Phytochemical profile and neuropharmacological potential of *Erythrina velutina* Willd. (Fabaceae): An integrative preclinical review

Gabriela Acunha Razzera[1], Elize Musachio[1,2,3,4], Fernanda dos Santos Trombini[1,2], Cindhy Suely da Silva Medeiros[1,3], Maria Denise Schimith[2], Euler Esteves Ribeiro[4] & Fernanda Barbisan[1,3,5]

[1] Biogenomics Laboratory, Federal University of Santa Maria; 97105-900, Brazil

[2] Postgraduate Program in Nursing, Federal University of Santa Maria; 97105-900, Brazil

[3] Postgraduate Program in Gerontology, Federal University of Santa Maria; 97105-900, Brazil

[4] Open University for the Third Age Foundation; 69029-040, Brazil

[5] Postgraduate Program in Pharmacology, Federal University of Santa Maria; 97105-900, Brazil

Correspondence: Fernanda Barbisan, Biogenomics Laboratory, Federal University of Santa Maria, Santa Maria, Brazil. E-mail: fernandabarbisan@gmail.com

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Abstract

Medicinal plants constitute an important source of bioactive compounds for the discovery of novel neuroactive agents. *Erythrina velutina* Willd. (Fabaceae). Popularly known as mulungu, has been traditionally used in the treatment of anxiety, insomnia, and other conditions related to the central nervous system (CNS), which has motivated extensive pharmacological and preclinical investigations. This integrative review critically synthesizes the available evidence on the phytochemical profile and neuropharmacological potential of *E. velutina*. The literature search was conducted in PubMed, SciELO, Web of Science, and the Virtual Health Library, including preclinical in vitro and in vivo studies, with no language or publication-year restrictions. The analyzed studies indicate a complex phytochemical composition characterized primarily by alkaloids, flavonoids, and other phenolic compounds. Preclinical evidence demonstrates anxiolytic, sedative, anticonvulsant, antioxidant, neuroprotective, and anticholinesterase activities associated with modulation of GABAergic and cholinergic neurotransmission, as well as with reductions in oxidative stress and neuronal protection. The available toxicological data suggest low acute toxicity and the absence of genotoxic effects at the experimentally evaluated doses. However, the lack of standardized extracts, compound-guided pharmacological studies, long-term toxicological assessments, and clinical investigations limits the translational extrapolation of the findings. Therefore, future studies focused on bioprospecting, elucidation of mechanisms of action, and clinical validation are required to consolidate the pharmacological potential of *Erythrina velutina*.

Keywords: medicinal plants, alkaloids, flavonoids, neuroactive compounds, oxidative stress.

Perfil fitoquímico e potencial neurofarmacológico de *Erythrina velutina* Willd. (Fabaceae): Uma revisão integrativa pré-clínica

Resumo

As plantas medicinais constituem uma importante fonte de compostos bioativos para a descoberta de novos agentes neuroativos. *Erythrina velutina* Willd. (Fabaceae), popularmente conhecida como mulungu, tem sido tradicionalmente utilizada no tratamento da ansiedade, insônia e outras condições relacionadas ao sistema nervoso central (SNC), o que motivou extensas investigações farmacológicas e pré-clínicas. Esta revisão integrativa sintetiza criticamente as evidências disponíveis sobre o perfil fitoquímico e o potencial neurofarmacológico de *E. velutina*. A busca bibliográfica foi realizada nas bases de dados PubMed, SciELO, Web of Science e Biblioteca Virtual em Saúde, incluindo estudos pré-clínicos in vitro e in vivo, sem restrições de idioma ou de ano de

publicação. Os estudos analisados indicam uma composição fitoquímica complexa, caracterizada principalmente pela presença de alcaloides, além de flavonoides e de outros compostos fenólicos. Evidências pré-clínicas demonstram atividades ansiolíticas, sedativas, anticonvulsivantes, antioxidantes, neuroprotetoras e anticolinesterásicas, associadas à modulação da neurotransmissão GABAérgica e colinérgica, bem como à redução do estresse oxidativo e à proteção neuronal. Os dados toxicológicos disponíveis sugerem baixa toxicidade aguda e ausência de efeitos genotóxicos nas doses avaliadas experimentalmente. No entanto, a ausência de extratos padronizados, de estudos farmacológicos guiados por compostos, de avaliações toxicológicas de longo prazo e de investigações clínicas limita a extrapolação translacional dos achados. Dessa forma, são necessários estudos futuros voltados à bioprospecção, à elucidação dos mecanismos de ação e à validação clínica para consolidar o potencial farmacológico de *Erythrina velutina*.

Palavras-chave: plantas medicinais, alcaloides, flavonoides, compostos neuroativos, estresse oxidativo.

1. Introduction

Neurological disorders are among the leading causes of disability worldwide, affecting approximately 3.4 billion people, which corresponds to about 43% of the global population (WHO, 2021). These conditions represent a growing public health challenge, driven by progressive neuronal dysfunction, neurodegeneration, and the limited availability of effective disease-modifying therapies. In this context, identifying neuroprotective agents has become increasingly important, and natural products have emerged as a significant source of structurally diverse bioactive compounds with potential applications in the prevention and management of central nervous system (CNS) disorders. The use of medicinal plants integrates traditional knowledge with contemporary pharmacological research, providing a valuable framework for pharmacognostic investigation (Cerqueira et al., 2020).

The genus *Erythrina* (Fabaceae) comprises medium-sized, generally thorny trees with compound leaves and characteristic orange inflorescences. Species of this genus are widely distributed across tropical and subtropical regions of the Americas, Africa, and Asia, and exhibit a long history of ethnomedicinal use. This traditional relevance has stimulated sustained scientific interest, particularly due to the reported pharmacological activities and chemical diversity associated with the genus (Carvalho et al., 2009; Silva et al., 2020).

Among these species, *Erythrina velutina* Willd., commonly known as mulungu, has been traditionally used to manage CNS-related conditions, including anxiety, insomnia, and depressive symptoms (Ramos et al., 2020; Ferreira et al., 2021; Souza et al., 2022). Beyond its therapeutic use, the species is also associated with symbolic and ritual practices, particularly due to the presence of alkaloids in the bark. From a pharmacognostic perspective, these alkaloids represent compounds of considerable interest due to their central bioactivity; however, reports of psychoactive effects underscore the need for careful toxicological and pharmacological evaluation (Vasconcelos et al., 2007; Adetunji et al., 2024).

Phytochemical investigations of *E. velutina* have identified a diverse array of secondary metabolites, particularly alkaloids, flavonoids, and other phenolic compounds. These classes of compounds are widely recognized for their antioxidant, neuroactive, and anti-inflammatory properties and have frequently been implicated in modulating oxidative stress pathways and neurotransmission systems relevant to CNS disorders (Fahmy et al., 2020). Nevertheless, the available evidence is derived predominantly from heterogeneous preclinical models, often using non-standardized extracts and variable experimental designs, which complicate direct comparisons among studies and limit mechanistic interpretation.

Despite the availability of pharmacological therapies for CNS disorders, current treatments remain constrained by modest efficacy, adverse effects, and a predominant focus on single molecular targets, which often fail to address the multifactorial nature of neuropsychiatric and neurodegenerative conditions (Lombardo; Maskos, 2015). In this context, natural products continue to play a central role in neuroactive drug discovery due to their structural diversity and capacity to modulate multiple biological pathways simultaneously. Plant-derived secondary metabolites, particularly alkaloids and flavonoids, have provided important molecular scaffolds for developing CNS-active agents, underscoring the relevance of pharmacognosy-driven bioprospecting strategies (Fahmy et al., 2020). Within this framework, *Erythrina velutina* emerges as a strategically relevant species, not only because of its extensive ethnopharmacological use, but also due to the growing body of preclinical evidence supporting its multitarget neuropharmacological profile (Souza et al., 2022).

In this context, the present integrative review aims to critically synthesize current knowledge on the pharmacognostic and phytochemical profile of *Erythrina velutina*, as well as its reported neuropharmacological effects, highlighting methodological limitations in compound-guided studies, and challenges related to

standardization and translational relevance.

2. Materials and Methods

This study is an integrative review conducted between January and August 2025. The guiding research question was: *Which bioactive compounds have been identified in E. velutina*, *and what are their reported neuropharmacological effects?* This question was structured using the PICO framework, in which **P** represents *in vitro* and *in vivo* preclinical studies, **I** refers to bioactive compounds and extracts obtained from *E. velutina*, **C** was not applicable, and **O** corresponds to reported pharmacological and neurobiological outcomes.

No temporal restrictions were applied, and all publications available up to August 2025 were considered eligible. Literature searches were conducted in the PubMed, SciELO, Web of Science, and Virtual Health Library (BVS) databases. The search strategy (Figure 1) employed the descriptors *mulungu*, *E. velutina*, phytochemical compounds, bioactive molecules, pharmacological activities, neuropharmacology, central nervous system, and traditional uses, combined using the Boolean operators "AND" and "OR."

Original experimental studies (*in vitro* and *in vivo*) and ethnopharmacological reports addressing CNS-related effects of *E. velutina* were included. Studies with insufficient methodological description, unclear outcome measures, or lacking direct relevance to phytochemical characterization or neuropharmacological activity were excluded. Data were extracted and analyzed descriptively, and the included studies were categorized according to plant part used, identified phytochemical classes, experimental model, and reported pharmacological outcomes.

No clinical studies evaluating the neuropharmacological effects of *E. velutina* were identified in the literature search. Therefore, the evidence discussed in this review is restricted to ethnopharmacological reports and preclinical *in vitro* and *in vivo* studies, which limits direct clinical extrapolation and was considered during data interpretation. No formal risk-of-bias assessment was performed, which represents a limitation of this integrative review and was taken into consideration during the interpretation of the findings.

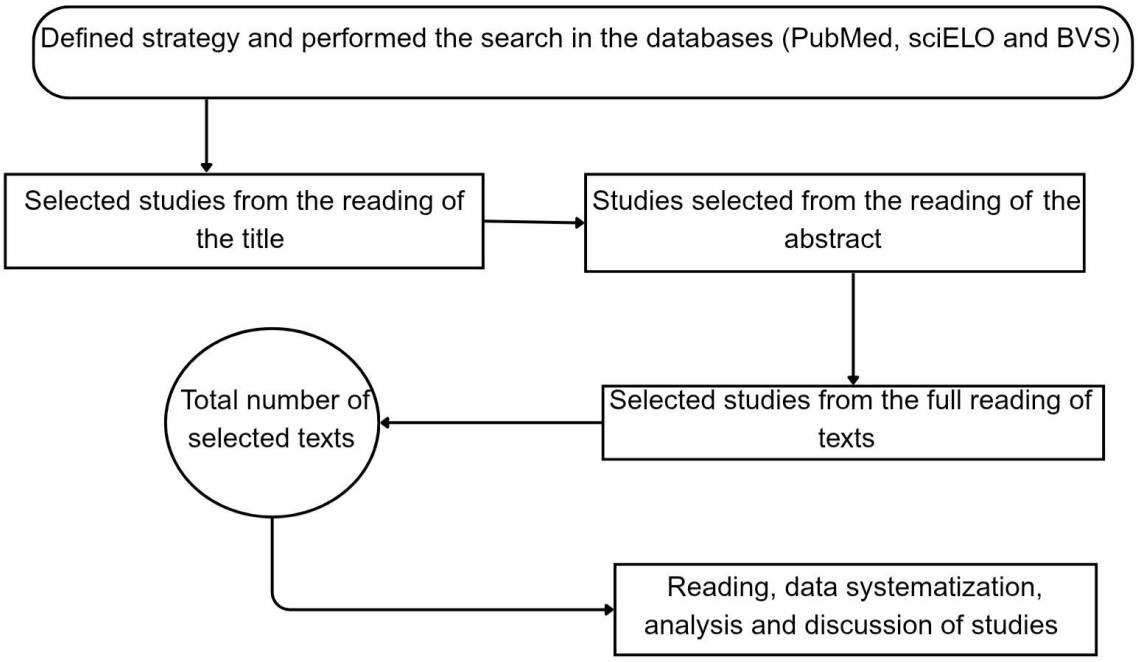

Figure 1. Study selection flowchart. Source: Authors, 2026.

3. Results

Initially, 207 articles were identified across the databases. After title and abstract screening, 106 studies were screened, of which 48 met the predefined inclusion criteria. After removing duplicate publications, 20 studies were retained for full-text analysis and constituted the final dataset for this integrative review (Figure 2). It is important

to note that the included studies comprise different levels of evidence, including ethnopharmacological reports, *in vitro* assays, and *in vivo* animal models, which limit direct extrapolation to clinical contexts and require cautious interpretation of the findings.

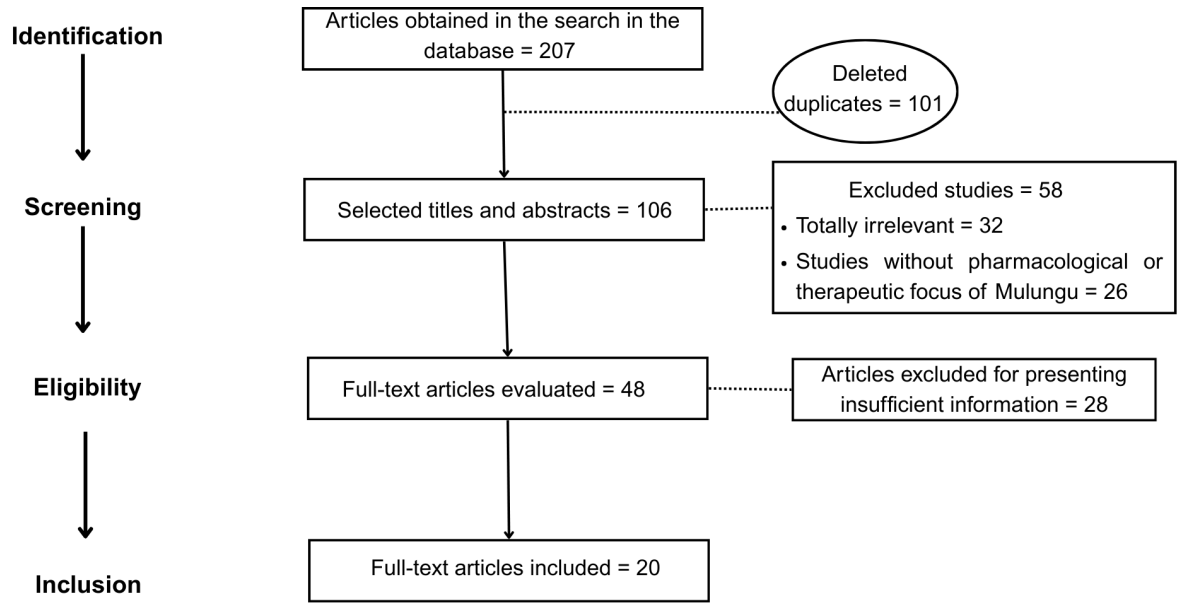

Figure 2. Study inclusion flowchart. Source: Authors, 2026.

To systematize and synthesize the studies included in this integrative review, (Table 1) was developed. It summarizes key information from the selected articles, including the authors and years of publication, study designs, plant parts investigated, major phytochemical classes identified, evaluated pharmacological activities, and the main conclusions reported. Although Table 1 provides an integrated overview of the available studies, the pronounced heterogeneity in experimental designs, biological models, plant parts investigated, extraction procedures, and outcome measures limits direct comparison among findings and hampers the establishment of robust compound–effect relationships

Table 1. Selected studies on the phytochemical composition, neuropharmacological activities, and safety of *Erythrina velutina*.

Author/year	Type of study	Part of the Plant	Main Compounds	Main Findings
Vasconcelos et al. 2004	*in vivo*	Peel and Sheets	Alkaloids	Sedative and CNS depressant activity in mice.
Silva et al. 2016	*in vitro*	Sheets	Phenolic compounds	Neuroprotective effect reduced 6-hydroxidopamine-induced neurotoxicity and preserved cell viability.
Craveiro et al. 2008	*in vivo*	Sheets	Alkaloids and flavonoids	The orally administered species was shown to have no observable acute toxicity in adult Wistar rats, no mortality, or adverse clinical signs.

Simokomaki et al. 2023	*in vivo*	Seeds	Alkaloids	Antinociceptive effect in hot plate tests and moderate anxiolytic effect in open field and elevated cross maze tests with Wistar rats, indicating modulating action on the CNS.
Silva et al. 2020	*Ethnopharmacological*	Shell, leaves, and flowers	Alkaloids and flavonoids	Studies show that the alkaloids erytravin and 11-hydroxy-erytravin are mainly responsible for the control of anxiety and insomnia in preclinical I.N. live tests in mice. These findings suggest pharmacological relevance in preclinical models.
Chacon et al. 2022	Molecular study	Sheets	Flavonoids	Identification of genes involved in the biosynthesis of pharmacological interest.
Albuquerque et al. 2007	Ethnopharmacological s	Peel and leaves	Alkaloids and flavonoids	Popular use of the species with calming, sedative, and anxiolytic effects, especially in the treatment of nervous system disorders.
Dias et al. 2019	*in vivo*	Sheets	Alkaloids and flavonoids	It attenuated schizophrenia-like behaviors and reduced oxidative stress parameters in mice.
Ozawa et al. 2008	*in vivo*	Hypaphorin seeds	Alkaloids	Anticonvulsant activity in a mouse model.
Santos et al. 2012	*In vitro* and *ex vivo*	Sheets	Alkaloids	Effect on inhibitory activity on AChE and BuChE
Faggion et al.2011	*in vivo*	Flowers	Alkaloids	Anticonvulsant action in models of *Wistar* rats with epilepsy.
Rosa et al.2012	*in vivo*	Flowers	Alkaloids	Anticonvulsant and anxiolytic effects in mice.
Carvalho et al. 2009	*in vivo* and *in vitro*	Sheets	Alkaloids	Suggests a pharmacological mechanism associated with the sedative effect.
Rodrigues et al. 2017	*in vivo*	Sheets	Phenolic and alkaloid compounds	Mice subjected to transient cerebral ischemia, the plant was able to attenuate neurological deficits and modulate parameters of oxidative stress, indicating a neuroprotective effect.
Ramos et al. 2020	*in vitro*	Peel and leaves	Phenolic compounds and flavonoids	Antioxidant activity associated with the phytochemical profile.
Ferreira et al. 2021	Pharmacotechnical study	Barks	Tannins, alkaloids, flavonoids, and Phenolic	Characterization of quality parameters of *Erythrina velutina*.

compounds.

Oliveira et al. 2018	*in vivo*	Leaves	Alkaloids and flavonoids	Absence of genotoxic effects on hematopoietic cells of adult Wistar rats, indicating a toxicological safety profile.
Dantas et al. 2004	*in vivo*	Leaves	Alkaloids and phenolic compounds	It promoted increased pentobarbital-induced sleep time and reduced motor activity and open field exploration, suggesting a depressive effect on the CNS in a mouse model.
Ribeiro et al. 2006	*in vivo*	Barks	Alkaloids and flavonoids	It reduced anxiety-related behaviors in rats, comparable to the effect of diazepam, indicating experimental central anxiolytic activity.
Lacerda 2025	*in vivo*	Leaves	Phenolic compounds and flavonoids	The species presented a consistent phytochemical profile and antioxidant activity, reinforcing its pharmacological potential.

Source: Authors, 2026.

4. Discussion

The findings synthesized in this integrative review indicate that *E. velutina* exhibits a complex phytochemical profile and a consistent spectrum of neuropharmacological activities across different preclinical models. The predominance of alkaloids, together with flavonoids and other phenolic compounds, underlies a multitarget pharmacological profile that modulates neurotransmission, reduces oxidative stress, and protects neurons. However, the marked heterogeneity in experimental designs, plant parts, extraction methods, and outcome measures limits direct comparison among studies and constrains translational interpretation. In this context, the following sections discuss the available evidence in an integrated manner, addressing botanical aspects, traditional uses, chemical composition, pharmacological effects, and toxicological considerations relevant to the pharmacognostic evaluation of *E. velutina*.

4.1 Botany

A member of the Fabaceae, mulungu is a thorny tree reaching 8–12 meters in height. The species is native to tropical regions of South America, including Brazil, and also occurs in other Central and South American countries (Carvalho et al., 2008; Souza et al., 2022). From a pharmacognostic perspective, accurate botanical identification is essential to ensure reproducibility and reliability of phytochemical and pharmacological studies. It exhibits high ecological adaptability, thriving in both humid and dry climates, with average temperatures ranging from 22.4 °C to 26.6 °C (Wanda et al., 2015). Taxonomic and environmental variability may alter alkaloid profiles and affect the consistency of neuropharmacological findings. Accurate botanical identification of *Erythrina velutina* is essential for reproducibility in pharmacognostic research.

4.2 Traditional uses

Erythrina velutina is traditionally used in folk medicine to treat anxiety, insomnia, and nervous system agitation. These traditional indications have guided experimental investigations into their neuropharmacological potential, particularly regarding sedative and anxiolytic effects.

It is important to note that preparation methods for teas or infusions directly influence the phytochemical profile and concentration of bioactive compounds, thereby affecting therapeutic outcomes. Furthermore, the use of

mulungu preparations is not recommended for individuals with heart failure or arrhythmia, and the seeds should be avoided, as their higher alkaloid content raises toxicological concerns (Ozawa et al., 2008; Gilbert, 2012).

Although traditional use strongly supports the calming and sedative reputation of *E. velutina*, ethnopharmacological indications alone do not allow for a distinction between anxiolytic, hypnotic, or general CNS depressant effects. This distinction is crucial, as different preparation methods, plant parts, and alkaloid concentrations can result in markedly different neuropharmacological profiles.

4.3 Chemical constituents

Erythrina velutina and are consistently associated with its neuropharmacological effects. However, the predominance of erythrinan-type alkaloids in the literature contrasts with the relatively limited chemical characterization of other potentially bioactive constituents, such as flavonoids and phenolic acids (Dantas et al., 2004; Ribeiro et al., 2006; Carvalho et al., 2009; Ramos et al., 2020).

The structural similarity among erythrinan alkaloids, including erysodine, erysothrine, erythravine, and 11-hydroxy-erythravine, suggests shared molecular targets and partially overlapping mechanisms of action. The chemical structures of the major alkaloids were drawn using ChemDraw 2020 with accurate stereochemical representation and are presented in (Figure 3). Conversely, the presence of structurally distinct compounds, such as the indole alkaloid hypaphorine, highlights the chemical heterogeneity underlying the species' multitarget pharmacological profile.

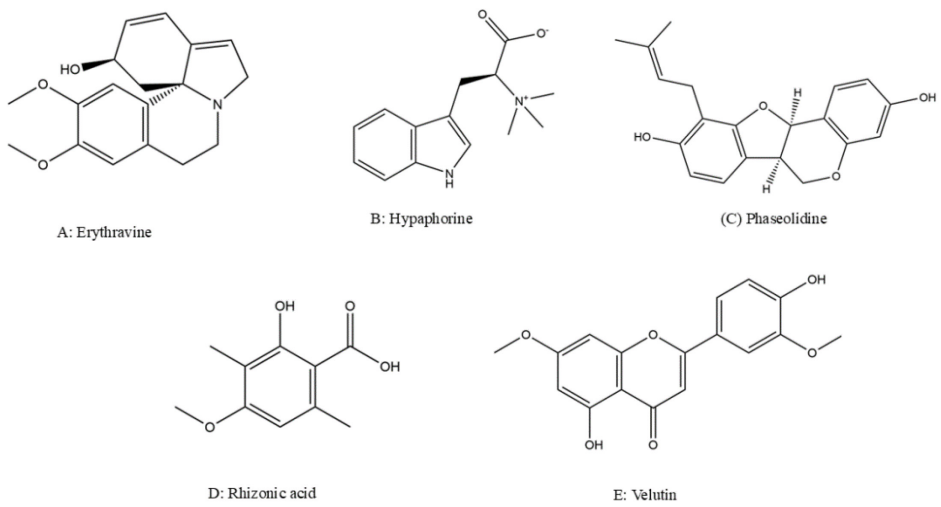

Figure 3. Chemical structures of major bioactive compounds identified in *Erythrina velutina*. (A) Erythravine, (B) Hypaphorine, (C) Phaseolidine, (D) Rhizonic acid, and (E) Velutin. Structures were drawn using ChemDraw v.2020, with accurate stereochemical representation based on previously reported phytochemical studies. Source: Authors, 2026.

In addition to erythrinan alkaloids, other classes of bioactive compounds have been reported from various plant parts, thereby contributing to the chemical diversity underlying the species' neuropharmacological profile. The main phytochemical classes reported include alkaloids, flavonoids, and, to a lesser extent, fatty acids and saponins (Fahmy; Balbuena, 2020) (Figure 4). These compounds have been extensively investigated for their antioxidant properties and modulatory effects on the central nervous system (Santos et al., 2012).

Among these constituents, alkaloids constitute the most thoroughly studied class, with emphasis on tetracyclic compounds such as erysodine, erysothrine, and hypaphorine. Erysodine exhibits central nervous system–modulatory properties and has been associated with the sedative and anxiolytic effects traditionally attributed to the species. Erysothrine has been linked to modulation of GABAergic neurotransmission, contributing to anxiolytic and sedative effects (Rosa et al., 2012). Hypaphorine, primarily isolated from the seeds, exhibits anticonvulsant activity and may act synergistically with other alkaloids to enhance sedative responses (Ozawa et al., 2011).

Flavonoids represent another highly relevant group, with compounds such as erythravine and erythratine isolated

from the leaves and bark of *E. velutina*. These phenolic metabolites exhibit antioxidant, neuroprotective, and anxiolytic activities, modulating the glutamatergic system, regulating GABA neurotransmitter levels, and protecting against oxidative stress. Experimental evidence also indicates their ability to modulate ion channels and neuronal receptors, reinforcing their contribution to neurochemical balance and the prevention of neurodegenerative diseases (Carvalho et al., 2009). Experimental evidence suggests that these phenolic metabolites contribute to antioxidant and neuroprotective effects, although their direct molecular targets remain insufficiently characterized.

In addition, compounds such as long-chain fatty acids and saponins have also been detected, suggesting an overall pharmacological profile with anti-inflammatory and calming activities (Chacon et al., 2022). Thus, the synergistic action among alkaloids, flavonoids, and other constituents underlies the diverse pharmacological activities of *Erythrina velutina,* including anxiety reduction, sleep induction, and neuronal protection (Souza et al., 2022). Despite the identification of multiple bioactive compounds, most studies do not evaluate isolated constituents and standardized extracts in parallel, thereby precluding robust attribution of pharmacological effects to individual molecules, limiting mechanistic interpretation, and hampering the assessment of potential synergistic interactions.

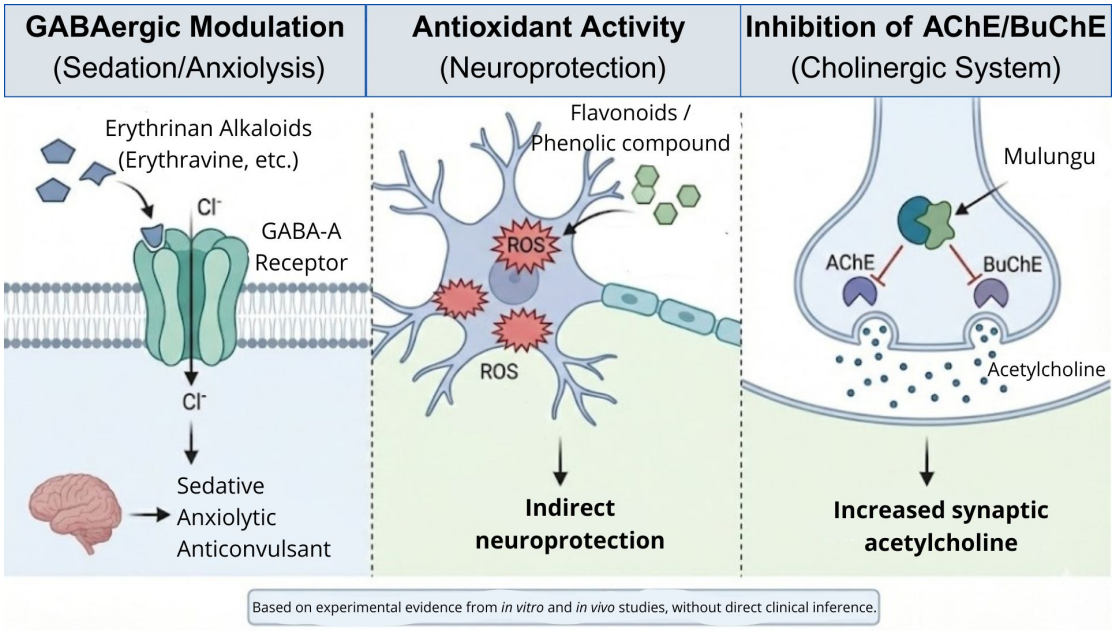

Figure 4. Schematic representation of the main proposed neuropharmacological mechanisms of *Erythrina velutina*. Source: Prepared by the authors using an artificial intelligence-assisted tool (Google Gemini, 2025).

4.4 Antioxidant effect

In addition, *E. velutina* exhibits notable antioxidant activity, which is essential in combating oxidative stress—a key factor associated with cellular aging and the pathophysiology of neurodegenerative diseases (Dias et al., 2019). Experimental studies demonstrated that hydroethanolic extracts of *Erythrina velutina* leaves significantly increased glutathione (GSH) levels and reduced malondialdehyde (MDA) concentrations, a marker of lipid peroxidation, in brain regions such as the prefrontal cortex, hippocampus, and striatum of mice subjected to a ketamine-induced schizophrenia model. These findings indicate that the extract protects neuronal cells against damage caused by reactive oxygen species (ROS), which initiate oxidative processes that contribute to aging and the development of various diseases, including neurodegenerative damage (Silva et al., 2016; Dias et al., 2019).

However, it should be emphasized that antioxidant outcomes inferred from biochemical markers do not necessarily reflect direct modulation of redox signaling pathways. Such effects may arise indirectly from improved neuronal viability, metabolic modulation, or attenuation of excitotoxic processes, rather than from primary radical-scavenging mechanisms.

This antioxidant protection is associated with the presence of natural bioactive compounds, such as alkaloids (erythravine and hypaphorine), flavonoids (phaseolidine), and rhizonic acid, which act by directly neutralizing ROS (Santos et al., 2012; Iqbal et al., 2013). Silva et al. (2016) demonstrated that in ethanolic extracts of *E. velutina,*

erythrine acid and rhizonic acid exhibited neuroprotective properties in neuronal cells, primarily due to their capacity to scavenge reactive species.

Collectively, these findings support the potential relevance of *E. velutina*–derived compounds in the context of disorders associated with oxidative stress. Excessive ROS production contributes to oxidative damage of biomolecules, contributing to premature aging and the progression of neurodegenerative diseases such as Alzheimer's and Parkinson's disease, in which oxidative stress is described as a central pathogenic mechanism (Lombardo; Maskos, 2015).

In this context, detailed mechanistic investigations addressing the effects of erythrine and rhizonic acid on cellular signaling pathways involved in redox homeostasis and neurodegeneration, such as the Nrf2–Keap1 axis, remain scarce. Elucidating how these compounds influence gene expression, protein synthesis, and intracellular signaling is essential to strengthen causal interpretation and pharmacological relevance (Iqbal et al., 2013) (Figure 5).

Overall, the available evidence indicates that standardized extracts of *E. velutina* and its bioactive constituents exhibit consistent antioxidant and neuroprotective activities. Nevertheless, despite the recurrent reporting of these effects, further studies employing standardized preparations and mechanistically oriented approaches are required to establish causality and better define their translational potential.

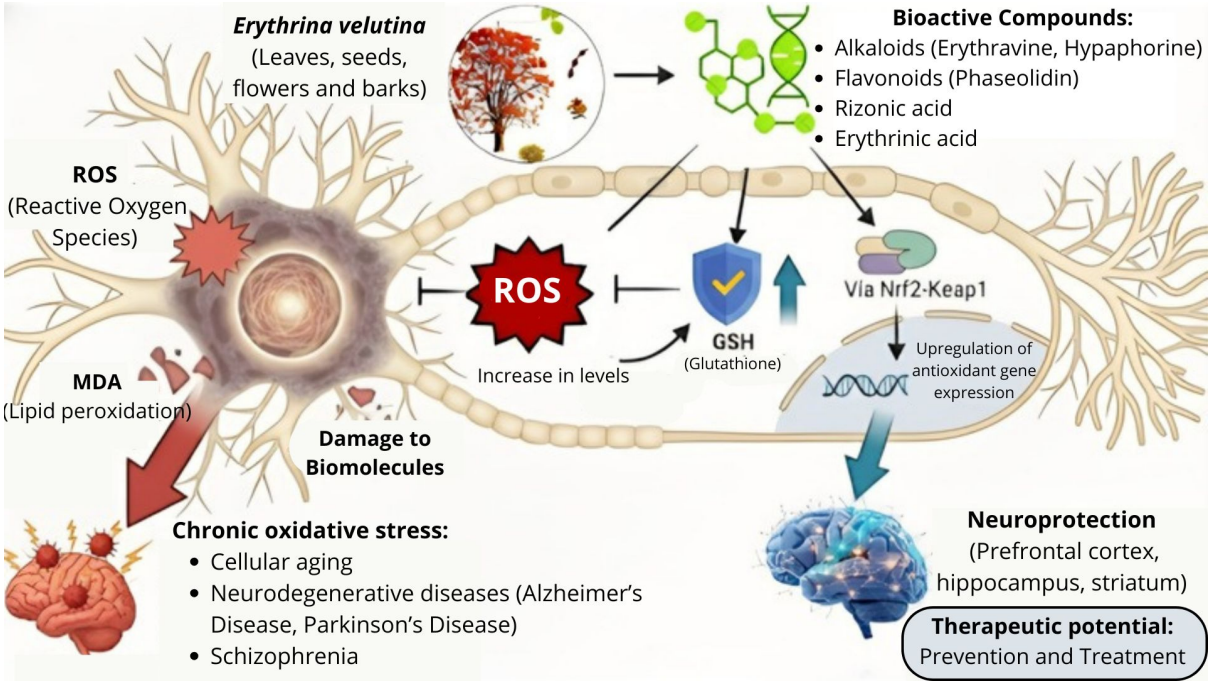

Figure 5. Modulatory effects of *Erythrina velutina* on oxidative stress markers and protection against neurodegenerative damage. Source: Prepared by the authors using images from Canva.

4.5 Anticholinesterase effect

Another relevant therapeutic aspect of *E. velutina* is its ability to inhibit cholinesterase, enzymes that play a crucial role in regulating acetylcholine levels in the central nervous system. Acetylcholine is a neurotransmitter involved in learning, memory, and cognitive functions in neurodegenerative diseases such as Alzheimer's disease. A cholinergic deficit results from the rapid degradation of acetylcholine by acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) (Rodrigues et al., 2017). This reduction is associated with progressive cognitive decline and other neurological impairments characteristic of these conditions.

Studies conducted by Santos et al. (2012) evaluated the effects of aqueous leaf extracts of *E. velutina* in experimental mouse models. The study demonstrated that the extract acts as a dose-dependent inhibitor of AChE and BuChE, with IC_{50} values (concentration required to inhibit 50% of enzyme activity) of 0.57 mg/mL and 2.95 mg/mL, respectively. However, the relatively high IC_{50} values indicate moderate inhibitory potency when compared to clinically approved cholinesterase inhibitors, limiting direct therapeutic extrapolation. This

distinction is critical to avoid overestimation of the clinical relevance of the observed anticholinesterase activity.

Although these results suggest that the extract is capable of reaching central targets, it should be noted that direct evidence of blood–brain barrier permeation was not formally demonstrated, and central effects are inferred from functional outcomes rather than pharmacokinetic measurements.

The mechanism of action is based on the interaction of bioactive compounds, primarily alkaloids, notably erythravine and 11-hydroxyerythravine, which exhibit inhibitory effects on AChE. Additionally, flavonoids present in *E. velutina* may also contribute to its anticholinesterase activity, although their exact mechanisms remain incompletely elucidated (Carvalho et al., 2009; Faggion et al., 2011). These compounds may bind to enzymes in a competitive or noncompetitive manner, thereby blocking acetylcholine hydrolysis and increasing its concentration in the synaptic cleft (Periasamy et al., 2009). This increase promotes greater stimulation of postsynaptic cholinergic receptors, improving cognitive functions impaired in neurodegenerative diseases.

Nevertheless, the predominance of studies employing crude extracts rather than isolated compounds or standardized preparations limits mechanistic interpretation and hinders the establishment of clear structure–activity relationships. Moreover, the absence of comparative analyses with reference drugs under standardized conditions further constrains translational interpretation.

Taken together, these findings suggest that *E. velutina* should be regarded not as a direct anticholinesterase therapeutic agent, but rather as a potential source of bioactive molecular scaffolds relevant to cholinergic modulation. Consequently, well-designed pharmacokinetic, toxicological, and clinical studies are required to determine its efficacy, safety, and therapeutic applicability in conditions associated with cholinergic dysfunction.

4.6 Toxicological effects

Investigation of the toxicity of plant species used in traditional medicine is essential to ensure safe use. Although the pharmacological potential of *E. velutina* has been described in the literature, toxicological studies remain limited. In an acute toxicity assay, Craveiro et al. (2008) reported no deaths, behavioral changes, or pathological findings at necropsy in Wistar rats treated orally with 5000 mg/kg of the aqueous extract, suggesting a low acute toxicity profile. Regarding genotoxicity, Oliveira et al. (2018) evaluated the alcoholic leaf extract using the *in vivo* micronucleus test in hematopoietic cells of rats.

The results did not indicate a significant increase in micronucleated polychromatic erythrocytes compared to controls, ruling out genotoxic effects at the tested concentrations. Subsequently, Craveiro et al. (2013) corroborated these findings, demonstrating the absence of mortality, behavioral alterations, and visible lesions at necropsy following administration of the aqueous extract. Overall, available data suggest that *E. velutina* exhibits low acute toxicity and no genotoxicity in animal models. However, these findings are largely restricted to short-term exposure paradigms, and their convergence does not allow extrapolation to long-term or repeated-use scenarios.

The absence of chronic toxicity, reproductive and developmental toxicity, and herb–drug interaction studies represents a critical gap for safe clinical translation. This limitation is particularly relevant given the high alkaloid content reported for certain plant parts, such as seeds and bark, which may present distinct toxicological profiles. From a pharmacognostic perspective, these gaps underscore the importance of plant-part selection, extract standardization, and dose definition in future toxicological evaluations. Comprehensive safety assessment, including long-term exposure and interaction studies, is therefore essential before considering translational or clinical applications of *E. velutina*.

Despite the growing body of preclinical evidence, the available literature on *E. velutina* presents important structural limitations. Pharmacokinetic data are lacking, preventing the determination of bioavailability, metabolism, and effective concentrations of bioactive compounds. In addition, blood–brain barrier permeability has not been quantitatively assessed, and central effects are inferred primarily from behavioral or biochemical outcomes. The absence of chronic toxicity and long-term exposure studies further restricts translational interpretation. Moreover, the limited use of standardized and phytochemically characterized extracts hampers reproducibility and cross-study comparability.

5. Conclusions

Based on the literature reviewed, Erythrina velutina demonstrates relevant neuropharmacological activity in preclinical models, particularly in studies addressing central nervous system disorders such as anxiety, insomnia, and neurodegenerative conditions. However, the available evidence is predominantly preclinical and

heterogeneous and should therefore be interpreted as suggestive rather than confirmatory of therapeutic efficacy.

The main bioactive constituents identified include alkaloids and flavonoids with reported antioxidant, neuroprotective, and anticholinesterase activities. From a pharmacognostic perspective, these findings indicate that the species represents a valuable source of neuroactive secondary metabolites rather than a fully established phytotherapeutic agent, highlighting its relevance for compound-oriented research and natural product–based lead discovery.

Despite the promising experimental data, substantial gaps remain. The absence of controlled clinical trials, the limited availability of comprehensive toxicological evaluations—particularly regarding safe dosage ranges, chronic exposure, and the higher alkaloid content of seeds—and the lack of standardized extracts and reproducible preparation methods significantly restrict the translational application of Erythrina velutina in clinical settings.

Future investigations should prioritize compound-guided pharmacological studies, extract standardization, and integrated pharmacokinetic and pharmacodynamic approaches to better define bioavailability and mechanisms of action. In addition, well-designed toxicological studies and carefully controlled clinical trials are essential to establish safety and efficacy. The development of phytochemically characterized formulations and advanced delivery strategies, including nanotechnological approaches, may further enhance the pharmacological consistency and translational potential of *Erythrina velutina*.

6. Acknowledgments

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7. Authors' Contributions

Gabriela Acunha Razzera: writing – original draft preparation. *Elize Musachio*: literature search. *Cindhy Suely da Silva Medeiros*: data curation. *Fernanda dos Santos Trombini*: methodological guidance. *Maria Denise Schimith*: funding acquisition. *Euler Esteves Ribeiro*: supervision. *Fernanda Barbisan*: review and editing.

8. Artificial Intelligence Statement

The authors declare that artificial intelligence–assisted tools were used exclusively for preparing schematic illustrations and graphical representations. No artificial intelligence tools were used for data analysis, data interpretation, or scientific writing. All scientific content and conclusions are the sole responsibility of the authors.

9. Conflicts of Interest

No conflicts of interest.

10. Ethics Approval

Not applicable.

11. References

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Institutional Review Board Statement

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Informed Consent Statement

The authors declare no conflict of interest.