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SHORT REVIEW

Ethnobotanical, Phytochemical and Pharmacological Activities of Genus *Erythroxylum*

Sabeena Hussain Syed[1*], Supriya Unavane[1], Poonam Taru[1], Amrita Thakur[1], Neeta Rai[1], Lida Sajimon[1], Sumit Deore[2] and Megha Shah[3]

[1]School of Pharmacy, Vishwakarma University, Kondhwa, Pune - 411048, Maharashtra, India; sabina.syed10@gmail.com

[2]School of Pharmaceutical Sciences, Sandip University, Trimbak Road, Nashik - 422212, Maharashtra, India

[3]AISSMS College of Pharmacy, Kennedy Road, Pune - 411001, Maharashtra, India

Abstract

Erythroxylum P. Browne represents the largest genus in the Erythroxylaceae family, comprising around 230 species. It is widely distributed in South America, Madagascar, Asia, and Australia. A significant number of species from the genus have been employed in traditional medicine to alleviate a variety of health issues. Except for cocaine-producing species, the genus has not received substantial chemical investigation. However, phytochemicals such as terpenoids and flavonoids from other species have also been found in *Erythroxylum*. Thus, the review aims to collect and analyze the scientific data available about the *Erythroxylum* species in terms of their phytoconstituents and pharmacological actions. The review also focuses on summarizing past study results and analyzing future directions of *Erythroxylum* species research.

Keywords: *Erythroxylum*, Erythroxylaceae, Phytochemistry, Pharmacology

1. Introduction

From early times, plants and their derivatives were recognised as a valuable source for treating various ailments. It has been reported that more than 50% of curative medicines have been derived from natural sources, and more than 80% of the population depends upon herbal products[1]. Many systematic investigations have shown the importance and contribution of plant families like Asteraceae[2], Apocynaceae[3], Solanaceae[4], Apiaceae and Rutaceae[5] in curing various perilous diseases. Additionally, the active chemicals present in plants, namely alkaloids, glycosides, tannins, terpenoids, flavonoids, and phenolics have been successful strategies for the development of novel therapeutic agents[6]. As a result, gathering and organizing information on the use of medicinal plants with therapeutic benefits is essential.

The Erythroxylaceae family with therapeutic and phytochemical significance comprises four genera, namely *Nectaropetalum* Engl., *Aneulophus* Benth., *Pinacopodium* Exell and *Mendona.*, and *Erythroxylum* P. Browne. Among the four genera, *Erythroxylum* is the largest, with approximately 230 species. In 1907, Schulz classified this genus into 19 divisions, creating a useful approach for phytochemical comparisons[7].

Erythroxylum is widely distributed in South America, Madagascar, Asia, Malaysia, and Australia[8]. Traditionally, many species of *Erythroxylum* are used as diuretics, febrifuge, amenorrhea, astringents, laxatives, aphrodisiacs, tonics, liniments, inhalants for asthma, and antidiarrheal. Furthermore, it is used to combat fatigue and hunger[9,10]. The phytochemical investigation of the genus Erythroxylaceae was initiated with the isolation of tropane alkaloids from *E. coca*[11] and currently, over 200 molecules have been separated and identified using spectroscopic techniques. From the literature, it was found that the *Erythroxylum* genus was scientifically reported for anticancer[12,13], antihypertensive[14],

*Author for correspondence

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antioxidant[15], and hepatoprotective[16] activities. In this article, we bring together research on traditional medicinal uses, the advancements in phytochemical exploration encompassing all the substances extracted from this genus, as well as their pharmacological effects.

2. Methods

A Literature search was conducted using diverse search engines including Science Direct, Web of Science, PubMed, Research Gate, and Google Scholar. The search terms 'Erythroxylaceae', '*Erythroxylum*', '*Erythroxylum* ethnomedicine' '*Erythroxylum* phytochemistry', and '*Erythroxylum* pharmacological activity' were used. Only articles published in the English language from 1941 to December 2022 were included. In addition to scholarly articles, data regarding *Erythroxylum* species was also sourced from books. References mentioned in the collected articles were meticulously reviewed and cross-referenced.

3. Results and Discussion

3.1 Anatomical Features of the Genus *Erythroxylum*

The anatomical features of the plants have contributed to plant systematics for more than a century and a half. Furthermore, anatomical traits can help to supplement the construction of genetic relationships or phylogenetics[17].

Leaves of the genus show the presence of paracytic stomata, mucilage cells, and papillose abaxial epidermis. The midrib mostly showed the presence of a simple arc of collateral vascular tissue, very rarely a more complex vascular system with pith bundles. Epidermal hairs are absent[18]. Cystolith cells are observable, confined either to the bundle sheath or dispersed in the ground tissue of the petiole and midrib. Within certain *Erythroxylum* species, epidermal cells containing single calcium oxalate crystals have been identified[19].

The stems of Erythroxylaceae were found to have cortical vascular bundles[20]. Anatomy of the stem includes subepidermal cork and the cortical region showed the presence of gum-like contents in secretory cells. medullary rays are uniseriate- to triseriate, with occasional instances of being pluriseriate (up to 5 cells wide), while vessels show some simple perforations. Certain *Erythroxylum* species contain calcium oxalate prisms within their parenchyma[8].

The wood shows the presence of axial parenchyma. Throughout the genus, prominent vessels of varying diameters can be found. Phloem fibres in the wood show two fundamental patterns, both of which appear to be species-specific; (1) Isolated bundles lacking interconnections and (2) Successive or intermittent strands of fibres, interspread with layers of phloem tissues, create distinct patterns. These differing arrangements might also contribute to the unique variations in bark texture found among *Erythroxylum* species[20].

3.2 Traditional Uses

Traditionally, many species of *Erythroxylum* are used for various medicinal uses such as diuretics, febrifuge, amenorrhea, astringents, laxatives, aphrodisiacs, tonics, liniments, inhalants for asthma, as a remedy for different types of intestinal parasites, and antidiarrheal. Additionally, it is utilized to combat fatigue and hunger. Leaves of *E. ferrugineum* Cav., are used to prepare decoction that acts as an antidiarrheal. The leaves of *E. laurifolium* Lam., act as an astringent and diuretic, while fruit juice has a laxative effect. The plant is also used in the treatment of yellow fever[9].

Infusions and decoction prepared from the leaves of the plant *E. myrtoides* Bojer., are used as a carminative and diuretic, particularly in cases of urinary gravel, cystic and renal calculi, and kidney stones. The leaves of the plant have been reported to have antiblennorrhagic effects. A decoction of all plant parts from *E. pervillei* Bail. Is used for lenitive baths[21]. Roots and leaves of the plant *E. dekindtii* O. E. Schulz. Act as a febrifuge[22].

Leaves of *E. monogynum* Roxb. are used as diaphoretic, stimulant, diuretic, and stomachic. Decoction prepared from the leaves possesses antimalarial action. Bark and wood act as a febrifuge[23]. *E. vacciniifolium* Mart. Is notable for its tonic and aphrodisiac properties[24]. *E. cuneatum* (Miq.) Kurz. is said to be used as fish poison and as a tonic[25]. *E. revolutum* Mart., is used in folk medicine as an aphrodisiac and tonic herbal[26].

3.3 Phytochemical Investigation of the genus *Erythroxylum*

Apart from the species that produce cocaine, the genus has received limited chemical attention. Alkaloids are

abundant, particularly tropane, hydroxytropane, and pseudo-tropane alkaloids. Hygroline and ecgonine are alkaloids that appear to be confined to Erythroxylaceae and Rhizophoraceae[9]. Other secondary metabolites include tannins, flavonoids, and diterpenoids[8].

3.3.1 Alkaloids

The economically significant species within the genus are the four cultivated coca varieties *E. novogranatense* 0 *novogranatense*, *E. novogranatense* var. *truxillense, E. coca* var. *coca* and *E. coca* var. *ipadu*, due to the presence of cocaine[27]. Other tropane alkaloids include cinnamoyl cocaine, benzoylecgonine, methylecgonine, pseudotropine, and benzoyltropine. The plants also showed the presence of pyrrolidines (hygrine, cuscohygrine, and dihydrocuscohygrine) and pyridines (nicotine)[28]. The synthesis of the ecgonine moiety in the plant is thought to be a one-of-a-kind evolutionary event that hasn't been replicated in other species or genera.

Calystegines, hydroxylated nortropane alkaloids are reported in young leaves of *E. novogranatense.* var. *novograntense*. Additionally, the Truxillense variety of *E. novogranatense* contains dihydroxytropanes, namelyα-Truxilline and β-Truxilline[29].

The outer covering of the bark and leaves of *E. vacciniifolium* Mart., widely known as "Catuaba" in Brazil, is rich in alkaloidal content and shows the presence of cautabin A, B, and C, which are esters of tropane-1,3-diol[24].

From the same plant, approximately eight tropane alkaloidal aromatic esters (cautabine D, 7β-hydroxycatuabine D, cautabine E, 7β-hydroxycatuabine E, 7β-acetyl catuabine E, cautabin F, 7β-hydroxycatuabine F, cautabine G) are isolated from the stem bark of *E. vacciniifolium* Mart., The ester moieties of the separated alkaloids are important because they are specific to the species. Pyrrole-2-carboxylic and 1-methyl-pyrrole-2-carboxylic acid have been found only in this species[30].

Furthermore, nine methyl pyrrole tropane alkaloids (cautabine H, Isocautabine H, cautabine I, 7β-hydroxycautabine H, 7α-hydroxycautabine, 7β-hydroxycataubine I, cataubine E *N*-oxide, vaccinine A and vaccinine B) were isolated from the same stem bark of *E. vacciniifolium* Mart.[31].

Isolated catuabines are tropane alkaloids that have been di- or trioxygenated at the 3-, 6-, or 7-position. Vaccinines, which are deoxygenated at the 3-, 4-, or 6-position, represent a new class of tropane alkaloids. The esterifying unit of vaccinines, like that of catuabines, is located at C-4, while the hydroxyl group can be located at C-3 or C-6. Tropanes containing esters at the C-2 or C-4 positions are uncommon, whereas carboxyl groups (e.g., ecgonine derivatives) and hydroxyl groups (e.g., calystegines) at the same positions are common. As a result, *E. vacciniifolium* Mart. Provides a source of unique tropane alkaloids with distinct esterifying acids and ester positions.

E.hypericifolium Lam., showed the presence of alkaloids in the root bark. Tropan-3α-yl 3- hydroxyphenylacetate, (+)-tropane-3,6β-diol-3-phenylacetate, tropane-3α,6β-diol-3-phenylacetate-6-acetate, tropane-3α,6β,7β-triol-3-phenylacetate, nortropan-3-yl phenylacetate, tropan-3α-ylphenylacetate, tropane-3,6,7-triol, tropane-3α,6β,7β -triol 3-phenylacetate and nortropane-3-yl phenylacetate were isolated[32].

From the leaves of *E. hypericifolium* Lam. fifteen alkaloids were characterized, the majority of which were esters of cinnamic and benzoic acid. 3α-Cinnamoyloxytropan-6β-ol is the principal base. Other alkaloids reported are 3α-cinnamoyloxytropane, 3β- cinnamoyloxytropane, 3α-cinnamoyloxynortropane, 3α-cinnamoyloxynortropan-6-ol, 3α, 6β-dicinnamoyloxytropane, 3α-benzoyloxytropane, 3-cinnamoyloxynortropan-6-ol, 6β-acetoxy-3α-cinnamoyloxytropane and, tentatively, 6-phenylacetoxytropan-3-ol[33].

Furthermore, thirteen tropane alkaloids are characterized from the stem bark of the plant *E.hypericifolium* Lam. among which hygrine is the main base. Phenylacetic acid predominates in stem bark and asin root bark. Other alkaloids include, 6β-acetoxy-3α-benzoyloxytropane, 3α-benzoyloxynortropane, 3-benzoyloxytropan-6-ol, 3α-trimethoxycinnamoyloxytropane and cuscohygrine[34]. The distribution of other alkaloids obtained from the genus *Erythroxylum* is listed in Table 1 and figures of isolated alkaloids are shown in Figure 1.

3.3.2 Terpenoids

Terpenoids such as diterpenoids and triterpenoids are widely distributed in the genus *Erythroxylum* and they tend to deposit in the form of balsams (mixture of essential oil and resin). The principal organs of the plant where terpenoids are found are the wood and

Table 1. Alkaloids derived from *Erythroxylum*

Sr. No.	Plant Name	Plant Part	Alkaloids	References
1	*E. australe* F. Muell.	Root bark	Methylecgonidine;3α-(4-hydroxyphenyl acetoxy) tropane; 3-benzoyloxytropane-6,7-diol; 3-cinnamoyloxytropane-6,7-diol; 3α-cinnamoyloxytropan-6β-ol;	35
2	*E. bezerrae* Plowman.	Stem bark	Erythrobezerrine A; Erythrobezerrine B; Erythrobezerrine C; Erythrobezerrine D; Erythrobezerrine E; Erythrobezerrine F; 3α-(3,4,5-trimethoxycinnamoyloxy)-6β-(3,4,5-trimethoxybenzoyloxy)-7β-hydroxy-tropane;3α-(3,4,5-trimethoxycinnamoyloxy)-6β-(benzyloxy)-7β-hydroxy-tropane	36
3	*E. caatingae* Plowman.	Stem	3α,6β-dibenzoyloxytropane. 6β-benzoyloxy-3α-(4-hydroxy-3,5-dimethoxybenzoyloxy) tropane. 6β-benzoyloxy-3α-(3,4,5-trimethoxybenzoyloxy) tropane	37
4	*E. cuneatum* (Wall.) Kurz.	Leaves	tropacocaine; nicotine. (±)-3α,6β-Dibenzoyloxytropane. 6β-tigloyloxytropan-3α-ol. 6β-benzoyloxytropan-3α-ol.	35
5	*E. cuneatum* (Wall.) Kurz.	Stembark	tropacocaine; nicotine. (±)-3α,6β-Dibenzoyloxytropane.	35
6	*E. dekindtii* (Engl.) O. E.Schulz.	Root bark	1αH,5αH-tropan-3α-ylisovalerate. 1 αH,5αH-tropan-3α-ylphenylacetate; 1 αH,5αH-tropan-3α-yl 2-furoate; methylecgonidine; valeroidine; poroidine; isoporoidine and tropine.	22
7	*E. ecarinatum* Burck.	Leaves	tropacocaine;3α-benzoyloxynortropan-6β-ol.	35
8	*E. macrocarpum* O. E. Schulz.	Leaves	3α-Benzoyloxynortropane; tropan-3β-ol; tropacocaine; 3α-Benzoyloxynortropan-6β-ol.	38
9	*E. macrocarpum* O. E. Schulz.	Stem and Root bark	3α-Benzoyloxynortropane	38
10	*E. monogynum*	Root bark	Hygrine; Tropinone; Tropine; Pseudotropine; Cuscohygrine; Dihydrocuscohygrine; Isoporoidine; Butropine; Valeroidine; Tropacocaine; Convolamine; 3α -Cinnamoyloxytropane;3-Phenylacetoxynortropane.	39
11	*E. pervillei* Baill.	Stem bark	Pervilleine A; Pervilleine B; Pervilleine C; Pervilleine F; Pervilleine G; Pervilleine H; cis-Pervilleine B; cis-Pervilleine F;	40
12	*E. pungens* O. E. Schulz.	Leaves	3-Benzoyloxytropane. 3-(2-Methylbutyryloxy) tropan-6-propionyl-7-ol. 3-(3′,5′-Dimethoxy-4′-hydroxy) benzoyloxytropane;	41
13	*E. pungens* O. E. Schulz.	Roots	3-(4′-Methoxy) benzoyloxytropane; 3-Phenylacetoxytropane;3-Phenylacetoxynortropane;3-Phenyltropan-6-ol; N, N-Dimethyl-1-H-indole-3-ethanamine;3-(3′,5′-Dimethoxy-4′-hydroxy) benzoyloxytropane; 3-(2-Methylbutyryloxy) tropan-6-propionyl7-ol; pungencine.	42
14	*E. pungens* O. E. Schulz.	Stembark	3-(2-Methylbutyryloxy) tropan-6-acetyl-7-ol. 3-(2-Methylbutyryloxy) tropan-6-propionyl-7-ol. 3-(2-Methylbutyryloxy) tropan-6,7-diol. 3-(2-Methylbutyryloxy) nortropan-6,7-diol. 3-Isovaleryloxytropan-6-ol.	41

Table 1. Continued...

Sr. No.	Plant Name	Plant Part	Alkaloids	References
15	*E. rimosum* O. E. Schulz.	Leaves	7β-acetoxy-3β,6β-dibenzoyloxytropane.	43
16	*E. rotundifolium* Lunan.	Stem	7β-Hydroxy-6β-(3,4,5-trimethoxybenzoyloxy)- 3α-[(E)-3,4,5-trimethoxycinnamoyloxy] tropane; 6β -(Benzoyloxy)-3α-[(Z)-3,4,5-trimethoxycinnamoyloxy] tropane; (-)-6β-(Benzoyloxy)-3α-hydroxytropane; 6β-(Benzoyloxy)-3α-[(Z)-3,4,5-trimethoxycinnamoyloxy] tropane; 6β-(Benzoyloxy)-3α-[(E)-3,4,5-trimethoxycinnamoyloxy] tropan-7β -ol; 7β-(Acetoxy)-6β-(benzoyloxy)-3α-[(E)-3,4,5-trimethoxycinnamoyloxy] tropane. Erythrorotundine	44
17	*E. sideroxyloides* Lam.	Leaves	3α-Benzoyloxynortropan-6β-ol; 3α-benzoyloxytropan-6β-ol ;3α-benzoyloxynortropane. 3α-benzoyloxytropane; tropacocaine.	38
18	*E. sideroxyloides* Lam.,	Stem and Root bark	3α-Benzoyloxynortropane.	38
19	*E. subsessile* (Mart.) O. E. Schulz.	Leaves	6β,7β-dibenzoyloxytropan-3α-ol. 3α-benzoyloxynortropan-6β-ol and 3α,6β-dibenzoyloxytropane.	45
20	*E. zeylanicum* O. E. Schulz.	Roots	Erythrozeylanine A; 3α -(3′,4′,5′-Trimethoxybenzoyloxy) tropane; Erythrozeylanine B.	46
21	*E. zeylanicum* O. E. Schulz.	Leaves and twigs	Erythrozeylanine C.	46

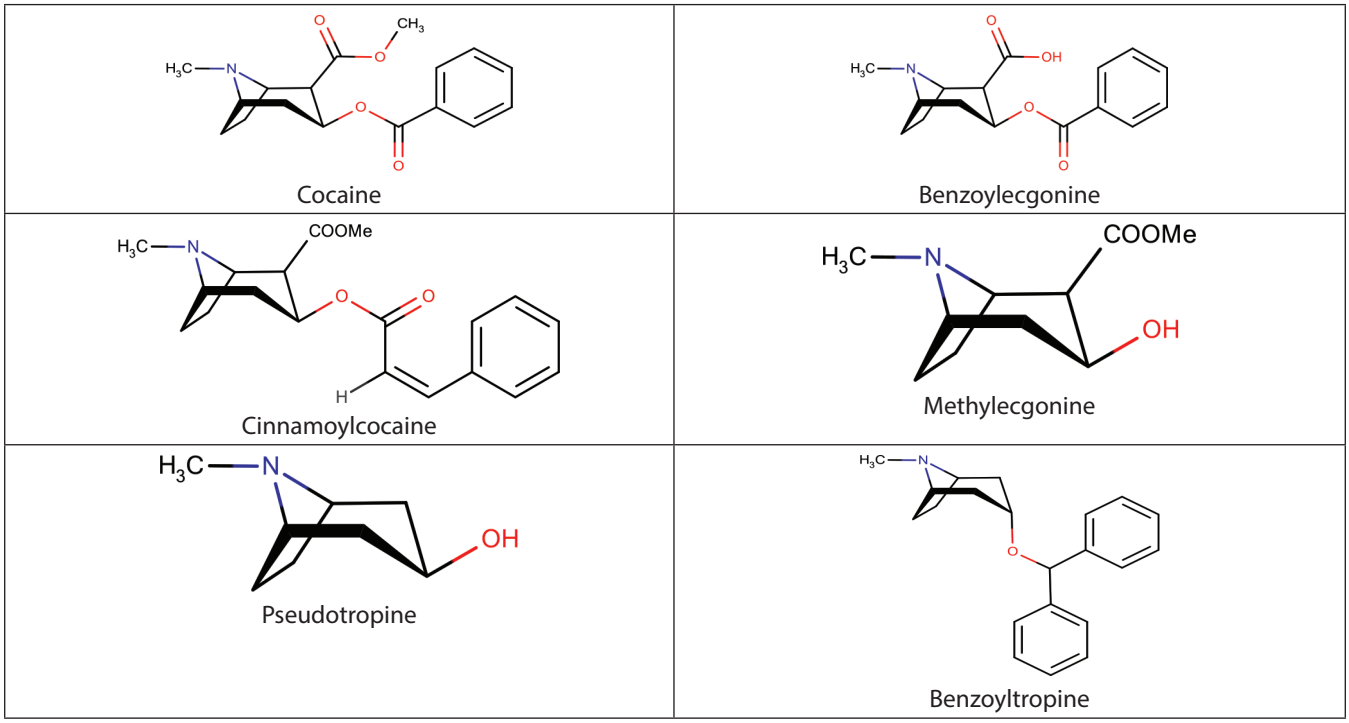
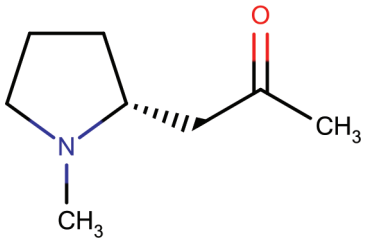
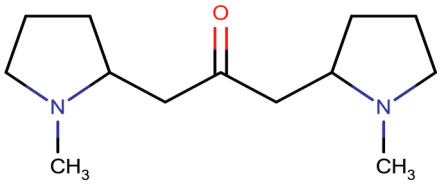


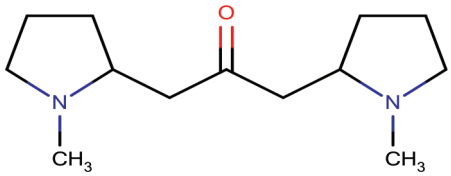
Figure 1. Alkaloids isolated from *Erythroxylum* plants.



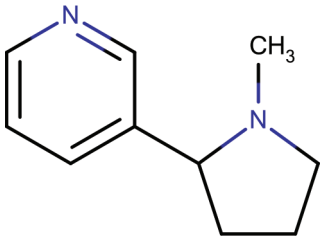
Hygrine



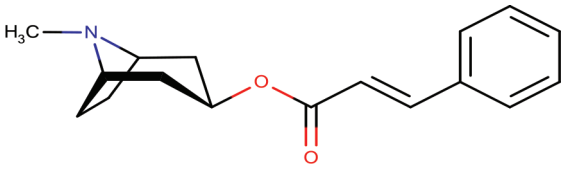
Dihydrocuscohygrine



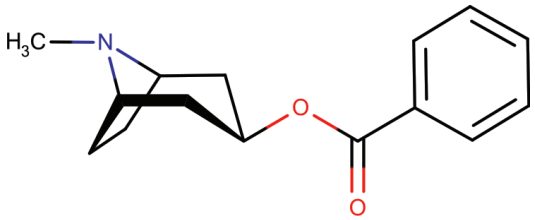
Cuscohygrine



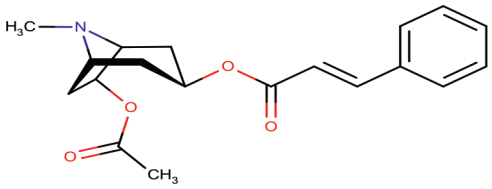
Nicotine



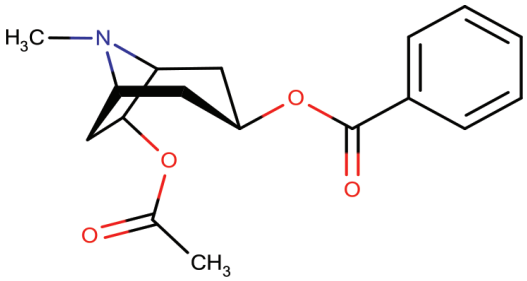
3α-cinnamoyloxytropane



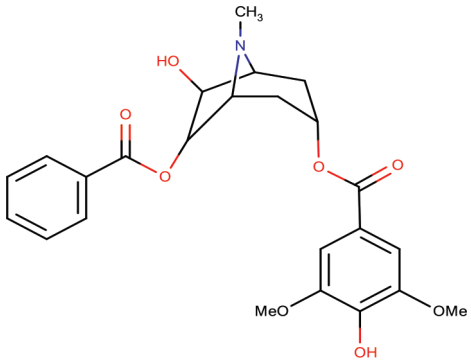
3α-benzoyloxytropane



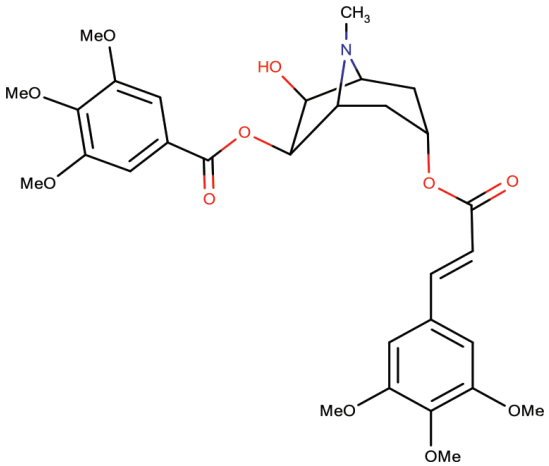
6β-acetoxy-3α-cinnamoyloxytropane



6β-acetoxy-3 -benzoyloxytropane



Erythrobezerrine A



3α-(3,4,5-trimethoxycinnamoyloxy)-6β-(3,4,5-trimethoxybenzoyloxy)-7β-hydroxy-tropane.

Figure 1. Continued...

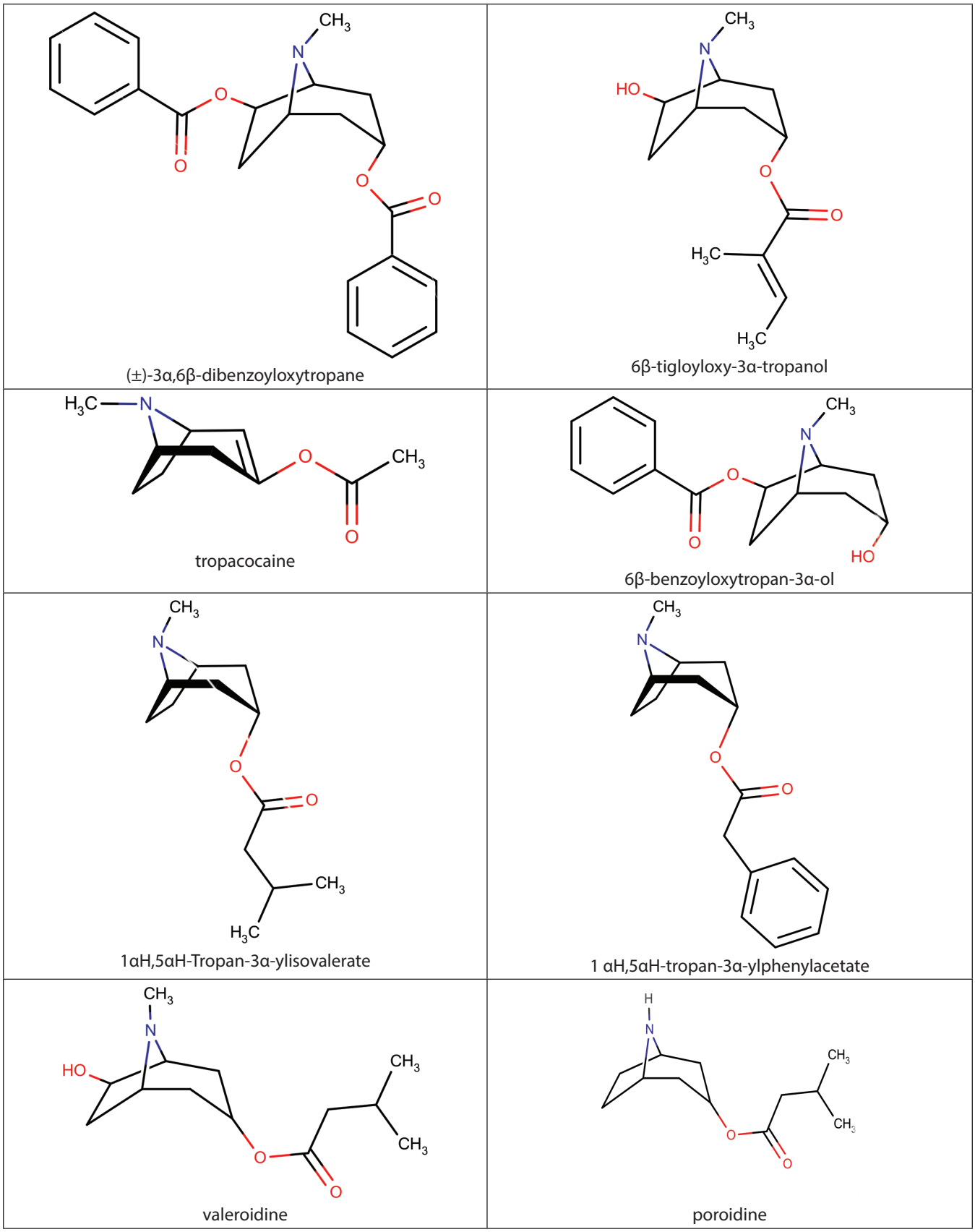


Figure 1. Continued...

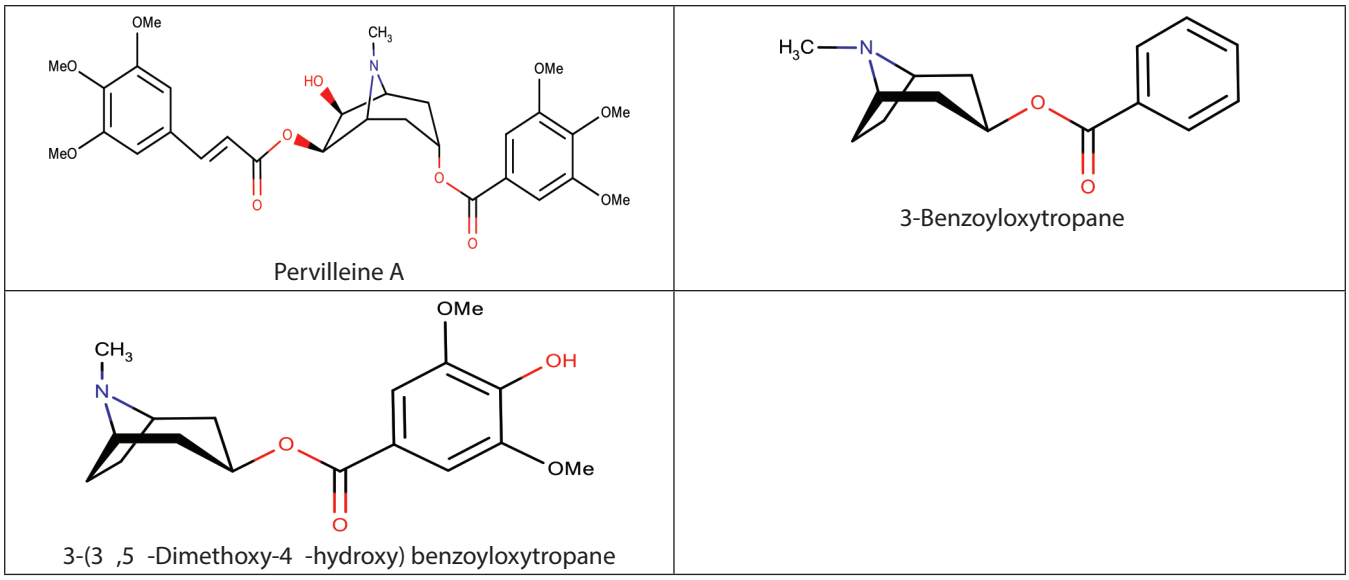


Figure 1. Continued...

stems. Triterpenoids were also found in leaves and fruit waxes[9].

Erythroxylum species are recognized for their composition of diterpenes such as ent-kaurane, ent-beyerane, ent-labdane, ent-rosane, ent-devadarane and ryanodine[47-50]. The distribution of terpenoids obtained from the genus *Erythroxylum* is presented in Table 2, and the structures of the isolated terpenoids are depicted in Figure 2.

3.3.2 Flavonoids

Flavonoids form an extensive and intricate class of plant-based compounds, exhibiting a variety of biological functions such as anticancer, antiulcer, antioxidant, anti-inflammatory and hepatoprotective activities among others[57]. In *Erythroxylum*, the most commonly occurring flavonoid compounds are flavonols. The main flavonols in *Erythroxylum* include kaempferol, ombuin, epicatechin and quercetin[9]. The distribution of flavonoids in *Erythroxylum* are enlisted in Table 3 and the structure of isolated flavonoids are depicted in Figure 3.

3.3.3 Other Constituents

Inamoside 6'-O-L-alpha-arabinofuranoside (also known as cuneatoside), a megastigmanediglycoside, was extracted from the branches and leaves of *E. cuneatum*[64]. Other constituents include citroside A, apocynol B, (6S,9R)-roseoside, vomifoliol-9-O-arabinofuranosyl-glucopyranoside, inamoside, and (3S,5R,6R,7E,9S)-megastigman-7-ene-3,5,6,9-tetrol-3-O-β-glucopyranoside. Two steroids, 4-methyl ergosta-7,23-dien-3β-ol and 4-methyl ergosta-7,24(28)-dien-3β-ol are isolated from the leaves of *E. monogynum*[65].

3.4 Pharmacological Studies of the Genus *Erythroxylum*

Extensive research has been conducted to explore the pharmacological actions of crude extracts obtained from the plants of the genus *Erythroxylum* (Table 4). Leaves and bark of the plant *E. pictum E. mey*., are reported for antibacterial action against *Bacillus subtilis* and *Klebsiella pneumonia*[66]. The hepatoprotective action of leaves of methanolic extract of *E. monogynum* Roxb. has been reported[16]. When compared to the toxic group, pre-administration of this extract normalized the increased levels of serum markers.

Four samples from *E. pungens* O. E. Schulz., 3α-(2- methylbutyryloxy) tropan-6endo,7endo-diol (1), N, N-dimethyltryptamine (DMT) (2), alkaloid-enriched extracts derived from the leaves (3) and stem (4) were evaluated for cytotoxic action. 3α-(2- Methylbutyryloxy) tropan-6endo, 7endo-diol cytotoxicity was variable, with potencies ranging from 0.3 to 1.0 mg/mL and better results against HeLa cells (50 per cent cell viability reduction). DMT (0.5 mg/

Table 2. Terpenoids derived from *Erythroxylum*

Sr. No.	Plant Name	Plant Part	Terpenoids	References
1	*E. aeriolatum*	Timber extract	ent-17-hydroxybeyer-15-en-1-one. *ent*-labda-8(17),14-dien-13R-ol. ent-rosan-5β,15,16-triol. ent-15ξ,16-dihydroxypict-4(18)-en-5-one; ent-devadaran1β,11β,15ξ,16-tetrol. ent-devadaran-11β,15ξ,16-triol. ent-1β-acetoxydevadaran-11β,15ξ16-triol.	49
2	*E. argentinum* O. E. Schulz.,	Timber extract	ent-dolabr-4(18)-en-15S,16-diol. ent-5α-dolabr-4(18)-en-15S,16-diol; ent-beyer-15-en-1-one. ent-beyer-15-en-17-ol. ent-labda-8(17),13E-diene-15,16-diol. ent-17-hydroxybeyer-15-en-1-one. ent-2,17-dihydroxybeyer-2,15-dien-1-one. ent-beyer-15-en-7-one.	49
3	*E. betulaceum* Mart.,	Wood	(-)-3-Oxomanool;(-)-3β-Hydroxymanool; ent-2β,19-dihydroxybeyer-15-en-1-one.	50
4	*E. cuneatum* (Miq.) Kurz,	Timber extract	ent-13R-hydroxylabda-8(17)-dien-3-one. ent-labda-8(17),14-dien-13R-ol. ent-rosan-5β,15ξ 16-triol. ent-labda-8(17),14-diene-3β,13R-diol; ent-pimara-8(14),15-dien-3β-ol. ent-15ξ,16-dihydroxypict-4(18)-en-5-one. ent-3β,11α-dihydroxypimara-8(14),15-diene.	49
5	*E. deciduum*	Timber extract	ent-labda-8(17),13E-dien-15-ol.	49
6	*E. delagoense* Schinz.,	Timber extract	ent-labda-8(17),14-diene-3β,13R-diol; ent-dolabr-4(18)-en-15S,16-diol; ent-5α-dolabr-4(18)-en-15S,16-diol; ent-15ξ,16-dihydroxypict-4(18)-en-5-one.	49
7	*E. leal-costae* Plowman.,	Leaves	β-amyrin; lupeol and lupenyl acetate.	51
8	*E. pictum*	Timber extract	ent-4,15ξ,16-trihydroxypictan-5-one; ent-15ξ,16-dihydroxy-4,18-epoxypictane-5-one; ent-4,15ξ,16,18-tetrahydroxypictan-5-one; ent-16-hydroxypictan-4(18)-ene-5,15-dione; ent-4,13α-dihydroxy-15ξ,16-bisnorpictan-5-one.	49
9	*E. macrocarpum*	Timber extract	ent-devadaran-15ξ,16-diol; ent-devadaran-11β, 15ξ,16-triol; ent-dolabr-4(18)-ene-11β, 15ξ,16-triol; ent-dolabr-4(18)-en-15S,16-diol.	49
10	*E. microphyllum*	Timber extract	ent-17-hydroxybeyer-15-en-1-one; ent-15ξ,16-dihydroxypict-4(18)-en-5-one; ent-2β-17-dihydroxybeyer-15-en-1-one; ent-2β,19-dihydroxybeyer-15-en-l-one; ent-2,19-dihydroxybeyer-2,15-dien-l-one. ent-1β, l9- dihydroxybeyer-15-en-2-one; ent-2,17-dihydroxybeyer-2,15-dien-1-one.	49
11	*E. monogynum* Roxb.,	Heartwood	ent-beyer-15-ene((+)-hibaene); ent-beyer-15-en-19-ol (erthroxylol A); ent-beyer-15-en-al; Erythroxylol B; erythroxydiol A. erythroxydiols X, Y and Z; (+)-devadarene. ent-devadarane-7β,15ξ,16-triol. ent-devadarane-15ξ,16-diol.	52

Table 2. Continued...

Sr. No.	Plant Name	Plant Part	Terpenoids	References
12	*E. nummularia* Peyr.,	Leaves	14-O-methyl-ryanodanol; β-amyrin; lupeol; erythrodiolpalmitate and stearate; palmitate of oleanolic acid and β-sitosterol.	[53,54]
13	*E. ovalifolium* Peyr.,	Stems	β-sitosterol; lupeol.	[55]
14	*E. passerinum* Mart.,	Ripe fruits	Ryanodanol and14-O-methyl-ryanodanol	[54]
15	*E. rotundifolium*	Timber extract	ent-13R-hydroxylabda-8(17)-dien-3-one. ent-labda-8(17),14-dien-13R-ol. ent-labda-8(17),14-diene-13R,18-diol; ent-dolabr-4(18)-en-15S,16-diol. ent-15ξ,16-dihydroxypict-4(18)-en-5-one; ent-kauran-16β,17-diol. ent-beyer-15-en-1-one. ent-beyer-15-en-7-one. ent-beyer-15-en-17-ol. ent-17-hydroxybeyer-15-en-1-one. ent-1β,17-dihydroxybeyer-15en-2-one; ent-2β-17-dihydroxybeyer-15-en-1-one.	[49]
16	*E. sideroxyloides*	Timber extract	ent-11β-acetoxydevadaran-15ξ,16-diol; ent-1β-acetoxydevadaran-11β,15ξ,16-triol. ent-rosan-5β,15ξ16-triol. ent-devadaran-15ξ,16-diol. ent-dolabr-4(18)-en-15S,16-diol. ent-devadaran-11β,15ξ,16-triol. ent-devadaran-1β,11β,15ξ,16-tetrol. ent-dolabr-4(18)-en-7α (,15R,16-triol; ent-dolabr-4(18)-ene-11β,15ξ,16-triol; ent-15ξ,16-dihydroxydolabr-4(18)-en-1-one. ent-1β-acetoxydolabr-4(18)-ene-11β, 15ξ,16-triol.	[49]
17	*E. suberosum* A.St.-Hil.,	branches	7-oxo-abiet-15(17)-en-16-ol. 7-oxo-16-hydroxy-abiet-15(17)-en-19- al. 7α,16-dihydroxy-abiet-15(17)-en-19-al; ent-12α-hydroxy-kaur-16-en-19-al; methyl ent-7α,15β-dihydroxy-kaur-16-en-19-oate.	[56]
18	*E. subsessile* (Mart.). O.E.Schulz.,	Stems	β-sitosterol; friedelin.	[55]
19	*E. zambesiacum* N. Robson.,	Timber extract	ent-rosan-5β,15ξ,16-triol. ent-labda-8(17),13E-dien-15-ol. ent-15ξ,16-dihydroxypict-4(18)-en-5-one; ent-beyer-15-ene; ent-15,16-epoxybeyerane; ent-beyer-15-en-17-ol; ent-beyer-15-en-19-ol; ent-beyer-15-en-1-one; ent-5α-ros-1(10)-en-15ξ,16-diol; ent-11β-acetoxy-5α-ros-1(10)-en-15ξ,16-diol; ent-2-oxo-ros-1(10),15-diene; ent-beyer-15-en-12-ol; ent-beyer-15-en-19-al.	[49]

mL) from *E. pungens* O. E. Schulz., roots reduced cell viability by 50% in HeLa, SiHa, PC3, and 786-0 cells[42]. The presence of alkaloids can be attributed to their cytotoxic activity, as they can modulate key signalling pathways involved in proliferation, the cell cycle, and metastasis making them key ingredients of several anticancer agents[67].

The alkaloidal leaf extract of *E. cuneatum* was evaluated for its antioxidative and anti-inflammatory properties. The highest dose (50 mg/kg) of extract

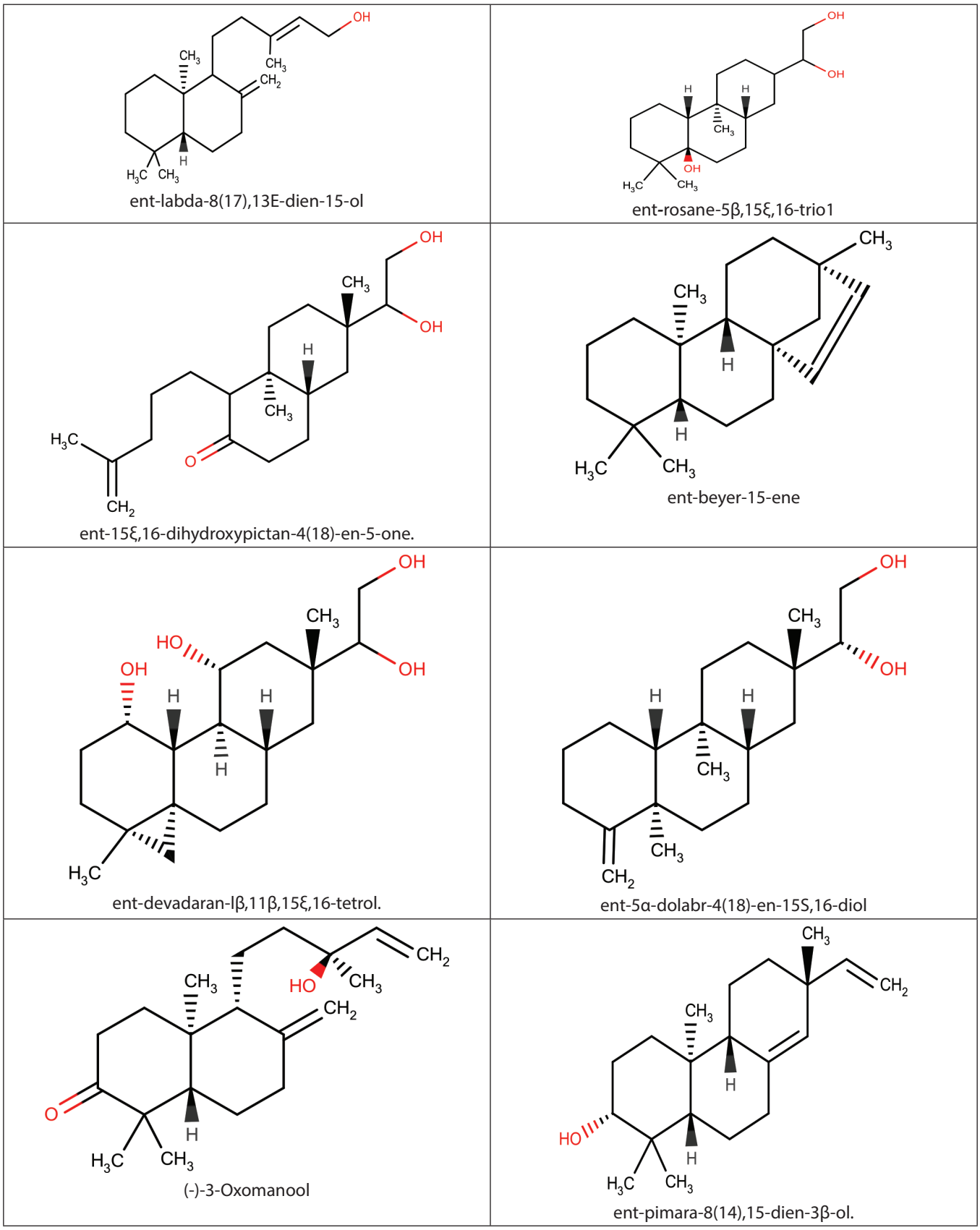


Figure 2. Terpenoids isolated from *Erythroxylum* plants.

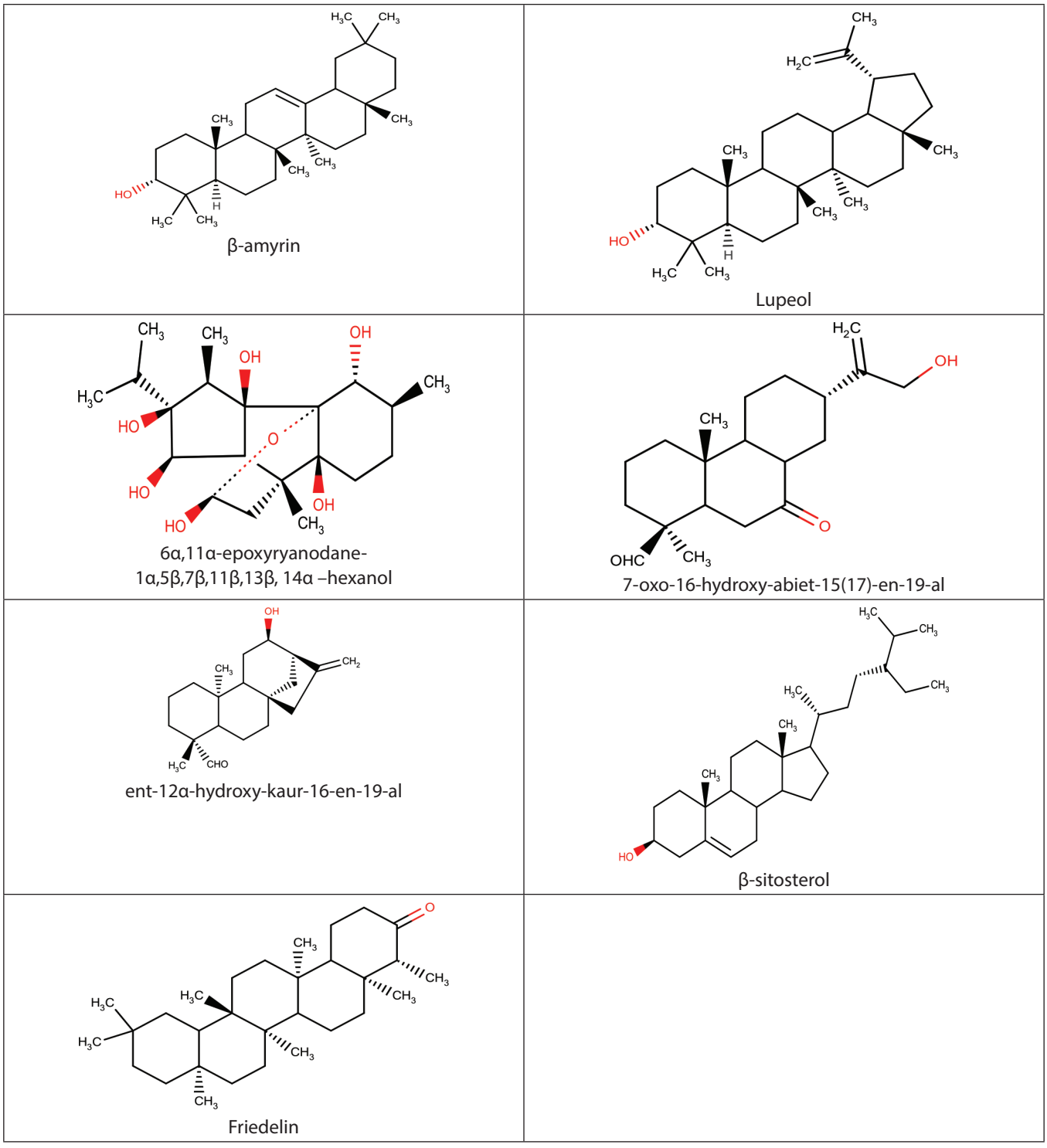


Figure 2. Continued...

had similar effects to aspirin in terms of paw thickness reduction, leucocyte infiltration, and collagen disruption[15].

The ethanolic extract of *E. passerinum* Mart. Causes hypotension as well as endothelial-dependent and independent vasorelaxation, likely mediated through nitric oxide and potassium channels. The hypotensive activity of the extract is assumed to be due to the presence of phenols. The hypotensive effect is believed to be attributable to the existence of phenols in the extract[68].

Table 3. Flavonoids obtained from *Erythroxylum* plants

Sr. No.	Plant Name	Plant part	Chemical Constituents	References
1	*E. alaternifolium* var. *alaternifolium* A. Rich.	Leaves	quercetin-3-O-rutinoside; ombuin-3-O-rutinoside.	[57]
2	*E. argentinum* O. E. Schulz.	Aerial parts of the plant	quercetin-3-rutinoside; quercetin-3-α-L-rhamnoside. 7,4′dimethylquercetin 3-rutinoside. 7,4′dimethylquercetin-3-rutinoside-5-glucoside.	[58]
3	*E. australe*	Leaves	2-methyl-3-O-rhamnosyl-dihydro-orobol; 3-O-rhamnosyl-7-O-glucosyl-dihydro-orobol. 3-O-rhamnosyl-7-O-glucosyl-quercetin. 4-O-dirhamnosyl-dihydro-orobol. 5-O-rhamnosyl-7-methoxy-dihydro-orobol. 7-O-rhamnosyl-5,3,4-OH-eriodictyol. 5-dehydroxy-7,3-O-glucosyl-dihydro-orobol.	[59]
3	*E. coca var. ipadu* Plowman.,	Leaves	Kaempferol; quercetin; 3-O-mono and diglycosides.	[60]
4	*E. leal-costae* Plowman.,	Leaves	quercetin 3-rhamnoside; epicatechin; 8-hydroxy luteolin 8-rhamnoside; 6-hydroxy luteolin 6-rhamnoside;	[51]
5	*E. nummularia* Peyr.,	Leaves	7,4-dimethyl-quercetin; quercetin-3-O-b-D-glycopyranoside.	[53]
6	*E. ovalifolium* Peyr.,	Stem	Quercetin; rutin.	[55]
7	*E. pulchrum* A. St.-Hil.,	Leaves	quercetin-3-O-α-L-rhaminoside; ombuin-3-ruthinoside; ombuin-3-ruthinoside-5-glucoside.	[61]
8	*E. rufum* Cav.,	Dried leaf extract	ombuin-3-O-rhamnosylglucoside. quercetin-3-O- mono- and diglycosides. Kaempferol;	[62]
9	*E. subsessile* (Mart.) O.E.Schulz.,	Stem	quercitrin; kaempferol-3-O-rhamnoside.	[55]
10	*E. ulei* O. E. Schulz.,	Dried leaf extract	Kaempferol; quercetin; myricetin 3-O-glycosides; the gallic acid conjugates of the glucosides; naringenin-7-O-glucoside; dihydroquercetin.	[62]
11	*E. ulei* O. E. Schulz.,	Leaves	Baptigenin; quercetin; genistein; 2,3-dihydro-2-methyl genistein ;2-hydroxy orobol; 2,3-dihydro-2-methyl orobol.	[63]

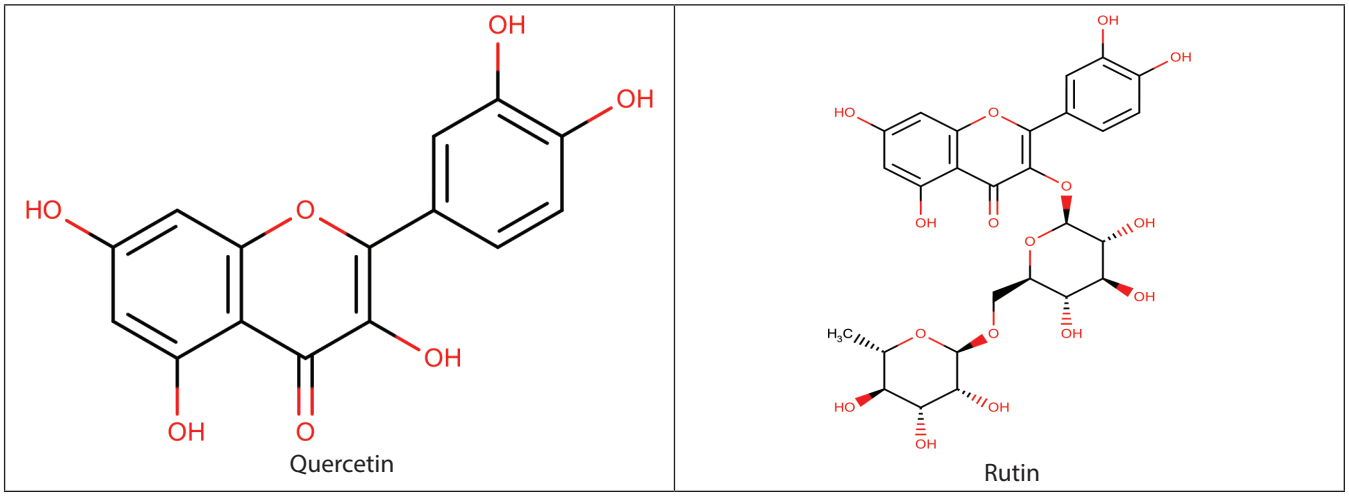


Figure 3. Flavonoids isolated from *Erythroxylum* plants.

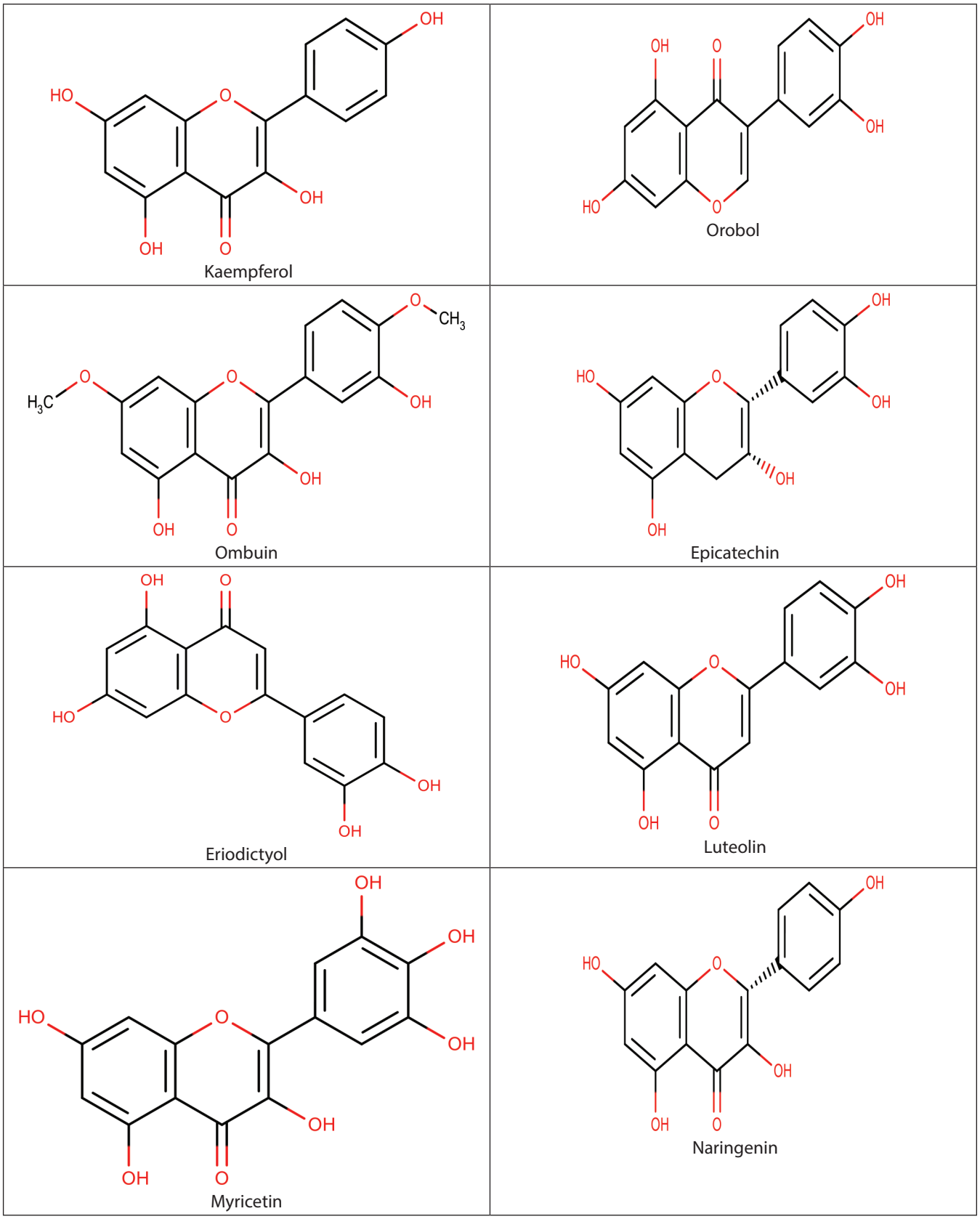


Figure 3. Continued...

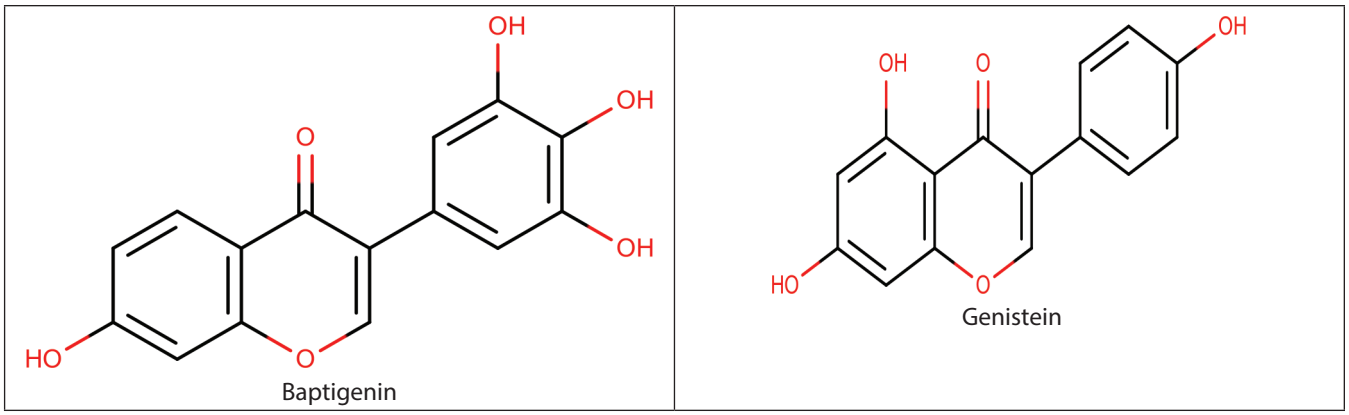


Figure 3. Continued...

Table 4. Biological activities of *Erythroxylum* plants

Sr. No.	Plant Name	Plant Part	Type of Study	Bioactivity	MOA	References
1	*E. caatingae* Plowman.	Leaves	*In-vivo*	relaxant effect on ovine cervical contractions	Intracellular calcium sequestration.	[69]
2	*E. cuneatum*	Leaves	*In-vitro*	anti-dependence property against morphine	↑α-synuclein, calmodulin	[70]
3	*E. confusum* Britton., and *E. minutifolium*Griseb. var. *minutifolium*	Leaves	*In-vitro*	Hepatoprotective	Antioxidant ↓MDH levels ↑GSH levels	[71]
4	*E. daphnites* Mart.	Leaves	*In-vitro*	Anticancer	↓ cyclines D and E ↑p21, caspase 3	[12]
5	*E. laurifolium* Lam.	leaves	*In-vitro*	Antihypertensive	↓Angiotensin-converting enzyme	[72]
6	*E. subsessile* (Mart.) O. E. Schulz.,and *E. ovalifolium* Peyr.	Stem	*In-vitro* and *In-vivo*	Protective effect against the adverse effects caused by the venom of the Lachesismuta snake.	Inhibition of hemolysis, proteolysis, haemorrhage, coagulation, or oedema.	[55]
7	*E. pervillei* Baill.,	Roots	*In-vitro*	Bioavailability enhancer for anticancer drugs	By inhibiting P-glycoprotein	[73]
8	*E. pungens* O. E. Schulz.	Roots	*In-vivo*	Anti-hypertensive	By $\downarrow[Ca2+]_i$ in vascular smooth muscle cells.	[14]
9	*E. suberosum* A.St.-Hil.	Leaves	*In-vitro*	Anticancer	Unknown	[13]
10	*E. vaccinifolium*Mart.	Stem bark	*In-vitro* and *In-vivo*	Anticancer	Cytotoxic to L1210 mouse leukaemia cells	[74]

3. Conclusion and Future Prospective

This review represents the anatomical, traditional, phytochemical, and pharmacological results of *Erythroxylum* species from the period of 1941-2022. Alkaloids, terpenoids, and flavonoids are the three major groups of phytoconstituents present in the genus. Over 200 phytochemicals were detected and subjected to structural characterization, offering valuable insights into the phytochemical composition of *Erythroxylum* plants. Noticeably, Hygroline and Ecgnonine alkaloids appear to be confined to the *Erythroxylum*.

Alkaloids, identified as prominent constituents of *Erythroxylum* species, are known for their significant cytotoxicity, making them promising candidates as potent anticancer agents. Other pharmacological actions of the plants, their extracts, and isolated compounds include antihypertensive, antioxidant, anti-inflammatory, antihepatotoxic, and antivenom activities. However, existing pharmacological activities were insufficient to establish a link between clinical applications and mechanisms of action. Therefore, future research on the pharmacological mechanism and structure-activity relationships of secondary metabolites obtained from the *Erythroxylum* species must be expanded. Furthermore, the quality control of *Erythroxylum* species has received little attention. Hence, well-developed analytical techniques are required to ensure consistency, safety, and efficacy.

In conclusion, this review article offers a comprehensive analysis of the anatomical, ethnobotanical, phytochemical, and pharmacological findings regarding the *Erythroxylum* genus. This overview can serve as an initial reference for researchers interested in the medicinal potential of genus *Erythroxylum*, aiding in the exploration of new bioactive compounds and potential therapeutic uses.

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