities associated with them. Extracts of the *Erythrina* genus are known to be rich in various phytochemicals, including alkaloids, flavonoids, tannins, and terpenoids (Fahmy et al., 2020). Some of the specific compounds found in *Erythrina* extracts include erythrinin, erythraline, erythratidine, and erysodine (Hussain et al., 2016). These compounds exhibit a wide range of pharmacological properties, encompassing anxiolytic, anticonvulsant, neuroprotective, anti-inflammatory, analgesic, antioxidant, and antimicrobial effects. Over the past few decades, a significant amount of research has documented the pharmacological properties and the connection to the traditional medicinal applications of *Erythrina* genus species. For instance, reports have highlighted the anti-inflammatory capabilities of *E. indica* Lam. (Verma et al., 2005), *E. variegata* L. (Santhiya et al., 2016), and *E. abyssinica* Lam. (Nasimolo et al., 2014). These findings corroborate the traditional medicinal usage of these species for addressing various inflammatory conditions. While the ethnomedicinal uses, phytochemistry, and pharmacological activities of certain *Erythrina* species have been thoroughly reviewed and documented, comprehensive reports on certain extensively studied species, such as *E. velutina* Willd., are absent. Furthermore, previous reviews on *Erythrina* species, particularly *E. velutina*, have focused on specific aspects such as alkaloid type and distribution (Fahmy et al., 2020) and biotechnological

potential (Souza et al., 2022). However, none of these reviews have comprehensively integrated the traditional uses, chemical constituents, and pharmacological activities of *E. velutina*. As a result, there is a lack of groundwork for selecting bioactive substances for potential drug discovery. Therefore, this review aims to fill this gap by presenting a comprehensive analysis of various aspects of *E. velutina*, including its medicinal uses, bioactive compounds, pharmacological potentials, and toxicity for the first time. By synthesizing existing information on *E. velutina*, this review seeks to facilitate the identification and development of new therapeutic agents while also contributing to the conservation and sustainable utilization of this valuable plant.

2. Methodology

Relevant information on the ethnomedicinal uses, phytochemistry, pharmacological activities and toxicology of *E. velutina* were obtained by searching through various scientific databases such as Google Scholar, Scopus, Web of Science, Springer, PubMed, and ScienceDirect. Additionally, insights were drawn from dissertations and scholarly books. ChemDraw software facilitated the generation of precise chemical structures for the compounds. The accuracy of plant nomenclature was validated using “World Flora Online” (www.worldfloraonline.org).

3. Results

3.1. Taxonomy (Botany) and geographic distribution of *E. velutina*

The *Erythrina* genus, which encompasses around 120 tropical species, is distributed across warm-temperature regions and various biomes globally (da Silva et al., 2013). The genus name originates from the Greek term “erythros,” signifying red, referencing the pigment present in flowers and seeds (Souza et al., 2022). Brazil harbors twelve species of this genus, with eight being indigenous to the northeast region (da Silva et al., 2013). Although the genus’s exact place of origin remains uncertain, evidence suggests it likely originated in South America, given that the majority of primitive groups within the genus are found there (Jiménez-Cabrera et al., 2021). The genus predominantly thrives in littoral forests on sandy soil and occasionally in coastal forests at elevations up to 250 m (Chu et al., 2019).

Erythrina velutina Willd., commonly referred to as mulungu and belonging to the Fabaceae family and Papilionaceae subfamily, is a thorny forest tree (Fig. 1A) that reaches a height of 8 to 12 m. This tree is indigenous to northeastern and southeastern Brazil, encompassing states like Ceará, Minas Gerais, Rio de Janeiro, and São Paulo. However, its presence has also been noted in other countries such as the Antilles, Venezuela, northern Colombia, Ecuador, Peru, and Central America (Dantas et al., 2004; Souza et al., 2022).

The mulungu tree predominantly flourishes in riparian forests of the Caatinga biome, high-altitude wetlands, open ombrophylous forests, rupestrian fields, savannas, Atlantic forest biomes, coastal regions of all north and northeast Brazilian states, as well as the broad-leaved semi-deciduous forests of Minas Gerais (Dantas et al., 2004; Souza et al., 2022). However, its presence is scarce in certain Brazilian regions due to overexploitation and habitat destruction (Souza et al., 2016). This plant is native to the plains and riverbanks of semi-arid regions in northeast Brazil (Vasconcelos et al., 2003), and it can adapt to areas with both humid and dry climates, enduring annual rainfall ranging from 326 to 2500 mm and temperatures spanning 22.4 °C–26.6 °C. This adaptability is due to its high plasticity and wide distribution (Souza et al., 2020).

Erythrina velutina has six synonyms, namely *Chirocalyx velutinus* (Willd.) Walp., *Corallodendron velutinum* (Willd.) Kuntze, *E. aculeatissima* Desf., *E. aurantiaca* Ridl., *E. velutina* f. *aurantiaca* (Ridl.) Krukoff and *E. splendida* Diels (Wanda et al., 2015). This arboreal species has a high trunk and branches that are not sharply pointed (Vasconcelos et al., 2003; Gomes et al., 2022). The tree can be recognized by its aculeate branches (Gomes et al., 2022). The trunk of *E. velutina* has a diameter of



Fig. 1. *Erythrina velutina* (A) Tree (B) Flowers (C) Stem bark (D) Seeds. (Photo: © Breno Farias) <https://uk.inaturalist.org/photos/153217668> (CC BY-NC 4.0).

80 cm (Wanda et al., 2015). Its leaves are imparipinnate with three foliate leaflets that alternate and are supported by a 6–10 cm petiole (Gomes et al., 2022). These tough and flexible leaflets (Carvalho et al., 2009) are ternate, with an obtuse apex and symmetrical base (da Silva et al., 2013).

During a very dry period, *E. velutina* trees bloom synchronously with flowers (Fig. 1B) developing from pseudoraceme, pedicelled inflorescences that are quite conspicuous since the plant usually blossoms without leaves (Silva, et al., 2020; Gomes et al., 2022). The inflorescence is fascicle type (da Silva et al., 2013), and each one develops 10–26 flowers, with daily 1–8 newly opened flowers, which are large and odourless. The flowers have a typical papilionaceous corolla in pale yellow to rich orange, composed of poorly developed keel and wing petals on the upper side and expanded vexillum below. The flowers open between 06h00–06h30, and the powdery pollen is dispersed on the first day of opening (Sazima et al., 2010). The zygomorphic orange flowers contain a nectariferous chamber where nectar is continuously secreted but only during the first day of anthesis (Teixeira et al., 2019; Silva et al., 2020; Gomes et al., 2022). These flowers occur between July and February (Silver, 2020).

The legume fruits are sessile and dehiscent, with an acute apex and base, measuring 5–8 cm in length. Each fruit contains 1–3 kidney-shaped seeds (Fig. 1D), which are dark red to orange red in color. These seeds are elongated, stenopermic, with a rounded apex and truncated base. They have a smooth surface with a varnish-like appearance, giving them a marple-leather texture (Teixeira et al., 2019; Silva et al., 2020; Gomes et al., 2022; Guariz et al., 2022).

3.2. Ethnomedicinal and other uses of *E. velutina*

Mulungu is a native species of the Brazilian flora, used in folk medicine in some regions of Northeastern Brazil as a sudorific, soothing,

pectoral emollient, and local anesthetic (Raupp et al., 2008; Souza et al., 2022). It has a long history of use in countries like Brazil and Peru, mainly as a tranquilizer for stress, anxiety, agitation, depression, and insomnia (Raupp et al., 2008; Souza et al., 2022). Moreover, it has a traditional application in treating inflammation, toothache, headache, and nervous cough, among other ailments (Table 1). The stem bark (Fig. 1C) is the most used part of the plant for medicinal purposes, followed by the seeds, flowers, fruits, and leaves. Typically, Mulungu is prepared as an infusion or decoction and taken orally.

Other general uses of *E. velutina* has been reported. Its lightweight, softwood is used for wooden shoes, toys, crates, and rafts (Raupp et al., 2008; Souza et al., 2022). It is also harnessed for woodworking, handicrafts, and industrial purposes, like dyeing clothes (Wanda et al., 2015). Additionally, it is cultivated in gardens and parks for its attractive flowers (Da-cunha et al., 1996), and also used for afforestation in streets and gardens as it is drought-resistant and has quick growth and nitrogen-fixing capacity (Ribeiro et al., 2018). Due to its pivoting root system and swift growth, it proves valuable in restoring degraded areas and rehabilitating riparian vegetation (Pereira et al., 2014). Finally, it is used in beekeeping (Silver, 2020).

3.3. Phytochemistry of *E. velutina*

Erythrina velutina has been a subject of extensive phytochemical research since erythraline and hypaphorine were first isolated from it in 1940 (Folkers and Koniuszy, 1940). To date, researchers have identified at least 244 phytochemicals from stem barks, seeds, leaves, and flowers of the plant (Table 2). These include alkaloids, flavonoids, fatty acids, carbohydrates, essential oils, saponins, coumarins, lignins, triterpenoids, nucleic acids, terpenes, glycerolipids, and other compounds. The major phytochemicals in *E. velutina* are alkaloids, flavonoids, essential oils, and fatty acids, and they have been the subject of study for their

Table 1
Traditional medicinal use of *Erythrina velutina*.

Country and local names	Ailments/Traditional uses	Plant parts used	References
Brazil(Mulungu)	Used as natural sedative and tranquilizer for stress, anxiety, agitation, depression and insomnia.	Bark, seeds	(Raupp et al., 2008; Rodrigues et al., 2008; Souza et al., 2022)
Brazil(Mulungu)	Used for insomnia, anxiety, depression, sclerosis, hypertension, cystitis, epilepsy, urinary insufficiency, gingivitis and asthmatic bronchitis.	Bark	Pereira Sousa et al. (2021)
Brazil(Mulungu)	Insomnia, coughs and as vermifuge	Stem bark	Agra et al. (2008)
Brazil(Mulungu)	Toothache	Dried fruit	Agra et al. (2008)
Peru(Porotillo)	To clean the intestine	Flowers, leaves and stem (fresh or dried)	Bussmann and Sharon (2006)
Brazil(Mulungu)	Used against several central nervous system disorders such as anxiety, insomnia, convulsions, and nervous cough.	Fresh stem bark	Santos et al. (2012)
Brazil(Mulungu)	Anti-inflammatory	Bark, leaves and flowers	(Júnior et al., 2011; Figueirêdo Júnior et al., 2022)
Brazil(Mulungu)	Menopause (climacteric) and improving circulation	Stem inner bark	(Carvalho et al., 2009; Saraiva et al., 2015; Macêdo et al., 2018)
Brazil(Mulungu)	Tooth inflammation, odontalgia, headache, fever, maternal milk production, diabetes, hypertension, cough, bronchitis, nervous disturbance, insomnia, hemorrhoids, helminthiasis, calmative, sinusitis, tranquilizer.	Bark, flowers, fruits, seeds	(De Albuquerque et al., 2007a, 2007b)
Brazil(Mulungu)	Used for nervous excitation, sleepiness, convulsions and nervous coughs.	Stem bark	Dantas et al. (2004)
Brazil(Mulungu)	Headache, fever, sedative and galactagogue.	Inner bark	De Almeida et al. (2005)
Brazil(Mulungu)	Tranquilizer and cough suppressant. To treat bronchitis, hemorrhoids and parasitic intestinal infections.	Bark	Teixeira et al. (2019)
Brazil(Mulungu)	Toothache, sleep disturbance, sneezing, tooth extraction.	Bark, seeds, and inner stem bark (fresh powder)	(Do Nascimento Magalhães et al., 2019)
Brazil(Mulungu)	Wound healing and for inflammation and nerve pains	Bark	(De Albuquerque and De Oliveira, 2007; De Sousa Araújo et al., 2008)
Brazil(Mulungu)	Helps to bring gum abscesses to maturity	Bark	Wanda et al. (2015)

properties and pharmacological functions.

3.3.1. Alkaloids

Alkaloids were the first group of phytochemicals to be extracted from *E. velutina*. In 1940, Folkers and colleagues successfully isolated erythraline (1) and hypaphorine (2) from the seed of the plant (Folkers and Koniuszy, 1940). Subsequently, Vasconcelos and colleagues reported the isolation of 5,7-3'-trihydroxyl-5'-p-enyl-6-methoxyisoflavonone as the next alkaloid compound from *E. velutina* (Vasconcelos et al., 2003). Later, 14 alkaloids (3–15) from the seeds of *E. velutina* were identified and isolated (Ozawa et al., 2009, 2011; Todoroki et al., 2021). Furthermore, Chacon et al. (2021) isolated 55 alkaloids (16–70) from the leaves and seeds of the plant. As of now, at least 71 alkaloids have been identified and isolated from *E. velutina*. Alkaloids make up approximately 27% of the total phytochemicals extracted from the plant.

3.3.2. Flavonoids

The first flavonoid, eryvellutinone (76), was isolated from the stem bark of *E. velutina* (Da-cunha et al., 1996). Additionally, five other flavonoids (74, 121–123) were also extracted from the stem bark (Silva et al., 2016; Rabelo et al., 2001). Three flavonoids (75, 77–78) were isolated in the plant's leaves (Passos et al., 2013; Dias et al., 2019). Chacon et al. (2022) isolated 42 flavonoids (79–120) from both the leaves and seeds of *E. velutina*. Overall, at least 50 flavonoids belonging to different categories like isoflavones, flavonols, chalcones, anthocyanins, and auronones have been identified in the plant (Chacon et al., 2022).

3.3.3. Fatty acids

Teixeira et al. (2019) identified and isolated 12 fatty acids (124–135) from the black and red seeds of *E. velutina*, with oleic acid, palmitic acid, and behenic acid being the major ones. The black seeds contained 28% saturated fatty acids, 53% monounsaturated fatty acids, and 10% polyunsaturated fatty acids, while the red seeds contained 27% saturated fatty acids, 52% monounsaturated fatty acids, and 16%

polyunsaturated fatty acids. Similarly, Chacon et al. (2022) isolated 13 fatty acids (136–148) from the leaves and seeds of *E. velutina*.

3.3.4. Essential oils

In 2019, Teixeira et al. isolated 59 essential oils (149–208) from the orange and red flowers of *E. velutina*. (E)-caryophyllene is the primary component of orange flower oil, while (E)-asarone is the primary component of red flower oil. Phenylpropanoids are the major chemical constituents of both flower oils (Teixeira et al., 2019).

3.3.5. Other compounds

Diaryl propanoid glycosides (71–73), amino acids and analogues (209–215), nucleic acids (216–220), phenylpropanoids (221–222), carbohydrates (223–226), coumarins and derivatives (227–231), terpenes (232–235), phenolic acid (236), saponins (237–238), lignans (239), glycerolipids (240–241), and other compounds (242–244) have been isolated from the leaves and seeds of *E. velutina* (Chacon et al., 2022; Todoroki et al., 2021; Vasconcelos et al., 2003, 2004).

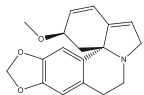
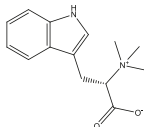
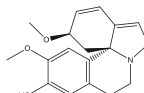
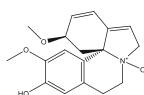
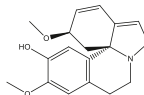
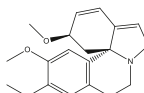
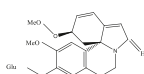
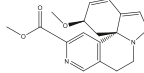
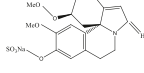
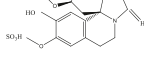
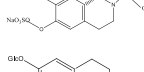
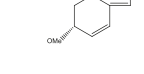
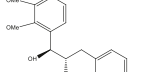
3.4. Pharmacological effects of *E. velutina*

Erythrina velutina has been reported to exhibit a diverse range of pharmacological properties. These include anxiolytic, anti-insomnia, anti-agitation, analgesic, anti-inflammatory, antibacterial, antinociceptive, anticonvulsant, neuroprotective, anti-odontalgic, anthelmintics, antitumor, anticoagulant, anti-elastase, gastroprotective, anesthetic, antioxidant, anticholinesterase, cardioprotective, antiulcer, and central nervous system modulating activities. These properties are presented in Table 3 and Fig. 2 and further discussed below.

3.4.1. Tranquilizer for central nervous system disorders

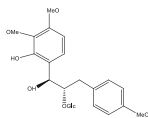
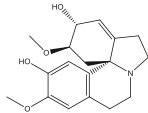
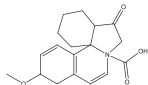
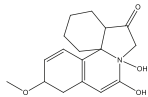
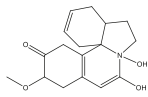
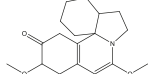
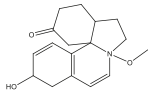
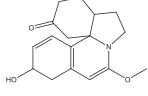
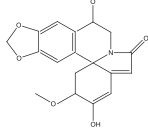
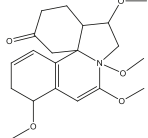
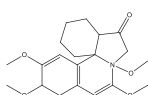
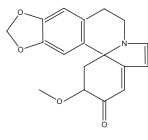
Erythrina velutina is a common tranquilizer used in Brazil for the treatment of central nervous system diseases. In a study conducted by Vasconcelos et al. (2004), the central behavioral effects of

Table 2Phytochemicals isolated from *Erythrina velutina*.

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
Alkaloids	(1)	Erythraline		Seeds	Silica gel chromatography	Folkers and Koniuszy (1940)
	(2)	Hypaphorine		Seeds	Silica gel chromatography	(Folkers and Koniuszy, 1940; Ozawa et al., 2008)
	(3)	Erysodine		Seeds	Silica gel chromatography	Ozawa et al. (2009)
	(4)	Erysodine-N-oxide		Seeds	Silica gel chromatography	Ozawa et al. (2009)
	(5)	Erysovine		Seeds	Silica gel chromatography	Ozawa et al. (2009)
	(6)	Erysotrine		Seeds	Silica gel chromatography	Ozawa et al. (2009)
	(7)	Glycoerysodine		Seeds	Silica gel chromatography	Ozawa et al. (2009)
	(8)	Erymelanthine		Seeds	Silica gel chromatography	Ozawa et al. (2009)
	(9)	Sodium erysovine 15-O-sulfate		Seeds	¹ H and ¹³ C-NMR, (HR)-MS	Ozawa et al. (2011)
	(10)	Erysopine 15-O-sulfate		Seeds	¹ H and ¹³ C-NMR, (HR)-MS	Ozawa et al. (2011)
	(11)	Sodium erysovine N-oxy-15-O-sulfate		Seeds	¹ H and ¹³ C-NMR, (HR)-MS	Ozawa et al. (2011)
	(12)	16-O-β-D-glucopyranosyl coccoline		Seeds	¹ H and ¹³ C-NMR, (HR)-MS	Ozawa et al. (2011)
	(13)	(3 R)-16-O-β-D-glucopyranosyl erysodine N-oxide		Seeds	NMR, MS, CC, and HPLC	Todoroki et al. (2021)

(continued on next page)

Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(14)	(3 R)-16-O- β -D-glucopyranosyl-10,11-dehydrococcoline		Seeds	NMR, MS, CC, and HPLC	Todoroki et al. (2021)
	(15)	Erysosalvine		Seeds	NMR, MS, CC, and HPLC	Todoroki et al. (2021)
	(16)	11-methoxy-5-oxo-2H,4H,5H,10H,11H-indolo [7a,1-a] isoquinoline-7-carboxylic acid		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(17)	7,8-dihydroxy-11-methoxy-2H,4H,5H,10H,11H-indolo [7a,1-a] isoquinolin-5-one (11-oxoerysopine)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(18)	7,8-dihydroxy-11-methoxy-4H,5H,10H,11H,12H-indolo [7a,1-a] isoquinolin-12-one (2,3-demethoxyerythratinone)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(19)	8,11-dimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7a,1-a] isoquinolin-12-one (coccudinone)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(20)	11-hydroxy-7-methoxy-2H,4H,5H,10H,11H-indolo [7a,1-a] isoquinolin-2-one		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(21)	11-hydroxy-8-methoxy-2H,4H,5H,10H,11H-indolo [7a,1-a] isoquinolin-2-one		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(22)	18-hydroxy-11,19-dimethoxy-5,7-dioxo-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,10} .0 ^{4,8}]icosa-2,4 (8),9,15,17-pentaen-14-one		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(23)	5,7,8,10-tetramethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a] isoquinolin-2-one		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(24)	7,8,11,12-tetramethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a] isoquinolin-5-one		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(25)	19-methoxy-5,7-dioxo-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,10} .0 ^{4,8}]icosa-2 (10),3,8,14,16-pentaen-18-one (3-oxo-erythraline)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)

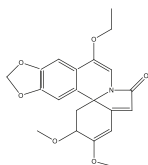
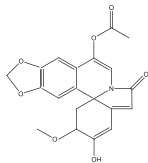
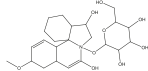
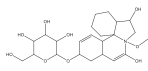
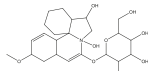
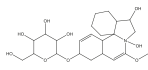
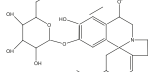
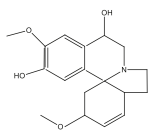
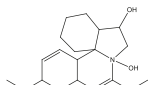
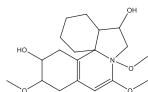
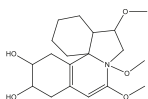
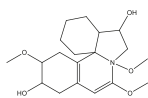
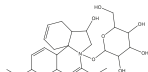
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(26)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,10} .0 ^{4,8}]icosa-2,4 (8),9,15,17-pentaen-11-one (11-oxo-erythraline)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(27)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,10} .0 ^{4,8}]icosa-2,4 (8),9,15,17-pentaen-14-one (8-oxo-erythraline)		Seeds, Leaves	Silica Gel Chromatography; HR-LC-MS/MS	(Ozawa et al., 2008; Chacon et al., 2021)
	(28)	7,11-dimethoxy-2H,10H,11H-indolo [7a,1-a]isoquinolin-2-one		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(29)	8,11-dimethoxy-2H,10H,11H-indolo [7a,1-a]isoquinolin-2-one		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(30)	7-hydroxy-8,11-dimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinolin-5-one (11-oxoerysodine)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(31)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,10} .0 ^{4,8}]icosa-2,4 (8),9,16-tetraen-18-one (erythratrone)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(32)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,10} .0 ^{4,8}]icosa-2,4 (8),9,16-tetraen-14-one (8-oxoerysodine)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(33)	8,11-dimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinolin-2-one (coccolinine)		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(34)	7,11-dimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinolin-2-one (isococcolinine)		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(35)	7,8,11-trimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinoline-4,5-dione (10,11-dioxoerysotrine)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(36)	7,8,11-trimethoxy-4H,5H,10H,11H,12H-indolo [7a,1-a]isoquinoline-5,12-dione		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(37)	19-methoxy-14-oxo-5,7-dioxa-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,10} .0 ^{4,8}]icosa-2,4 (8),9,11,15,17-hexaen-11-yl acetate		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)

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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(38)	11-ethoxy-18,19-dimethoxy-5,7-dioxo-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,16} .0 ^{4,8}]icosa-2,4 (8),9,11,15,17-hexaen-14-one		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(39)	18-hydroxy-19-methoxy-14-oxo-5,7-dioxo-13-azapentacyclo [11.7.0.0 ^{1,16} .0 ^{2,16} .0 ^{4,8}]icosa-2,4 (8),9,11,15,17-hexaen-11-yl acetate		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(40)	2-({5,8-dihydroxy-11-methoxy-1H,2H,4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinolin-7-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(41)	2-({5,8-dihydroxy-7-methoxy-1H,2H,4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinolin-11-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(42)	2-({5,7-dihydroxy-11-methoxy-1H,2H,4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinolin-8-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(43)	2-({5,7-dihydroxy-8-methoxy-1H,2H,4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinolin-11-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(44)	2-({7-hydroxy-5,11-dimethoxy-1H,2H,4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinolin-8-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(45)	7,11-dimethoxy-1H,2H,4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinoline-5,8-diol		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(46)	8,11-dimethoxy-1H,2H,4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinoline-5,7-diol		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(47)	7,8,11-trimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7a,1-a]isoquinoline-5,12-diol (11-hydroxyerythratidine or 11-hydroxyepierythratidine)		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(48)	5,7,8-trimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7a,1-a]isoquinoline-11,12-diol		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(49)	7,8,12-trimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7a,1-a]isoquinoline-5,11-diol		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(50)	2-({5-hydroxy-8,11-dimethoxy-4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinolin-7-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)

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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(51)	2-({5-hydroxy-8,11-dimethoxy-4H,5H,10H,11H,13aH-indolo [7a,1-a]isoquinolin-7-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(52)	7,11,12-trimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7 ^a ,1-a]isoquinolin-8-ol		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(53)	7,8,11-trimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7 ^a ,1-a]isoquinolin-12-ol (erythratidine)		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(54)	8,11,12-trimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7 ^a ,1-a]isoquinolin-7-ol		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(55)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ¹ , ^{1a} .0 ² , ^{1a} .0 ⁴ , ^a]icosa-2,4 (8),9,16-tetraene-11,18-diol (11-hydroxyerythratine or 11-hydroxyepierythratine)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(56)	5,7-dihydroxy-8,11-dimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7a,1-a]isoquinolin-12-one (11-hydroxyerysotinine)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(57)	5,8-dihydroxy-7,11-dimethoxy-1H,2H,4H,5H,10H,11H,12H-indolo [7a,1-a]isoquinolin-12-one (11-hydroxyerysosalvinone)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(58)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ¹ , ^{1a} .0 ² , ^{1a} .0 ⁴ , ^a]icosa-2,4 (8),9,15-tetraen-11-ol		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(59)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ¹ , ^{1a} .0 ² , ^{1a} .0 ⁴ , ^a]icosa-2,4 (8),9,15-tetraen-18-ol (erythratine or epierythratine)		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(60)	7,11-dimethoxy-4H,5H,10H,11H,13aH-indolo [7 ^a ,1-a]isoquinoline-5,8-diol (11-hydroxyerysovin (alpha or beta))		Leaves	HR-LC-MS/MS	Chacon et al. (2021)

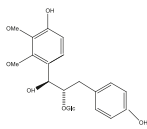
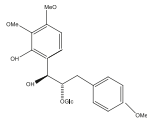
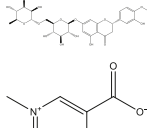
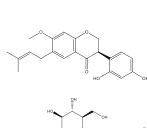
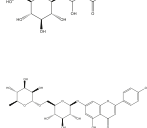
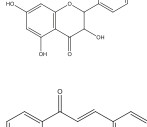
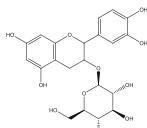
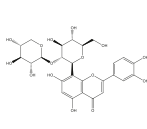
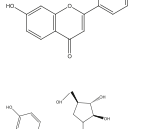
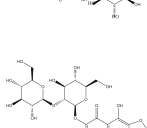
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(61)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ¹ , ¹⁶ .0 ² , ¹⁰ .0 ⁴ , ⁸]icosa-2,4 (8),9,17-tetraen-11-ol		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(62)	2-({5,12-dihydroxy-8,11-dimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinolin-7-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(63)	2-({11,12-dihydroxy-5,8-dimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinolin-7-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(64)	2-({5,12-dihydroxy-7,11-dimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinolin-8-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(65)	2-([4,5-dihydroxy-2-({19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ¹ , ¹⁶ .0 ² , ¹⁰ .0 ⁴ , ⁸]icosa-2,4 (8),9,17-tetraen-11-yl}oxy)oxan-3-yl]oxy)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(66)	2-(hydroxymethyl)-6-({7,8,11-trimethoxy-2H,4H,5H,10H,11H-indolo [7a,1-a]isoquinolin-5-yl}oxy)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(67)	2-({18-hydroxy-19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ¹ , ¹⁶ .0 ² , ¹⁰ .0 ⁴ , ⁸]icosa-2,4 (8),9,15,17-pentaen-11-yl}oxy)-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(68)	7,8,12-trimethoxy-10H,11H,12H,13H,13aH-indolo [7a,1-a]isoquinolin-11-ol		Leaves	HR-LC-MS/MS	Chacon et al. (2021)
	(69)	7,8,11-trimethoxy-1H,2H,4H,5H,12H-indolo [7a,1-a]isoquinolin-12-ol		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
	(70)	19-methoxy-5,7-dioxa-13-azapentacyclo [11.7.0.0 ¹ , ¹⁶ .0 ² , ¹⁰ .0 ⁴ , ⁸]icosa-2,4 (8),9,14,17-pentaen-11-ol (erythrine)		Leaves, Seeds	HR-LC-MS/MS	Chacon et al. (2021)
Diarylpropanoid glycosides	(71)	Eryvelutioside A		Seeds	NMR, MS, CC, and HPLC	Todoroki et al. (2021)

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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
Flavonoids	(72)	Eryvelutioside B		Seeds	NMR, MS, CC, and HPLC	Todoroki et al. (2021)
	(73)	Eryvelutioside C		Seeds	NMR, MS, CC, and HPLC	Todoroki et al. (2021)
	(74)	Hesperitin		Stem bark	HPLC-PDA	Silva et al. (2016)
	(75)	Trigonelline		Leaves	Reversed phase HPLC	Dias et al. (2019)
	(76)	Eryvellutinine		Stem bark	NMR, CC	Da-cunha et al. (1996)
	(77)	Apigenin 6,8-di-C-β-glucoside (vicenin II)		Leaves	LC-DAD-MS	Passos et al. (2013)
	(78)	Apigenin-7-O-rutinoside (isorhoifolin)		Leaves	LC-DAD-MS	Passos et al. (2013)
	(79)	Dihydrokaempferol		Leaves	LC-MS/MS	Chacon et al. (2022)
	(80)	Chalcone		Seeds	LC-MS/MS	Chacon et al. (2022)
	(81)	(2R,3R,4S,5S,6R)-2-[[2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3,4-dihydro-2H-chromen-3-yl]oxy]-6-(hydroxymethyl)oxane-3,4,5-triol		Seeds	LC-MS/MS	Chacon et al. (2022)
	(82)	8-[(2S,3R,4S,5S,6R)-4,5-dihydroxy-6-(hydroxymethyl)-3-[(2S,3R,4S,5R)-3,4,5-trihydroxyoxan-2-yl]oxyoxan-2-yl]-2-(3,4-dihydroxyphenyl)-5,7-dihydroxychromen-4-one		Leaves	LC-MS/MS	Chacon et al. (2022)
	(83)	7,4'-Dihydroxyflavone		Leaves	LC-MS/MS	Chacon et al. (2022)
	(84)	Flavonoid 8-C-glycosides		Leaves	LC-MS/MS	Chacon et al. (2022)
	(85)	7-[(2S,3R,4S,5S,6R)-4,5-dihydroxy-6-(hydroxymethyl)-3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyoxan-2-yl]oxy-9-hydroxy-6-(4-hydroxyphenyl)-[1,3]dioxolo [4,5-g]chromen-8-one		Seeds	LC-MS/MS	Chacon et al. (2022)

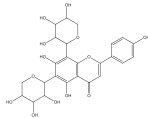
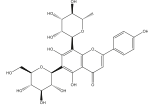
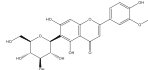
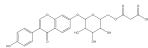
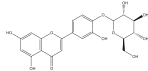
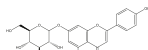
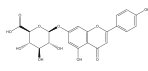
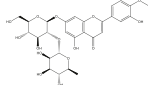
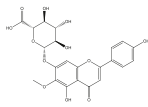
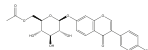
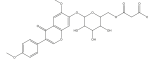
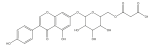
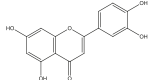
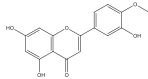
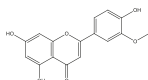
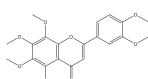
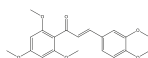
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(86)	2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-[(2S,3R,4S,5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxychromen-4-one		Seeds	LC-MS/MS	Chacon et al. (2022)
	(87)	Daidzein-8-C-glucoside		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(88)	3,5,7,3',4'-Pentahydroxyflavanone (dihydrotricitin)		Seeds	LC-MS/MS	Chacon et al. (2022)
	(89)	5,7-dihydroxy-2-(4-hydroxyphenyl)-6,8-bis [3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]chromen-4-one		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(90)	Daidzin		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(91)	5,7-dihydroxy-2-(4-hydroxyphenyl)-8-[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]-6-(3,4,5-trihydroxyoxan-2-yl)chromen-4-one		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(92)	2-[4-[3-[3,4-dihydroxy-4-(hydroxymethyl)oxolan-2-yl]oxy-4,5-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]-7-hydroxy-2,3-dihydrochromen-4-one		Seeds	LC-MS/MS	Chacon et al. (2022)
	(93)	Luteolin-6-C-glucoside		Leaves	LC-MS/MS	Chacon et al. (2022)
	(94)	Flavone base + 3O, O-HexA-HexA		Leaves	LC-MS/MS	Chacon et al. (2022)
	(95)	Apigenin-8-C-glucoside		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(96)	3-(4-hydroxyphenyl)-7-methoxy-5-[(3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxychromen-4-one		Leaves	LC-MS/MS	Chacon et al. (2022)
	(97)	Astragalin		Leaves	LC-MS/MS	Chacon et al. (2022)
	(98)	(2S,3S,4S,5R,6S)-6-[2-(3,4-dihydroxyphenyl)-5-hydroxy-4-oxochromen-7-yl]oxy-3,4,5-trihydroxyoxane-2-carboxylic acid		Leaves	LC-MS/MS	Chacon et al. (2022)

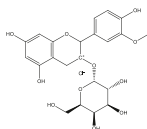
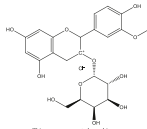
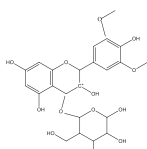
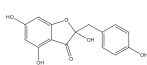
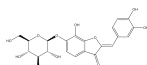
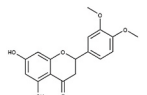
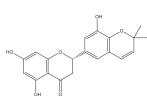
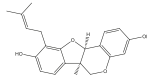
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(99)	5,7-dihydroxy-2-(4-hydroxyphenyl)-6,8-bis(3,4,5-trihydroxyoxan-2-yl)chromen-4-one		Leaves	LC-MS/MS	Chacon et al. (2022)
	(100)	5,7-dihydroxy-2-(4-hydroxyphenyl)-6-[(2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]-8-[(2S,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]chromen-4-one		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(101)	3'-O-methyluteolin 6-C-glucoside (isoscoparine)		Leaves	LC-MS/MS	Chacon et al. (2022)
	(102)	Isoflavone base + 2O, O-MalonylHex		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(103)	Luteolin-4'-O-glucoside		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(104)	Apigenin-7-O-glucoside		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(105)	(2S,3S,4S,5R,6S)-3,4,5-trihydroxy-6-[5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl]oxyoxane-2-carboxylic acid		Leaves	LC-MS/MS	Chacon et al. (2022)
	(106)	Neodiosmin		Seeds	LC-MS/MS	Chacon et al. (2022)
	(107)	(2S,3S,4S,5R,6S)-3,4,5-trihydroxy-6-[5-hydroxy-2-(4-hydroxyphenyl)-6-methoxy-4-oxochromen-7-yl]oxyoxane-2-carboxylic acid		Leaves	LC-MS/MS	Chacon et al. (2022)
	(108)	6''-O-acetylidaizn		Seeds	LC-MS/MS	Chacon et al. (2022)
	(109)	Isoflavone base + 1O, 2MeO, O-malonylHex		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(110)	Isoflavone base + 3O, O-malonylHex		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(111)	Luteolin		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(112)	Diosmetin		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(113)	5,7-dihydroxy-2-(4-hydroxy-3-methoxyphenyl)chromen-4-one		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(114)	Nobiletin		Leaves	LC-MS/MS	Chacon et al. (2022)
	(115)	(E)-3-(3,4-dimethoxyphenyl)-1-(2,4,6-trimethoxyphenyl)prop-2-en-1-one		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)

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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(116)	Petunidin-3-O- β -glucoside		Seeds	LC-MS/MS	Chacon et al. (2022)
	(117)	Peonidin 3-galactoside	 This name appears to be ambiguous	Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(118)	Anthocyanidin base + 4O, 2MeO, O-Hex		Seeds	LC-MS/MS	Chacon et al. (2022)
	(119)	2,4,6-trihydroxy-2-[(4-hydroxyphenyl)methyl]-1-benzofuran-3-one		Seeds	LC-MS/MS	Chacon et al. (2022)
	(120)	Maritimetin-6-O-glucoside		Seeds	LC-MS/MS	Chacon et al. (2022)
	(121)	Homohesperetin		Stem bark	HPLC-PDA	(Silva et al., 2016; Rabelo et al., 2001)
	(122)	Sigmoidin C		Stem bark	HPLC-PDA	Silva et al. (2016)
	(123)	Phaseollidin		Stem bark	HPLC-PDA	Rabelo et al. (2001)
Fatty acids	(124)	Myristic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(125)	Palmitic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(126)	Palmitoleic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(127)	Stearic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(128)	Oleic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(129)	Linoleic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(130)	Behenic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(131)	Eicosanoic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(132)	Eicosadienoic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(133)	Dihomo- γ -linolenic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(134)	Erucic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(135)	Docosadienoic acid		Seeds	GC-MS	Teixeira et al. (2019)
	(136)	5-Hydroxyeicosapentaenoic acid (5-HEPE)		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(137)	Phytosphingosine		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)

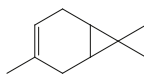
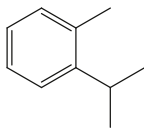
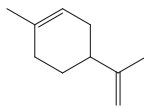
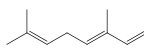
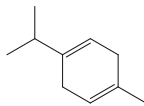
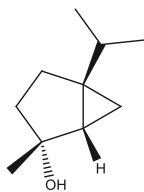
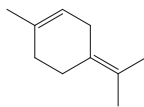
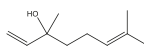
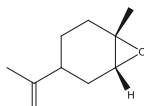
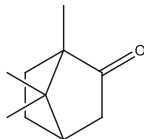
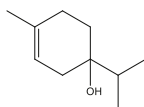
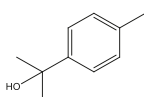
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
Essential oils	(138)	9,12,15-octadecatrienoic acid, 3-(hexopyranosyloxy)-2-hydroxypropyl ester, (9Z,12Z,15Z)		Leaves	LC-MS/MS	Chacon et al. (2022)
	(139)	1-palmitoyl-2-hydroxy-sn-glycero-3-phosphoethanolamine		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(140)	Palmitoyllysleothithin		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(141)	1-hexadecanoyl-sn-glycero-3-phosphocholine		Seeds	LC-MS/MS	Chacon et al. (2022)
	(142)	1-(9Z-octadecenoyl)-sn-glycero-3-phosphoethanolamine		Seeds	LC-MS/MS	Chacon et al. (2022)
	(143)	13-keto-9Z,11E-octadecadienoic acid		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(144)	1-hexadecanoyl-sn-glycerol		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(145)	Monoolein		Seeds	LC-MS/MS	Chacon et al. (2022)
	(146)	1,2-dioleoyl-sn-glycero-3-phosphoethanolamine-N-methyl		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(147)	Glycerol 1-stearate		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(148)	13-docosenamide		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(149)	(4Z)-hexenol		Red flowers	GC-MS	Teixeira et al. (2019)
	(150)	Isopropyl-2-methyl butyrate		Red flowers	GC-MS	Teixeira et al. (2019)
	(151)	α -thujene		Red flowers	GC-MS	Teixeira et al. (2019)
	(152)	α -Pinene		Red flowers	GC-MS	Teixeira et al. (2019)
	(153)	Sabinene		Red flowers	GC-MS	Teixeira et al. (2019)
	(154)	β -Pinene		Red flowers	GC-MS	Teixeira et al. (2019)
	(155)	Myrcene		Red flowers	GC-MS	Teixeira et al. (2019)
	(156)	α -phellandrene		Red flowers	GC-MS	Teixeira et al. (2019)

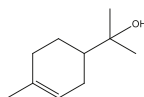
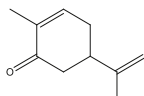
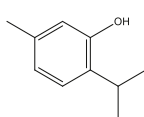
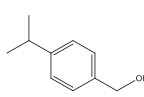
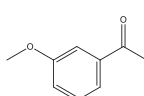
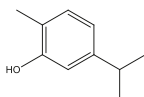
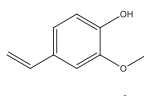
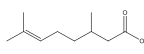
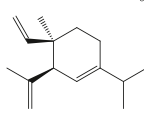
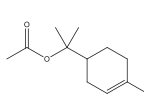
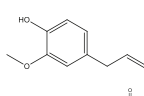
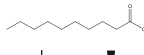
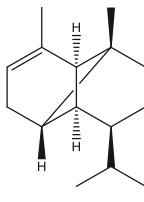
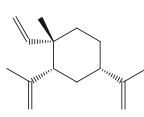
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(157)	δ -3-carene		Red flowers	GC-MS	Teixeira et al. (2019)
	(158)	o-cymene		Red flowers	GC-MS	Teixeira et al. (2019)
	(159)	Limonene		Red flowers	GC-MS	Teixeira et al. (2019)
	(160)	(E)- β -ocimene		Red flowers	GC-MS	Teixeira et al. (2019)
	(161)	γ -terpinene		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(162)	cis-sabinene hydrate		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(163)	Terpineolene		Red flowers	GC-MS	Teixeira et al. (2019)
	(164)	Linalool		Red flowers	GC-MS	Teixeira et al. (2019)
	(165)	cis-limonene oxide		Red flowers	GC-MS	Teixeira et al. (2019)
	(166)	Camphor		Red flowers	GC-MS	Teixeira et al. (2019)
	(167)	Terpinen-4-ol		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(168)	p-cymen-8-ol		Red and orange flowers	GC-MS	Teixeira et al. (2019)

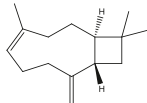
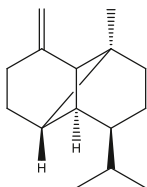
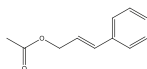
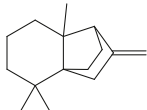
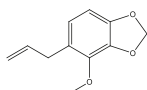
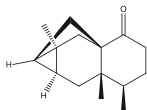
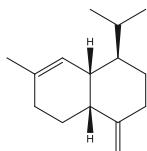
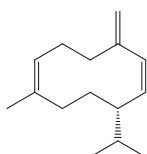
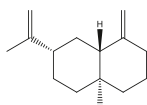
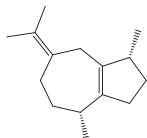
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(169)	α -terpineol		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(170)	Carvone		Orange flowers	GC-MS	Teixeira et al. (2019)
	(171)	Thymol		Orange flowers	GC-MS	Teixeira et al. (2019)
	(172)	p-cymen-7-ol		Orange flowers	GC-MS	Teixeira et al. (2019)
	(173)	3-methoxy-acetophenone		Red flowers	GC-MS	Teixeira et al. (2019)
	(174)	Carvacrol		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(175)	p-vinyl-guaiacol		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(176)	Citronellic acid		Orange flowers	GC-MS	Teixeira et al. (2019)
	(177)	δ -elemene		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(178)	α -terpinyl acetate		Red flowers	GC-MS	Teixeira et al. (2019)
	(179)	Eugenol		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(180)	Decanoic acid		Orange flowers	GC-MS	Teixeira et al. (2019)
	(181)	α -copaene		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(182)	β -elemene		Orange flowers	GC-MS	Teixeira et al. (2019)

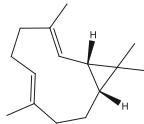
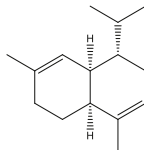
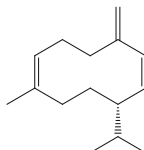
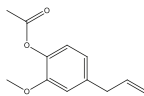
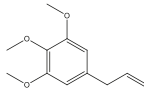
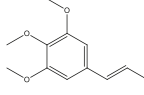
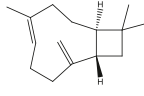
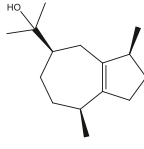
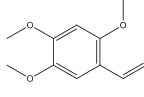
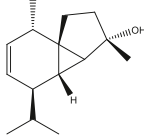
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(183)	E-caryophyllene		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(184)	β -copaene		Orange flowers	204.35	Teixeira et al. (2019)
	(185)	(E)-cinnamyl acetate		Orange flowers	GC-MS	Teixeira et al. (2019)
	(186)	Myltayl-4 (12)-ene		Orange flowers	GC-MS	Teixeira et al. (2019)
	(187)	Croweacin		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(188)	Ishwarone		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(189)	γ -muurolene		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(190)	Germacrene D		Orange flowers	GC-MS	Teixeira et al. (2019)
	(191)	β -selinene		Orange flowers	GC-MS	Teixeira et al. (2019)
	(192)	cis- β -guaiene		Orange flowers	GC-MS	Teixeira et al. (2019)

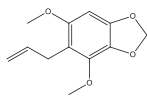
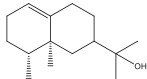
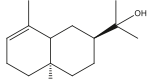
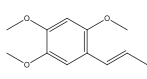
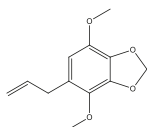
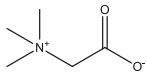
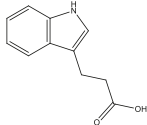
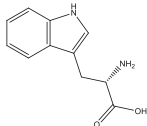
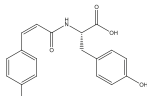
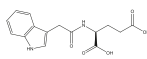
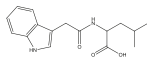
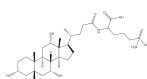
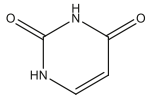
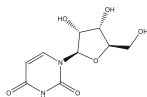
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(193)	Bicyclogermacrene		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(194)	α -muurolene		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(195)	Germacrene A		Orange flowers	GC-MS	Teixeira et al. (2019)
	(196)	Eugenol acetate		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(197)	Elemicin		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(198)	Geranyl butanoate		Orange flowers	GC-MS	Teixeira et al. (2019)
	(199)	(Z)-isoelemicin		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(200)	Caryophyllene oxide		Red flowers	GC-MS	Teixeira et al. (2019)
	(201)	Guaiol		Red flowers	GC-MS	Teixeira et al. (2019)
	(202)	(Z)-asarone		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(203)	1-epi-cubebol		Red flowers	GC-MS	Teixeira et al. (2019)

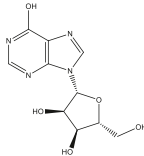
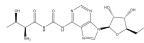
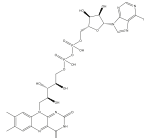
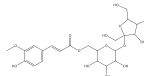
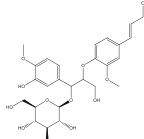
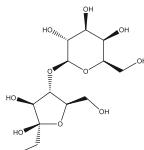
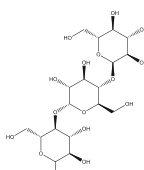
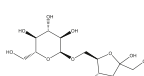
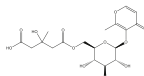
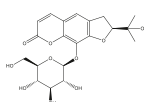
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(204)	Exalatacin		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(205)	Valerianol		Red flowers	GC-MS	Teixeira et al. (2019)
	(206)	7-epi- α -eudesmol		Red flowers	GC-MS	Teixeira et al. (2019)
	(207)	E-asarone		Red and orange flowers	GC-MS	Teixeira et al. (2019)
	(208)	Apiole		Red and orange flowers	GC-MS	Teixeira et al. (2019)
Amino acids and Analogues	(209)	Betaine		Leaves	Reversed phase HPLC	Dias et al. (2019)
	(210)	3-indolepropionic acid		Seeds	LC-MS/MS	Chacon et al. (2022)
	(211)	(S)-2-amino-3-(3-indolyl)propionic acid		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(212)	(2S)-3-(4-hydroxyphenyl)-2-[[[(Z)-3-(4-hydroxyphenyl)prop-2-enoyl]amino]propanoic acid		Leaves	LC-MS/MS	Chacon et al. (2022)
	(213)	Indole-3-acetyl-L-glutamic acid		Seeds	LC-MS/MS	Chacon et al. (2022)
	(214)	Indole-3-acetyl-L-leucine		Leaves	LC-MS/MS	Chacon et al. (2022)
	(215)	Arginine conjugated cholic acid		Leaves	LC-MS/MS	Chacon et al. (2022)
Nucleic acids	(216)	Uracil		Leaves	Reverse - phase HPLC	Dias et al. (2019)
	(217)	Uridine		Leaves	Reverse - phase HPLC	Dias et al. (2019)

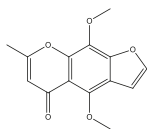
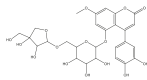
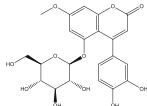
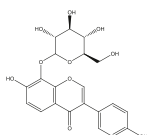
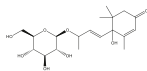
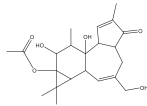
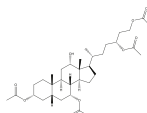
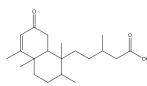
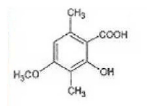
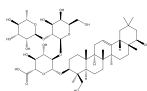
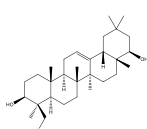
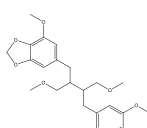
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(218)	Inosine		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(219)	N6-threonylcarbamoyladenine		Leaves	LC-MS/MS	Chacon et al. (2022)
	(220)	Flavin adenine dinucleotide		Leaves	LC-MS/MS	Chacon et al. (2022)
Phenylpropanoid	(221)	[6-[3,4-dihydroxy-2,5-bis(hydroxymethyl)oxolan-2-yl]oxy-3,4,5-trihydroxyoxan-2-yl]methyl (E)-3-(4-hydroxy-3-methoxyphenyl)prop-2-enoate		Seeds	LC-MS/MS	Chacon et al. (2022)
	(222)	3-Hydroxy-1-(3-hydroxy-4-methoxyphenyl)-2-{4-[(1E)-3-hydroxy-1-propen-1-yl]-2-methoxyphenoxy}propyl-β-D-glucopyranoside		Leaves	LC-MS/MS	Chacon et al. (2022)
Carbohydrates	(223)	Lactulose		Seeds	LC-MS/MS	Chacon et al. (2022)
	(224)	Maltotriose		Seeds	LC-MS/MS	Chacon et al. (2022)
	(225)	Isomaltulose		Seeds	LC-MS/MS	Chacon et al. (2022)
	(226)	2-Methyl-4-oxo-4H-pyran-3-yl 6-O-(4-carboxy-3-hydroxy-3-methylbutanoyl)-β-D-glucopyranoside		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
Coumarins and derivatives	(227)	Rutarin		Seeds	LC-MS/MS	Chacon et al. (2022)

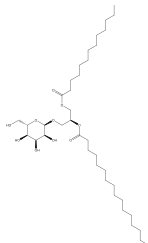
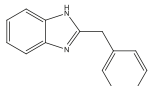
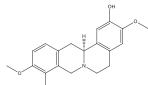
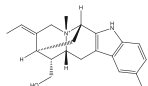
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Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
	(228)	4,9-dimethoxy-7-methylfuro [3,2-g]chromen-5-one		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(229)	5-[6-[[[3,4-dihydroxy-4-(hydroxymethyl)oxolan-2-yl]oxymethyl]-3,4,5-trihydroxyoxan-2-yl]oxy-4-(3,4-dihydroxyphenyl)-7-methoxychromen-2-one		Seeds	LC-MS/MS	Chacon et al. (2022)
	(230)	4-(3,4-dihydroxyphenyl)-7-methoxy-5-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxychromen-2-one		Seeds	LC-MS/MS	Chacon et al. (2022)
	(231)	N-pyridin-3-yl-2-[(4,8,8-trimethyl-2-oxo-9,10-dihydropyrano [2,3-H]chromen-5-yl)oxy]acetamide		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
Terpenes and derivatives	(232)	2-cyclohexen-1-one, 4-[(1E)-3-(beta-D-glucopyranosyloxy)-1-buten-1-yl]-4-hydroxy-3,5,5-trimethyl		Leaves	LC-MS/MS	Chacon et al. (2022)
	(233)	7 b,9-dihydroxy-3-(hydroxymethyl)-1,1,6,8-tetramethyl-5-oxo-1,1a,1 b,4,4a,5,7a,7 b,8,9-decahydro-9aH-cyclopropa [3,4] benzo [1,2-e]azulen-9a-yl acetate		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(234)	(3R,6R)-6-((3R,5S,7R,8R,9S,10S,12S,13R,14S,17R)-3,7-diacetoxy-12-hydroxy-10,13-dimethylhexadecahydro-1H-cyclopenta [a]phenanthren-17-yl)heptane-1,3-diyl diacetate		Leaves	LC-MS/MS	Chacon et al. (2022)
	(235)	5-(1,2,4a,5-tetramethyl-7-oxo-3,4,8,8a-tetrahydro-2H-naphthalen-1-yl)-3-methylpentanoic acid		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
Phenol acid	(236)	Rizonic acid		Stem bark	HPLC-PDA	Silva et al. (2016)
Saponins	(237)	Soyasaponin I		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(238)	Soyasapogenol B		Leaves	LC-MS/MS	Chacon et al. (2022)
Lignans	(239)	6-[3-[(3,4-dimethoxyphenyl)methyl]-4-methoxy-2-(methoxymethyl)butyl]-4-methoxy-1,3-benzodioxole		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)

(continued on next page)

Table 2 (continued)

Classification	No.	Compound name	Structure	Plant part	Method of isolation	References
Glycerolipids	(240)	Monogalactosylmonoacylglycerol		Leaves	LC-MS/MS	Chacon et al. (2022)
	(241)	Putative Monogalactosyl Diacylglycerol (MGDG)		Leaves	LC-MS/MS	Chacon et al. (2022)
Other	(242)	2-Benzyl-1H-benzimidazole		Leaves and Seeds	LC-MS/MS	Chacon et al. (2022)
	(243)	Scoulerine		Leaves	LC-MS/MS	Chacon et al. (2022)
	(244)	Spegatrine		Seeds	LC-MS/MS	Chacon et al. (2022)

hydroalcoholic extracts from *E. velutina* stem bark were evaluated in mice using the elevated plus maze, open field, and rota rod tests. Female mice were administered with 200, 400 or 800 mg/kg of the hydroalcoholic extracts of *E. velutina* stem bark orally and intraperitoneally. The administration of hydroalcoholic extract of *E. velutina* stem bark resulted in a decrease in locomotor activity in the open field test, reduction in rearing and grooming frequency, as well as a decrease in the number of entries in the open and closed arms of the elevated plus maze, indicating a depressant effect on the central nervous system. Dantas et al. (2004) reported that *E. velutina* aqueous extract extended sleep duration induced by sodium pentobarbital by blocking the acquisition of foot shock memory, decreasing the crossing and rearing numbers, interfered with mnemonic process, and possessed sedative and neuromuscular blocking actions. Carvalho et al. (2009) assessed the possible mechanisms of the pharmacological actions of *E. velutina* leaves aqueous extract (EVLAE). In the terminal segments of the guinea pig ileum, the effects of EVLAE were assessed and contractions were observed. EVLAE was incubated alongside other drugs with known pharmacological mechanisms. EVLAE significantly induced contractions. This can be attributable to gamma-aminobutyric acid (GABA) receptor activation, acetylcholine release, muscarinic receptor activation, and increased calcium ion entry through L-type calcium channels all playing a role to produce contractions.

In another study, Ximenes et al. (2019) investigated the effects of standardized *E. velutina* stem bark ethanolic extract on the ketamine induced schizophrenia-like behaviours. Schizophrenia was induced by administering 20 mg/kg ketamine to Swiss mice for 14 days. On days 8–14, 200–400 mg/kg of the extract were co-administered. On day 14, the mice were assessed for schizophrenia like symptoms viz: pre-pulse inhibition of the startle reflex, locomotor activity (open field test), spatial recognition memory (Y-maze task) and social interaction test. Ketamine administration resulted in reduction in pre-pulse inhibition of the startle reflex, hyperlocomotion in the open field test and also a decrease in the social interaction test when compared with the control. There was a reversal in these ketamine induced behavioural patterns

following treatment with the standardized *E. velutina* stem bark ethanolic extract. The study concluded that the standardized *E. velutina* stem bark ethanolic extract may be a drug candidate for the treatment of schizophrenia.

Overall, the interactions between *E. velutina* extracts and neurotransmitter systems, such as gamma-aminobutyric acid (GABA) and acetylcholine, hold promise for unraveling novel pharmacological mechanisms. Further investigations into the precise receptors and pathways modulated by the plant's compounds can deepen the comprehension of its CNS effects. Exploring synergistic effects between *E. velutina* compounds and existing pharmacological agents used in the treatment of CNS disorders could lead to innovative combination therapies, potentially enhancing therapeutic outcomes.

3.4.2. Anxiolytic effects

Erythrina velutina extracts have been reported to possess anxiolytic like effects. The effect of hydroalcoholic extract of *E. velutina* stem bark (HEEVSb) in mice subjected to elevated plus-maze, forced swim, spontaneous locomotor activity, and habituation to active chamber tests was reported by Raupp et al. (2008). Acute and chronic administration of HEEVSb increased the open arm entries percentage and impaired habituation. The study concluded that HEEVSb possess anxiolytic properties, could be a potential novel treatment option for anxiety. Another study by (Ribeiro et al., 2006) assessed the effects of acute and chronic administration of a water: alcohol extract of *E. velutina* stem bark (WAEVSb) (7:3) in rats subjected to elevated T-maze model of anxiety. This model was chosen due to its ability to display definite subtypes of anxiety available in clinical practise. The WAEVSb impaired the elevated T-maze avoidance latencies, without altering escape, in the same manner as diazepam, the reference drug. The study concluded that WAEVSb exerts anxiolytic-like effects on a specific subset of defensive behaviours which have been associated with generalized anxiety disorder. Teixeira-Silva et al. (2008) also assessed the anxiolytic effects of *E. velutina* leaves alcohol extract (EVLAE) in animals using the elevated plus maze test. In the elevated plus maze test,

Table 3Summary of the pharmacological activities of *Erythrina velutina*.

Pharmacological activity	Extracts/ compounds	Plant part used	Type of study	Cell/ Animal used	Dosage used	Effect	References
Antioxidant activity	Ethanol extract	Bark	<i>In vitro</i>	–	10, 25, 50, 100, 200 µg/mL	Scavenged free radicals	Silva et al. (2016)
Neuroprotective effect	Ethanol extract	Bark	<i>Ex vivo</i>	SH-SY5Y cell	0.0025, 0.025, 0.25, 0.5, 1 µg/mL	Reduced neurotoxicity induced by 6-hydroxy-dopamine in SH-SY5Y cells	Silva et al. (2016)
Neuroprotective effect	Ethanol extract	Bark	<i>In vivo</i>	Mice	200, 400 mg/kg	Reversed memory deficit, decreased excitatory amino acid concentrations in the prefrontal cortex, hippocampus, and striatum, taurine concentration, and increased inhibitory amino acid levels in ischemic mice	Rodrigues et al. (2017)
Sleep - inducing effect	Hypaphorine	Seeds	<i>In vivo</i>	Mice	1, 30, 300 mg/kg	Increased non-rapid eye movement (NREM) sleep time by 33% in mice	Ozawa et al. (2008)
Selective apoptosis of cancer cells	Erythraline, erysodine, and erysovine	Seeds	<i>Ex vivo</i>	Jurkat cells	5–25 mg/kg	Enhanced cytotoxicity against Jurkat cells when combined with tumour necrosis factor-related apoptosis-inducing ligand	Ozawa et al. (2009)
Anti-nociceptive activity	Aqueous extract	Leaves	<i>In vivo</i>	Mice	300 and 600 mg/kg	Showed analgesic effects in formalin and acetic acid-induced writhing models	Marchioro et al. (2005)
Central nervous system effects	Aqueous extract	Leaves	<i>In vivo</i>	Swiss mice and Wistar rats	10, 50, 200 mg/kg	Interfered with mnemonic process for different tasks, had sedative and neuromuscular blocking actions	Dantas et al. (2004)
Anticonvulsant effect	Hydroalcoholic extracts	Stem bark	<i>In vivo</i>	Mice	200, 400 mg/kg	Showed anticonvulsant effects in strychnine-induced seizure model and potentiated pentobarbital induced sleeping time	Vasconcelos et al. (2007)
Contractile response	Aqueous extract	Leaves	<i>In vivo</i>	Guinea-pigs	0.025, 0.05, 0.5, 1.0, 1.5, 2.0, and 2.5 mg/ml	Activated gamma-aminobutyric acid and muscarinic receptors, released acetylcholine, augmented calcium ion entry through L-type calcium channels and calcium release from the intracellular stores in the guinea-pig ileum	Carvalho et al. (2009)
Anxiolytic effect	Hydroalcoholic extract	Stem bark	<i>In vivo</i>	Mice	5, 10, 25, 50, and 100 mg/kg	Increased the percentage of open arm entries and exerted an anxiolytic-like effect on mice	Raup et al. (2008)
Antinociceptive effects	Hydroalcoholic extracts	Stem bark	<i>In vivo</i>	Mice	200 and 400 mg/kg	Inhibited abdominal contractions, reduced nociception produced by formalin	Vasconcelos et al. (2003)
Anticholinesterase activity	Aqueous extract	Leaf	<i>Ex vivo</i>	Swiss mice	100, 200, and 400 mg/kg	Inhibited acetylcholinesterase and butyrylcholinesterase activities	Santos et al. (2012)
Central nervous system effect	Alcohol extract	Leaves	<i>In vivo</i>	Swiss mice	10, 20, 100, and 500 mg/kg	Increased the percentage of entries into the open arms, increased the latency to death, and reduced the kindling behaviour induced by pentylenetetrazol	Teixeira-Silva et al. (2008)
Central nervous system depressant effects	Hydroalcoholic extracts	Stem bark	<i>In vivo</i>	Mice	200, 400, and 800 mg/kg	Decreased locomotor activity and the incidence of rearing, and grooming. Decreased the number of entries in the open and closed arms of the elevated plus maze	Vasconcelos et al. (2004)
Antipsychotic effect	Ethanol extract	Stem bark	<i>In vivo</i>	Mice	200 and 400 mg/kg	Reverted schizophrenia-like symptoms induced by ketamine	Ximenes et al. (2019)
Antiulcer effect	Protein isolates	Seeds	<i>In vivo</i>	Wistar rats	0.2 and 0.4 mg/kg	Showed a high affinity and inhibitory effect against human neutrophil elastase. Protected gastric mucosa, preventing haemorrhagic lesions, oedema, and mucus loss	Oliveira de Lima et al. (2017)
Antioxidant and behavioural effects	Erythrine	Leaves	<i>In vivo</i>	Mice	100, 200 and 400 mg/kg	Increased pre-pulse inhibition, glutathione concentration in prefrontal cortex and striatum, decreased malondialdehyde in the prefrontal cortex, hippocampus, and striatum in ketamine-induced schizophrenia model	Dias et al. (2019)
Anti-coagulation and anti-inflammatory effect	Peptides	Seeds	<i>In vitro</i> and <i>In vivo</i>	Mice	1 mg/kg	Showed anticoagulant activity and modulating activity in sepsis induced by caecal ligation and puncture, non-competitively inhibited trypsin, inhibited factor Xa and neutrophil elastase	Machado et al. (2013)
Cardioprotective effect	Ethyl acetate fraction	Leaves	<i>In vivo</i>	Guinea-pig and mice	50 and 500 mg/ml	Increased the cardiac contractile force by increasing the L-type calcium current and activating the adrenergic receptor pathway	Passos et al. (2013)
Anxiolytic-like effects	Water-alcohol extract	Stem bark	<i>In vivo</i>	Wistar rats	100, 200, and 400 mg/kg	Exerted anxiolytic-like effects on some defensive behaviours associated with generalized anxiety disorder	Ribeiro et al. (2006)
Antimicrobial activities	Hydroalcoholic extract	Stem bark	–	–	–	Inhibited <i>Staphylococcus aureus</i> and <i>Streptococcus pyogenes</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> and <i>Salmonella typhimurium</i>	Virtuoso et al. (2005)

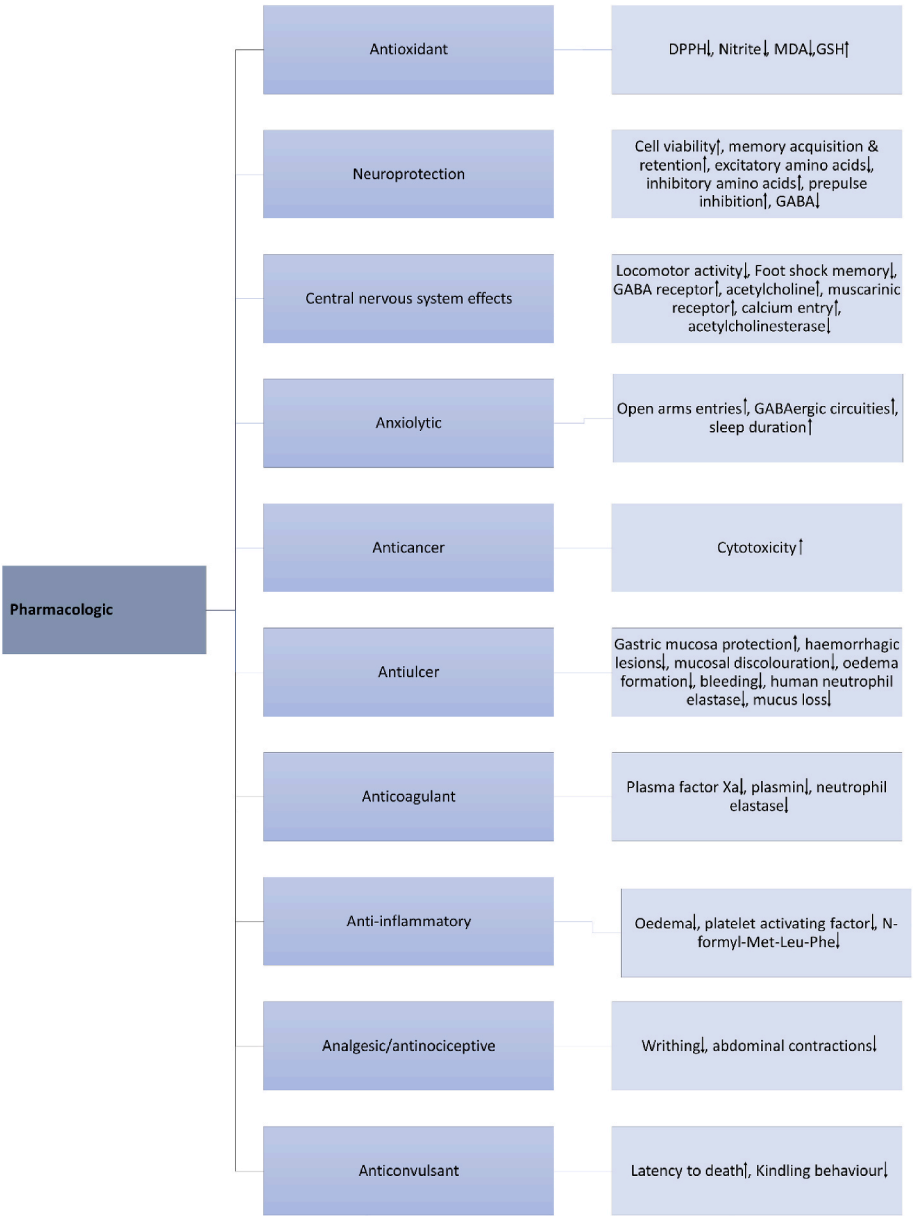


Fig. 2. Mechanisms of pharmacological activities of *Erythrina velutina*.

20 mg/kg EVLAE caused an increase in the percentages of entries into the open arm. The study concluded that the anxiolytic effects of *E. velutina* leaves alcohol extract was similar to that of benzodiazepines and maybe be due to the interaction of the extract with GABAergic circuitries. Ozawa et al. (2008) carried out a study to assess the sleep promoting effects of hypaphorine, an indole alkaloid isolated from *E. velutina* in mice. After 60 min of administration, hypaphorine significantly increased the non-rapid eye movement (NREM) sleep duration. When compared to the control mice, the experimental mice's NREM sleep period was increased by 33%. Vasconcelos et al. (2007) also assessed the effects of *E. velutina* stem bark hydroalcoholic extracts on the potentiation of pentobarbital-induced sleeping time in mice. The extract increased the sleep time compared with the control. Sleep disturbances, especially insomnia, are very typical in anxiety disorders and a common complaint of patients with the different anxiety types is insomnia or nightmares (Staner, 2022). Hence, *E. velutina* may alleviate anxiety by inducing sleep or prolonging sleep time. Despite the documented anxiolytic and sedative properties of *E. velutina*, the specific chemical constituents responsible for these effects remain unidentified.

This underscores the need for future research to isolate and characterize the precise chemical entities driving the anxiolytic and sedative actions of the plant. This endeavor not only deepens the comprehension of the plant's mechanisms but also holds promise for novel therapeutic agents targeting anxiety and related disorders.

3.4.3. Anticonvulsant activity

Erythrina velutina is an ornamental and medicinal tree that is commonly used against a myriad of disorders, convulsion inclusive (Santos et al., 2012). Vasconcelos et al. (2007) studied the anticonvulsant effects of *E. velutina* stem bark hydroalcoholic extracts on pentylenetetrazole and strychnine-induced seizure tests in mice. Following the oral administration of 200 and 400 mg/kg *E. velutina* stem bark hydroalcoholic extracts, there was an observed increase in the latency of convulsion and in the death time. The study concluded that *E. velutina* stem bark hydroalcoholic extracts possessed anticonvulsant effects in the strychnine-induced seizure model, implying their probable action in glycine system. Another study by Teixeira-Silva et al. (2008) evaluated the effect of alcohol extract of *E. velutina* leaves in

pentylene-tetrazol-induced convulsions and pentylene-tetrazol-induced kindling seizure in animals. Administration of 100 mg/kg alcohol extract of *E. velutina* leaves increased the latency to death compared with the control and decreased the pentylene-tetrazol-induced kindling behaviour. These findings collectively suggest that *E. velutina* extracts hold promise as anticonvulsant agents, potentially impacting the glycine system. However, further research is warranted to elucidate the exact mechanisms through which these extracts exert their anticonvulsant effects.

3.4.4. Neuroprotective activity

A study by Dias et al. (2019) examined the effects of the standardized extract (erythrine) from *E. velutina* leaves in behavioural parameters in the ketamine-induced schizophrenia model. After the administration of erythrine (100, 200 and 400 mg/kg), there was an increase in pre-pulse inhibition initially decreased by ketamine. The study concluded that the standardized extract of *E. velutina* can prevent behavioural symptoms. Rodrigues et al. (2017) examined the possible neuroprotective effect of the ethanolic extract of *E. velutina*. The animals were subjected to transient cerebral ischemia by blocking of both carotid arteries for 30 min and thereafter treated for 5 days with 200/400 mg/kg ethanolic extract of *E. velutina*. Treatment of the ischemic animals with *E. velutina* ethanolic extract caused a reversal in the damage induced by ischemia in the step down and Y-maze test, memory deficit in the object recognition test, decreased excitatory and increased inhibitory amino acid concentrations in the prefrontal cortex, hippocampus and striatum as well as reduced GABA concentration. The authors concluded that *E. velutina* ethanolic extract possess a neuroprotective effect and suggests that the likely mechanism of action maybe its effect on amino acid concentrations and is therefore a potential therapeutic tool in reducing the damage caused by ischemia. Silva et al. (2016) developed a standardized ethanol extract of *E. velutina* and investigated the neuroprotective potential of the extract and rizonic acid from *E. velutina* on neuronal cells. The standardized extract and rizonic acid significantly decreased the neurotoxicity induced by the neurotoxin 6-hydroxydopamine in SH-SY5Y cells. The extract and rizonic acid possess neuroprotective properties portraying their potential for future development as a therapeutic option for the treatment of neurodegenerative disease. The potential neuroprotective effects of *E. velutina* extracts, as suggested by Rodrigues et al. (2017), raise the possibility of clinical translation. Conducting preclinical trials involving animal models that closely mimic human ischemic conditions could provide a better understanding of the therapeutic potential of the extract in reducing damage caused by cerebral ischemia. Furthermore, bridging the gap between animal studies and human clinical trials is essential to determine the safety, efficacy, and optimal dosage regimens for potential therapeutic use in neurodegenerative diseases. Further research is necessary to elucidate the mechanisms underlying the cholinesterase inhibitory effects of EVLAE and to validate its potential as a therapeutic intervention. Clinical studies are essential to determine its safety, efficacy, and the extent of its impact on cognitive function in individuals with Alzheimer's disease or other related conditions. Additionally, exploring the specific bioactive compounds within EVLAE responsible for the observed effects could pave the way for the development of novel treatments targeting cholinergic pathways.

3.4.5. Analgesic/antinociceptive effects

The anti-nociceptive effects of *E. velutina* leaves aqueous extract were assessed using animal models of nociception. 600 mg/kg of the extract reduced the paw licking time in the formalin test by 96.5%. In the acetic acid induced writhing test, 300 and 600 mg/kg of the extract decreased the number of writhing by 88.8% and 96.4%, respectively. The study concluded that *E. velutina* leaves aqueous extract has anti-nociceptive activities (Marchioro et al., 2005).

Another study by Vasconcelos et al. (2003) assessed the anti-nociceptive effects of *E. velutina* stem bark hydroalcoholic extracts in

three experimental models of nociception in animals. 200/400 mg/kg of the extract was administered intraperitoneally to female mice. 88.6–95.5% abdominal contraction inhibition was observed when compared to the control. The extract also decreased the formalin-induced nociception in the first and second phases. In the hot plate test, 400 mg/kg of the extract also caused an increase in reaction time at 60 and 90 min when compared with the control. The authors concluded that *E. velutina* possesses antinociceptive proper independent of the opioid system. The existing studies on *E. velutina*'s anti-nociceptive effects provides a strong foundation for further research. Conducting comparative studies with other natural compounds or conventional pain medications could help assess the relative efficacy and safety of *E. velutina* extracts. This could involve evaluating the extract's effects in combination with existing analgesics or assessing its potential synergistic interactions. Although the studies above indicated effective doses, further investigation is needed to optimize dosage regimens for maximum anti-nociceptive effects while minimizing potential side effects. Dose-response studies could help determine the ideal concentration range for different models of nociception.

3.4.6. Anticholinesterase activity

A number of disorders, including Alzheimer's disease, are significantly impacted by the regulation of acetylcholine levels. Acetylcholine levels in the brain is known to be associated with cognitive decline in Alzheimer's disease. Hence, brain cholinesterase inhibition which increases acetylcholine concentrations, is a key therapeutic target for combating Alzheimer's disease (Santos et al., 2012; Lombardo and Maskos, 2015). According to Santos et al. (2012), *E. velutina* leaf aqueous extract (EVLAE) inhibited mouse brain cholinesterase activity (IC_{50} = 0.57 mg/mL) in a dose dependent manner. EVLAE also inhibited acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) *in vitro* dose dependently (IC_{50} AChE – 0.56 mg/mL, IC_{50} BuChE - 2.95 mg/mL). It was concluded that EVLAE may have crossed the blood-brain barrier to inhibit cholinesterase activity in the brain. EVLAE also showed inhibitory activities on AChE and BuChE. Cholinesterase inhibition, a strategy aimed at increasing acetylcholine levels, has emerged as a crucial therapeutic target for addressing the cognitive impairments associated with Alzheimer, a neurodegenerative condition. The observed inhibitory effects on cholinesterase enzymes raise the possibility that EVLAE may have successfully penetrated the blood-brain barrier, potentially leading to inhibition of cholinesterase activity in the brain itself. These results provide promising insights into the potential of EVLAE as a therapeutic agent for conditions like Alzheimer's disease, where cholinergic deficits contribute to cognitive decline. The demonstrated inhibitory activities of EVLAE on AChE and BuChE suggest its potential to modulate acetylcholine levels and subsequently improve cognitive function.

3.4.7. Anti-inflammatory effects

Vasconcelos et al. (2011) reported the anti-inflammatory activities of the *E. velutina* hydroalcoholic extracts in the carrageenan and dextran-induced mice hind paw oedema models. 200/400 mg/kg of the extracts were administered to the mice orally. In the dextran model, a decrease in the paw oedema was observed at 1, 2, 3, 4 and 24 h, implying an anti-inflammatory effect in the dextran model. It was concluded that *E. velutina* was efficacious against oedema through interfering with inflammatory processes in which mast cells play a key role. In another study by Monteiro (2011), it was observed that a chymotrypsin inhibitor from *E. velutina* seeds (0.017 and 0.035 mg/kg) had an anti-inflammatory property and acted antagonistically against platelet-activating factor and N-formyl-Met-Leu-Phe. Similarly, in a separate study, a Kunitz trypsin inhibitor from *E. velutina* seeds (1 mg/kg) in a sepsis model, displayed anti-inflammatory effect by strongly inhibiting trypsin (Machado et al., 2013). These studies have demonstrated the diverse anti-inflammatory properties of *E. velutina* and its bioactive compounds, shedding light on its potential therapeutic

applications in addressing inflammatory conditions. The multi-faceted mechanisms of action identified across these studies, from interference with inflammatory processes involving mast cells to the inhibition of specific enzymes, suggest that *E. velutina* holds promise as a source of natural anti-inflammatory agents. Further research is warranted to fully understand the molecular mechanisms underlying these effects and to explore their clinical implications for the management of various inflammatory disorders.

3.4.8. Anticoagulant effects

Machado et al. (2013) used a purified Kunitz trypsin inhibitor obtained from *E. velutina* seeds (EvTI) in a sepsis model. 1 mg/kg EvTI demonstrated anticoagulant effects by strongly inhibiting plasma factor Xa. According to Monteiro (2011), a chymotrypsin inhibitor from *E. velutina* seeds in a sepsis model, strongly inhibited plasmin, factor Xa, neutrophil elastase, and HNE, and hence, possess anticoagulant properties. The authors concluded that Kunitz inhibitors may be efficacious in interfering with blood coagulation and inflammation.

3.4.9. Antiulcer effects

A study reported by Oliveira de Lima et al. (2017) evaluated the gastroprotective and anti-elastase activities of protein inhibitors obtained from *E. velutina* seeds in an ethanol-induced ulcer model. Two protein isolates with chymotrypsin and trypsin inhibitory activities were obtained. They both possessed high affinity and inhibitory effect on human neutrophil elastase. The protein isolates both protected the gastric mucosa, prevented haemorrhagic lesions, oedema and loss of mucus. The protein isolates did not induce histologic damage in the liver and pancreas. These protein isolates were reported to possess gastroprotective potentials and may be suitable candidates for gastric ulcer drugs.

3.4.10. Anticancer effects

Alkaloids obtained from *E. velutina* were assessed for their cytotoxic activities against Jurkat cells in the presence or absence of 0.125 mg/ml TNF- related apoptosis-inducing ligand (TRAIL). TRAIL induces apoptosis in cancer cell lines selectively and does not have effect on normal cells. The IC₅₀ values for erythraline, erysodine, and erysovine were 23.0, 10.8, and 24.0 µg/ml respectively. Their cytotoxicity however, increased when in combination with TRAIL. 8-oxo-erythraline, erysotrine, and glucoerysodine only showed cytotoxic activities when combined with TRAIL with IC₅₀ values of 22.0, 7.2, and 44.0 µg/ml respectively (Ozawa et al., 2009). These results suggest a potential synergistic effect between the alkaloids and TRAIL, leading to increased cell death in cancer cells. It is therefore important to study the underlying mechanisms of the observed synergy between *E. velutina* alkaloids and TRAIL. Understanding how these alkaloids enhance the effects of TRAIL could provide insights into potential novel therapeutic approaches for treating cancer.

3.4.11. Antioxidant effects

A study by Dias et al. (2019) examined the effects of erythrine, a standardized extract from the *E. velutina* leaves in behavioural and oxidative parameters in the ketamine-induced schizophrenia model. Ketamine induced oxidative stress in the animal models, however, erythrine increased glutathione concentration, and decreased malondialdehyde concentrations in the prefrontal cortex, hippocampus and striatum of the animals. The study concluded that the standardized extract from the *E. velutina* leaves can prevent oxidative stress. Silva et al. (2016) reported that standardized ethanol extract of *E. velutina* and rizonic acid displayed neuroprotective properties on neuronal cells by scavenging free radicals. Hence, by acting as antioxidants, the extract and rizonic acids may have the potential of being developed into therapeutic agents for neurodegenerative disorders. Free radicals initiate oxidation, contributing to aging and various diseases in humans, including neurodegenerative disorders (Iqbal et al., 2013). Further

exploration of the impact of erythrine and rizonic acid on cellular pathways involved in oxidative stress and neurodegeneration, such as the Nrf2-Keap1 pathway, could provide insights into their mode of action. Investigating how these compounds modulate gene expression, protein synthesis, and other cellular processes would contribute to a more comprehensive understanding of their antioxidant and neuro-protective potential.

3.4.12. Antimicrobial activities

Virtuoso et al. (2005) evaluated the antibacterial activity of hydro-alcoholic *E. velutina* stem bark against eight pathogenic bacteria. The hydroalcoholic extract of *E. velutina* stem bark showed a minimal inhibitory concentration (MIC) of 9.77 mg/mL for *Staphylococcus aureus* and *Streptococcus pyogenes*. The extract also exhibited intermediary activity for other microorganisms, such as *Pseudomonas aeruginosa*, *Escherichia coli* and *Salmonella tiphymurium*. Other *Erythrina* species (including isolated compounds and extracts) have demonstrated antimicrobial properties against oral bacteria, throat infections, and urinary issues (de Lima et al., 2006; Sato et al., 2003; Virtuoso et al., 2005). Expanding antimicrobial research beyond the stem bark to other *E. velutina* parts like roots, leaves, and flowers is essential to uncover its full potential.

3.4.13. Cardioprotective effects

Heart failure is a condition characterized by dysfunction in either myocardial relaxation or cardiac contractility. This results in diminished efficiency in blood distribution by the vascular system (Passos et al., 2013). Passos et al. (2013) investigated the effects of *E. velutina* leaves ethyl acetate fraction on mammalian myocardium using guineapig left atria. *Erythrina velutina* leaves ethyl acetate fraction had a positive inotropic affect, increased atrial force by 164% (EC₅₀ = 157 ± 44 mg/ml), and enhanced L-type calcium current peak by 31.2%. About 10 flavonoids were reported to be present in *E. velutina* leaves ethyl acetate fraction, two of which were identified as vicenin II and isorhoifolin. The study concluded that *E. velutina* leaves ethyl acetate fraction by enhancing the L-type calcium current and activating the adrenergic receptor pathway, increases the heart contractile force. This study contributes to the understanding of the potential cardiovascular effects of *E. velutina* and its potential application in the context of heart function and health. Further research is necessary to elucidate the underlying mechanisms in more details and explore the clinical implications of these findings.

3.5. Toxicology

The assessment of the potential toxicity of medicinal plants before they are employed for therapeutic purposes is important. These studies can provide information on the potential adverse effects of such plants, their extracts and isolated compounds and help determine safe dosages for humans. Based on the available literature, the reported toxicity of *E. velutina* appears to be very few.

A study on the acute toxicity of aqueous extracts of *E. velutina* leaves in adult Wistar rats reported no signs of toxicity or mortality during a 14-day observation period following a limit dose of 5 g/kg. This may indicate that the extract is relatively safe and has a low risk of causing toxicity (Craveiro et al., 2008). In a more recent study, the genotoxic effects of the alcoholic extract of leaves of *E. velutina* in the bone marrow cells of adult Wistar rats was evaluated using micronucleus test (Oliveira et al., 2018). At the concentrations tested (25, 50, and 100 mg/kg), the study reported that *E. velutina* extract showed no genotoxicity.

Overall, the available studies suggest that the acute toxicity of *E. velutina* is relatively low, however, further research is needed to fully understand its potential toxicity and to determine safe dosage levels for humans.

4. Conclusion and future perspectives

Erythrina velutina has gained significance due to its medicinal, biotechnological, and economic importance, driving heightened research endeavors across time. This comprehensive review summarizes the research progress of *E. velutina* in order to advance its scientific exploration. Firstly, botanical attributes and ethnomedicinal applications of this plant are summarized. Then, an overview of its chemical constituents and associated pharmacological impacts are presented. Furthermore, the available toxicology studies of *E. velutina* are also reported.

Based on the review of literature, *E. velutina* has a rich history of traditional uses, particularly in South America, for various ailments such as tranquilizer for anxiety and stress, inflammation, pain, and infections. It also holds both biotechnological and pharmacological potential, substantiated by numerous investigations revealing bioactive compounds endowed with therapeutic attributes for human applications. According to existing data, more than 200 chemical compounds have been isolated from various parts of *E. velutina* mainly including alkaloids and flavonoids with numerous bioactivities. For example, the research by Passos et al. (2013) demonstrated that *E. velutina* leaves ethyl acetate fraction has a significant positive impact on mammalian myocardium and demonstrated cardiovascular effects. The observed enhancement in atrial force, coupled with the increase in L-type calcium current and activation of the adrenergic receptor pathway, collectively resulted in improved contractile force of the heart. The presence of flavonoids, including vicenin II and isorhoifolin, in the fraction suggests that these compounds could be responsible for the observed physiological effects. The unique combination of bioactive compounds such as flavonoids, terpenoids, alkaloids, phenolic compounds, and glycosides among others, makes *E. velutina* an intriguing subject of study for researchers interested in developing natural remedies, pharmaceuticals, and agricultural solutions particularly as an insecticide.

The foremost pharmacological effect linked to *E. velutina* is its anxiolytic and sedative properties. Numerous studies and anecdotal evidence indicate that the plant's extracts potentially induce calming and relaxation within the central nervous system, potentially mitigating anxiety and enhancing sleep. For instance, Raupp et al., (2008) findings suggest that the continual administration of the hydroalcoholic stem bark extract of *E. velutina* exhibits an anxiolytic-like impact on mice, presenting a novel avenue for anxiety treatment, albeit with a possible amnesic effect at lower doses. Similarly, Dantas et al. (2004) documented the extension of sleep duration induced by sodium pentobarbital with higher doses of *E. velutina*'s aqueous extract, while lower doses impeded foot shock memory acquisition. This prompted the authors to propose that *E. velutina* could potentially interfere with memory processes and deliver sedative effects. The anxiolytic and sedative properties of *E. velutina* are thought to be associated with its bioactive constituents mainly alkaloids and flavonoids.

Although there are reports on its bioactivities, there is a lack of rigorous scientific evidence to support some of its traditional uses. There are several promising avenues for future research on *E. velutina* that could build upon the findings from this review.

Firstly, whilst studies have consistently highlighted the potential therapeutic benefits of *E. velutina* extracts on anxiety and relaxation (the most important pharmaceutical effects), the specific bioactive compounds underlying these effects remain elusive. Thus, it becomes a compelling consideration for future research to isolate and characterize the exact chemical entities responsible for its anxiolytic and sedative actions. Identifying these compounds will not only enhance the understanding of the plant's mechanisms of action but also pave the way for the development of novel therapeutic agents for anxiety and related disorders.

The lack of clinical trials and mechanistic studies on the pharmacological activities of *E. velutina* represents a significant knowledge gap that needs to be addressed. There is a need for further research to

elucidate the underlying mechanisms of action of the plant's bioactive compounds and to investigate their potential therapeutic applications. For example, investigating the precise cellular and molecular mechanisms by which *E. velutina* extracts and their components interact with neuronal pathways could provide valuable insights into their mode of action. This could involve exploring their impact on neurotransmitter systems, receptor interactions, signal transduction pathways, and gene expression profiles.

Furthermore, while the stem bark of *E. velutina* is commonly utilized in ethnomedicine, other parts of the tree in various *Erythrina* species have displayed significant bioactivities. However, there remains a notable gap in the exploration of these alternative parts of *E. velutina* for potential therapeutic applications. Future research should extend beyond the stem bark of *Erythrina velutina* and encompass an investigation into the bioactivities of its other components. By studying various parts of the *E. velutina* tree, such as leaves, roots, and flowers, additional bioactive compounds that might possess valuable medicinal properties can be uncovered. This comprehensive exploration could potentially lead to the discovery of novel therapeutic agents and broaden the understanding of the medicinal potential of *E. velutina* as a whole.

Also, the limited number of toxicity studies available on *E. velutina* suggests that caution should be exercised in the use of this plant, particularly in high doses or for extended periods. There is a need for more comprehensive toxicological studies to establish the safety profile of *E. velutina* and its bioactive compounds. This could involve investigating the acute and chronic toxicity of *E. velutina* in animal models, as well as its potential for causing genotoxicity. Such studies could help to establish safe dosages and usage guidelines for *E. velutina*.

Finally, the overexploitation of this tree species for its wood and other purposes is a cause for concern and could lead to its depletion. There is a need for conservation efforts to prevent the overexploitation of *E. velutina* and other valuable tree species. This could involve promoting sustainable harvesting practices, establishing protected areas, and raising awareness of the importance of conserving this species for its medicinal, ecological and economic value.

In conclusion, *E. velutina* is a promising plant species with potential medicinal properties, but its traditional uses require further scientific validation. Future research efforts should focus on conducting more comprehensive toxicological studies, clinical trials, and mechanistic studies on *E. velutina*, as well as promoting conservation efforts to protect this valuable tree species.

Credit authorship contribution statement

Tomi Lois Adetunji: Conceptualization, Writing – original draft, Writing – review & editing. Marvellous Amarachi Acho: Writing – original draft: Victory Oghenetega Samel: Writing – original draft, Chinmerem Ruth Ohoro: Writing – original draft, Mmbulaheni Ramulondi: Writing – original draft.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors confirm that the data supporting the findings of this review are available within the article.

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