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Erythrina Alkaloids: An Updated Review with Neurological Perspective

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ABSTRACT

Erythrina is a genus comprising several plant species that are distributed in tropical and subtropical regions. This genus is a source of many phytoconstituents, with alkaloids and flavonoids as the main bioactive components. *Erythrina* alkaloids are characterized by a unique nucleus. One hundred ninety-eight alkaloids were isolated from *Erythrina* plants till early 2023. Recently, an increase in the number of isolated dimeric alkaloids has been witnessed. *Erythrina* plants have been used in the management of different conditions such as oxidative stress and diseases like cancer, inflammation, viral diseases, malaria, and diabetes, with the alkaloids showing a good potential against certain neurological disorders like anxiety, epilepsy, and Alzheimer's disease. All data on *Erythrina* alkaloids were collected from Google Scholar, ScienceDirect, SCOPUS, and SciFinder. For compounds isolated from multiple *Erythrina* species, the plant source was traced only from 2008 till 2023. The reported anxiolytic, anti-convulsant, and anti-Alzheimer's activities of *Erythrina* plant metabolites were traced from 2002 till 2023.

Keywords: *Erythrina; alkaloid; dimeric; Alzheimer's; anxiolytic; anticonvulsant.*

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1. Introduction

Erythrina is a genus of tropical and subtropical plants characterized by its velvety red flowers. The origin of the word Erythrina is from the word "*erythros*" meaning red in Greek. This genus belongs to the family Fabaceae, and it comprises 110 to 130 species **[1]**. The genus is a source of many secondary metabolites such as stilbenes, sterols, triterpenoids, phenolics, and coumarins, with flavonoids and alkaloids representing the main active constituents **[2]**. Studies have shown that *Erythrina* extracts and their isolated compounds have promising antidiabetic **[3-5]**, cytotoxic **[6-8]**, anti-inflammatory **[9, 10]**, anti-malarial **[11-14]**, antiviral **[15, 16]**, and antioxidant activities **[17-20]**. Many neurological activities were reported for *Erythrina* plants, these activities were mainly attributed to their alkaloid content **[21-27]**.

Neurological diseases are complex interlinked disorders that have a significant prevalence in the world's population. Epilepsy is a long-term neurological disease that affects 50 million people worldwide. Anxiety is a common psychiatric comorbidity associated with epilepsy where the prevalence of anxiety as comorbidity is 20% **[28, 29]** as compared to its prevalence (3.6%) in the general population globally.

Epilepsy can be also associated with progressive neurodegenerative diseases like Alzheimer's disease which accounts for 6% of early-onset epilepsy cases and up to 10% of people older than 65 years of age **[30]**.

The complex and interlinking nature of these diseases represents an urge to find a holistic safe treatment that can address all these disorders with minimal side effects. Traditional medicinal plants have long been used in the management of neurological diseases **[31–33]**. Being relatively safe and widely available, medicinal plants offer a great alternative to conventional medicine, especially in low-income countries.

This work presents an updated review of the reported *Erythrina* alkaloids till early 2023 arranged in tabular form, the most recent review was published by (Fahmy et al, 2019) **[34]** reporting 143 alkaloids. Over the past years, more alkaloids were isolated from *Erythrina* plants. This review also discusses the reported anxiolytic, anti-convulsant, and anti-Alzheimer's activities of some *Erythrina* alkaloids.

2. Methods and Materials

Literature Survey Databases and Methodology

All data on *Erythrina* alkaloids were collected from Google Scholar, ScienceDirect, SCOPUS, and SciFinder. For compounds isolated from multiple *Erythrina* species, the plant source was traced from 2008 till 2023. The reported anxiolytic, anti-convulsant, and anti-Alzheimer's activities of *Erythrina* plant metabolites were traced from 2002 till 2023.

3. Results and Discussion

3.1. Phytochemistry of *Erythrina* Alkaloids

Erythrina alkaloids (**Table. 1**) are composed of a tetracyclic spiro amine nucleus characterized by a 6,5,6,6-membered indoloisoquinoline skeleton. The erythrinan nucleus (**Fig. 1**) is formed of four ring system (A to D), based on the structure of these rings, erythrinan alkaloids can be classified into aromatic and non-aromatic erythrinan alkaloids.

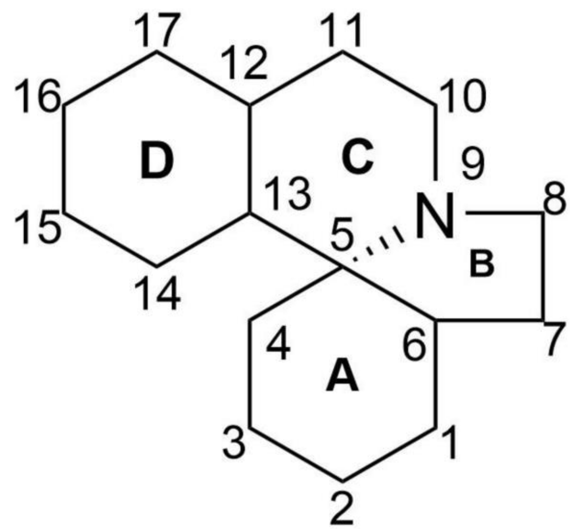


Fig. 1. The main nucleus of erythrinan alkaloids.

The former ones are characterized by the presence of an aromatic D-ring, and they represent most of *Erythrina* alkaloids, they are subclassified into dienoid (**Fig. 2-5**) and alkenoid alkaloids (**Fig. 6-8**). The majority of dienoid alkaloids are characterized by a conjugated diene system between C_1 and C_2 with C_6 and C_7, and a typical aromatic benzene D-ring which is substituted by an aza D-ring in erymelanthine (**74**) and melanacanthine (**75**) **[35]**. Some dienoid alkaloids display modifications in the conjugated diene system with the absence of one of the two double bonds between C_1 and C_7 (**Fig. 4**). Alkenoid alkaloids, on the other hand, are characterized by the presence of only a double bond in ring A between C_1 and C_6, however some alkenoid alkaloids display some modifications in their basic structure (**Fig. 8**). Non-aromatic erythrinan alkaloids are characterized by the absence of the aromatic D-ring which is substituted by an oxo D-ring like in lactonic alkaloids (**Fig. 9**).

Table.1 Reported alkaloids from genus *Erythrina*.

No.	Compound name	Plant part	Plant Source	Reference
I.	**Dienoid Alkaloids**			
(1)	Erysotramidine	Seeds	*E. crista-galli*	**[36]**
		Flowers	*E. herbacea*	**[37]**
		Seeds	*E. latissima*	**[38]**
(2)	10,11-Dioxoerysotramidine	Flowers	*E. latissima*	**[38]**
(3)	10-Hydroxyerysotramidine (Cristanines C)	Seeds	*E. crista-galli*	**[36]**
(4)	11*β*-Hydroxyerysotramidine	Flowers	*E. lysistemon*	**[39]**
		Leaves and stems	*E. stricta*	**[40]**
		Flowers	*E. arborescens*	**[41]**
		Flowers	*E. latissima*	**[38]**
(5)	11*β*-Methoxy-10-oxo erysotramidine	Flowers	*E. latissima*	**[38]**
(6)	11*α*-Methoxyerysotramidine	Leaves and stems	*E. stricta*	**[40]**
(7)	11*β*-Methoxyerysotramidine	Flowers	*E. lysistemon*	**[39]**
		Flowers	*E. latissima*	**[38]**
(8)	10*β*-Hydroxy-11*β*-methoxyerysotramidine	Barks	*E. stricta*	**[42]**
(9)	Erysotrine	Flowers	*E. corallodendron*	**[43]**
		Leaves and stems	*E. stricta*.	**[40]**
		Flowers	*E. arborescens*	**[41]**
		Seeds	*E. crista-galli*	**[15]**
		Seeds	*E. fusca*	**[44]**
		Bark and flowers	*E. verna*	**[21]**
		Fruits	*E. vespertilio*	**[45]**
		Seeds	*E. abyssinica*	**[46]**
		Flowers	*E. suberosa*	**[24]**
		Seeds	*E. falcata*	**[47]**
		Seeds	*E. addisoniae*	**[48]**
		Seeds	*E. velutina*	**[49]**
(10)	Eryalkal B	Roots	*E. corallodendron*	**[50]**
(11)	10,11-Dioxoerysotrine	Flowers	*E. arborescens*	**[41]**
		Seed pods	*E. latissima*	**[38]**
		Flowers	*E. herbacea*	**[37]**

No.	Compound name	Plant part	Plant Source	Reference
(12)	10-Hydroxy-11-oxoerysotrine	Flowers	*E. herbacea*	**[37]**
(13)	11*α*-Hydroxyerysotrine	Leaves and stems	*E. stricta*	**[40]**
		Stem bark	*E. suberosa*	**[51]**
		Flowers	*E. verna*	**[52]**
(14)	11*β*-Hydroxyerysotrine (erythrartine)	Leaves and stems	*E. stricta*	**[40]**
		Flowers	*E. herbacea*	**[37]**
		Flowers	*E. speciosa*	**[53]**
(15)	8α-Acetonylerysotrine	Barks	*E. stricta*	**[42]**
(16)	Erythrartine 11-*O*-*β*-D-glucose	Leaves	*E. arborescens*	**[54]**
(17)	10-Oxo-erythrartine 11-*O*-*β*-D-glucose			
(18)	Erysodine	Seeds	*E. crista-galli*	**[36,55]**
		Seeds	*E. abyssinica*	**[56]**
		Seeds	*E. fusca*	**[44]**
		Flowers	*E. suberosa*	**[24]**
		Seeds	*E. falcata*	**[47]**
		Seeds	*E. addisoniae*	**[48]**
		Seeds	*E. velutina*	**[49]**
(19)	11*α*-Hydroxyerysodine	Seeds	*E. lysistemon*	**[57]**
(20)	11*β*-Hydroxyerysodine	Flowers	*E. corallodendron* L.	**[43]**
(21)	11-Oxoerysodine		*E. senegalensis,* *E. excelsa,* *E. tabitensis* *E. arborescens* *E. caffra* *E. livingstoniana* *E. abyssinica*	**[58]**
(22)	11*β*-Hydroxyerysodine-glucose	Leaves	*E. crista-galli*, *E. falcata*	**[59]**
(23)	11-Methoxyerysodine	Seeds	*E. abyssinica*	**[56]**
(24)	8-Oxoerysodine		*E. tabitensis*	**[58]**
(25)	11*β*-Methoxyglucoerysodine	Leaves and stems	*E. stricta*	**[40]**
		Leaves	*E. falcata*	**[59]**
(26)	Glucoerysodine	Seeds	*E. addisoniae*	**[48]**
		Seeds	*E. velutina*	**[49]**
(27)	16-*O*-11*β*-*O*-Glucococcoline	Seeds	*E. velutina*	**[60]**
(28)	(3R)-16-*O*-*β*-D-Glucopyranosyl-10,11-dehydro-coccoline	Seeds	*E. velutina*	**[6]**
(29)	Rhamnoerysodine	Seeds	*E. lysistemon*	**[61]**
(30)	Erysoline	Seeds	*E. coralloides*	**[62]**

No.	Compound name	Plant part	Plant Source	Reference
(31)	Erysonine			**[62]**
(32)	Erysopine	Bark	*E. variegata* var. orientalis	**[63]**
		Seeds	*E. falcata*	
			E. addisoniae	**[47]**
		Seeds		
				[48]
(33)	11-Oxoerysopine		*E. tabitensis, E. arborescens*	**[58]**
(34)	11-Methoxyerysopine		*E. caffra*	**[58]**
(35)	Erysopine 15-*O*-sulfate	Seeds	*E. velutina*	**[64]**
(36)	15*β*-D-Glucoerysopine	Seeds	*E. latissima*	**[65]**
(37)	16*β*-D-Glucoerysopine	Leaves and stems	*E. stricta*	**[40]**
		Seeds	*E. crista-galli*	**[15]**
		Seeds	*E. latissimi*	**[65]**
(38)	Erysothiopine	Leaves	*E. crista-galli*	**[59]**
		Leaves	*E. falcata*	
(39)	Erysothiovine		*E. glauca, E. pallida, E. poeppigiana*	**[58]**
(40)	Erythravine	Flowers	*E. verna* (syn. *E. mulungu*)	**[52,66]**
(41)	11*α*-Hydroxyerythravine			
(42)	Erysovine	Seeds	*E. crista-galli*	**[67]**
		Bark	*E. verna*	**[68]**
		Bark	*E. varieigata var. orientalis*	**[69]**
(43)	11*β*-Hydroxyerysovine		*E. arobrescens, E. lysistemon, E. senegalensis*	
(44)	11 Oxoerysovine		*E. tabitensis , E. arborescens E. livingstoniana*	**[58]**
(45)	11*β*-Methoxyerysovine		*E. lysistemon , E. abyssinica*	
(46)	Sodium erysovine 15-O-sulfate	Seeds	*E. velutina*	**[64]**
(47)	11*β*-Methoxyglucoerysovine	Fruits	*E. vespertillo*	**[45]**
(48)	Erythristemine	Flowers	*E. corallodendron* L.	**[43]**
		Leaves and stems	*E. stricta*	**[40]**
		Leaves	*E crista-galli and E. falcata*	**[70]**
(49)	8*α*-Acetonyl erythristemine	Barks	*E. stricta*	**[42]**
(50)	Erythromotidienone	Flowers	*E. varieigata*	**[71]**
(51)	Erythrabine	Flowers	*E. corallodendron*	**[43]**
		Seeds	*E. fusca*	**[67]**
		Flowers	*E. arborescens*	**[41]**
		Flowers	*E. lysistemon*	**[57]**
		Seeds	*E. crista-galli*	**[44]**
(52)	Erytharborine H	Flowers		**[41]**

No.	Compound name	Plant part	Plant Source	Reference
(53)	Erytharborine A		*E. arborescens*	**[41]**
(54)	10,11-Dioxoerythraline	Flowers	*E. corallodendron* L.	**[43]**
(55)	8-Oxoerythraline	Flowers	*E. corallodendron* L.	**[43]**
		Leaves and stems	*E. stricta*	**[40]**
		Seeds	*E. crista-galli*	**[67]**
		Flowers	*E. arborescens*	**[41]**
		Bark	*E. verna*	**[68]**
		Seeds	*E. abyssinica*	**[46]**
(56)	8-Oxoerythrinine	Flowers	*E. corallodendron*	**[43]**
		Flowers	*E. arborescens*	**[41]**
		Bark	*E. crista-galli*	**[72]**
		Roots	*E. stricta*	**[73]**
(57)	10-Oxoerythrinine	Flowers	*E. corallodendron* L.	**[43]**
(58)	Erythrbidin B	Flowers	*E. ×bidwillii*	**[74]**
(59)	Erythraline	Flowers	*E. corallodendron*	**[43]**
		Bark	*E. brucei*	**[75]**
		Flowers	*E. addisoniae.*	**[41]**
		Bark	*E. verna*	**[68]**
		Bark	*E. crista-galli*	**[76]**
		Seeds	*E. abyssinica*	**[77]**
(60)	Eryalkal C	Roots	*E. corallodendron* L.	**[50]**
(61)	11-Oxoerythraline		*E. zeheri*	**[58]**
(62)	11 *β* Methoxy Erythraline	Flowers and seeds	*E. cafftra*	**[26]**
			E. vespertillo	**[58]**
(63)	8-Oxo-11 *β* methoxy erythraline	Flowers and seeds	*E. cafftra*	**[26]**
		Seeds	*E. lysistemon*	**[78]**
(64)	Erythraline-11*β*-*O*-glucopyranoside	Leaves	*E. arborescens*	**[54]**
		Seeds	*E. crista-galli*	**[15]**
(65)	10-Oxo-erythraline-11-*O*-*β*-D-glucose	Leaves	*E. arborescens*	**[54]**
(66)	Erythrinine	Flowers	*E. corallodendron*	**[43]**
		Stems and leaves	*E. stricta*	**[40]**
		Flowers	*E. arborescens*	**[41]**
		Bark	*E. verna*	**[68]**
		Bark	*E. crista-galli*	**[72]**
(67)	Erythrosotidienone	Flowers	*E. varieigata*	**[71]**

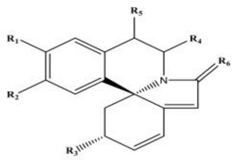
No.	Compound name	Plant part	Plant Source	Reference
(68)	Erytharborine B	Flowers	*E. arborescens*	**[41]**
(69)	Crystamidine	Seeds	*E. crista-galli*	**[67]**
		Bark	*E. crista-galli*	**[72]**
		Bark	*E. verna*	**[68]**
(70)	Erysodinophorine hydroxide		*E. arborescens*	**[58]**
(71)	Erysopinophorine hydroxide			
(72)	Erysophorine Chloride			
(73)	Isoerysopinophorine hydroxide			
(74)	Erymelanthine	Seeds	*E. Velutina*	**[100]**
		Seeds	*E. Melanacantha*	**[101]**
(75)	Melanacanthine	Seeds	*E. Melanacantha*	**[101]**
II.	**Dienoid Alkaloids with Modified Structure**			
(76)	8-Oxo-erythraline epoxide	Bark	*E. verna*	**[68]**
		Flowers	*E. ×bidwillii*	**[79]**
(77)	Erytharborine J	Stems	*E. corallodendron* L.	**[80]**
(78)	Erytharborine E	Flowers	*E. arborescens*	**[41]**
(79)	Erytharborine I	Stems	*E. corallodendron* L.	**[81]**
(80)	Cristanine F	Stems	*E. corallodendron* L.	**[81]**
III.	***N*-Oxide Dienoid Alkaloids**			
(81)	11α-Hydroxyerysotrine *N*-oxide	Flowers	*E. lysistemon*	**[39,57]**
(82)	11*β*-Hydroxyerysotrine *N*-oxide (erythrartine *N*-oxide)	Leaves and stems	*E. stricta*	**[40]**
		Flowers	*E. lysistemon*	**[39,57]**
		Flowers	*E. arborescens*	**[41]**
(83)	11*β*-Methoxyerysotrine *N*-oxide (erythristemine *N*-oxide)	Leaves and stems	*E. stricta*	**[40]**
		Flowers	*E. lysistemon*	**[57]**
(84)	Erysodine *N*-oxide	Seeds	*E. velutina*	**[49]**
(85)	Erysotrine *N*-oxide	Flowers	*E. mulungu*	**[82]**
		Leaves and stems	*E. stricta*	**[40]**
		Seeds	*E. crista-galli*	**[67]**
		Seeds	*E. fusca*	**[44]**
		Flowers	*E. herbacea*	**[37]**
		Flowers	*E. lysistemon*	**[57]**
(86)	(3R)-16-*O*-*β*-D-Glucopyranosyl erysodine *N*-oxide	Seeds	*E. velutina*	**[6]**
(87)	Erysovine *N*-oxide	Seeds	*E. addisoniae*	**[48]**
(88)	Sodium erysovine *N*-oxy-15-*O*-sulfate	Seeds	*E. velutina*	**[64]**

No.	Compound name	Plant part	Plant Source	Reference
(89)	Cristanine A	Bark	*E. brucei*	**[75]**
		Flowers	*E. arborescens*	**[41]**
		Bark	*E. crista-galli*	**[72]**
(90)	Erythrinine *N*-oxide-11-*O*-*β*-D-glucose	Leaves	*E. arborescens*	**[54]**
(91)	Erythrinine *N*-oxide	Flowers	*E. corallodendron* L.	**[43]**
IV.	**Alkenoid alkaloids**			
(92)	10,11-Dioxoepierythratidine	Bark	*E. subumbrans*	**[85]**
(93)	10,11-Dioxoerythratidinone			
(94)	11-Hydroxyerysotinone-rhamnoside	Leaves	*E. crista-galli* and *E. falcata*	**[59]**
(95)	11-Hydroxyerythratidinone	Bark	*E. verna*	**[69]**
(96)	*epi*-Erythratidine	Flowers	*E. corallodendron* L.	**[43]**
		Seeds	*E. fusca*	**[44,86]**
		Bark	*E. crista-galli*	**[72]**
(97)	11-Hydroxyepierythratidine		*E. variegate*, *E. poepgigiana*, *E. subumrans*	**[58]**
(98)	*epi*-Erythraditinone	Bark	*E. verna*	**[69]**
(99)	Erysosalvine		*E. sulciiflora* *E. salviiflora,* *E. latissimi* *E. arborescens* *E. livingstoniana,* *E. tahitensis ,* *E. burana ,* *E. salviiflora,* *E. oliviae* *E. melanacantha*	**[58]**
(100)	Erysosalvinone	Seeds	*E. addisoniae*	**[48]**
(101)	11-Hydroxyerysosalvinone		*E. berteroana*	**[58]**
(102)	Erysopitine	Bark	*E. variegata*	**[58]**
(103)	Erysotine	Flowers Leaves	*E. corallodendron* L. *E. americana*	**[87]**
(104)	Erysotinone		*E. salviflora*	**[88]**
(105)	11-Hydroxyerysotinone		*E. macrophylla*	**[58]**
(106)	Erysoflorinone		*E. salviflora, E. subumbrans*	**[58]**
(107)	11-Hydroxyerysotine		*E. berteroana*	**[58]**
(108)	Erythratidine	Bark	*E. crista-galli*	**[72]**
		Seeds	*E. crista-galli*	**[36]**
		Bark	*E. verna*	**[69]**
(109)	11-Hydroxyerythratidine	Flowers	*E. corallodendron* L.	**[43]**
(110)	11-Methoxyerythratidine	Leaves and stems	*E. stricta*	**[40]**
(111)	Erythratidinone	Flowers	*E. arborescens*	**[69,89]**
		Bark	*E. verna*	**[69,89]**

No.	Compound name	Plant part	Plant Source	Reference
(112)	10,11-Dioxoerythratine	Bark	*E. subumbrans*	**[85]**
(113)	10-Hydroxy-erythratine (Cristanines D)	Bark	*E. crista-galli*	**[67]**
(114)	11-Hydroxyerythratine	Flowers	*E. corallodendron* L.	**[43]**
(115)	11-Methoxyerythratine	Flowers	*E. crista-galli*	**[90]**
(116)	Erythramine		*E. variegate*	**[91]**
(117)	Erythratine	Flowers	*E. corallodendron* L.	**[43]**
		Leaves and stems	*E. stricta*	**[40]**
		Flowers	*E. arborescens*	**[41]**
		Bark and seeds	*E. crista-galli*	**[15,67,72]**
(118)	Epierythratine		*E. subumbrans*	
(119)	11-Hydroxyepierythratine			**[58]**
(120)	Erythratinone		*E. glauca, E. crista galli, E. variegata*	
(121)	Cristanine A	Bark	*E. crista-galli*	**[72]**
(122)	Eryalkal A	Roots	*E. corralodendron* L	**[50]**
(123)	Cristanine G	Stems	*E. corallodendron* L.	**[80]**
(124)	Erythaborine F			
(125)	Erythaborine C	Flowers	*E. arborescens*	**[41]**
(126)	Erythaborine D			
(127)	Cristanine H	Stems	*E. corallodendron* L.	**[80]**
(128)	Erythratidine *N*-oxide (cristanine E)	Seeds	*E. crista-galli*	**[67]**
(129)	11*β*-Hydroxyerythratidine *N*-oxide	Leaves and stems	*E. stricta*	**[40]**
(130)	3-Demethoxyerythratidinone		*E. variegate*	**[94]**
(131)	Erythaborine G	Flowers	*E. arborescens*	**[41]**
V.	**Alkenoid alkaloids with Modified Structure**			
(132)	Erysodienone	Bark	*E. variegate*	**[92]**
(133)	Erythritol	Flowers	*E. variegata*	**[93]**
(134)	Erythrivarine Z	Bark	*E. variegata L*	**[95]**
VI.	**Lactonic Alkaloids**			
(135)	*α*-Erythroidine			
(136)	8-Oxo-*α*-erythroidine		*E. poeppigiana*	
(137)	*β*-Erythroidine	Bark		**[83]**
(138)	8-Oxo-*β*-erythroidine			
(139)	8-Oxo-*α*-erythroidine epioxide	Wood	*E. poeppigiana*	**[84]**

No.	Compound name	Plant part	Plant Source	Reference
VII.	**Dimeric and Trimeric alkaloids**			
(140)	Erythrivarine A			**[96]**
(141)	Erythrivarine A1			
(142)	Erythrivarine A2			
(143)	Erythrivarine A3			
(144)	Erythrivarine A4			
(145)	Erythrivarine A5			
(146)	Erythrivarine A6			**[97]**
(147)	Erythrivarine A7	Flowers	*E. variegate*	
(148)	Erythrivarine A8			
(149)	Erythrivarine A9			
(150)	Erythrivarine A10			
(151)	Erythrivarine A11			
(152)	Erythrivarine A12			
(153)	Erythrivarine A13			**[96]**
(154)	Erythrivarine B			
(155)	Erythrivarine C			
(156)	Erythrivarine D			
(157)	Erythrivarine E	Flowers		**[98]**
(158)	Erythrivarine F		*E. variegate*	
(159)	Erythrivarine G			
(160)	Erythrivarine H			
(161)	Erythrivarine I	Leaves	*E. arobscence*	**[54]**
(162)	Erythrivarine J			
(163)	Erythrivarine K			
(164)	Erythrivarine L	Barks	*E. variegata* L	**[99]**
(165)	Erythrivarine M			
(166)	Erythrivarine N			
(167)	Erythrivarine O			
(168)	Erythrivarine P			
(169)	Erythrivarine Q			
(170)	Erythrivarine R			
(171)	Erythrivarine S	Barks	*E. variegata* L	**[95]**
(172)	Erythrivarine T			
(173)	Erythrivarine U			
(174)	Erythrivarine V			

No.	Compound name	Plant part	Plant Source	Reference
(175)	Erythrivarine W			
(176)	Erythrivarine X			
VIII.	**Other classes of alkaloids**			
(177)	Erythrivarine Y	Barks	*E. variegata* L	[95]
(178)	Erybidine	Leaves	*E. × bidwillii*	[102]
(179)	Erythrinarbine	Leaves and stems	*E. stricta*	[40]
		Stems	*E. arobscence*	[103]
(180)	Stachydrine	Leaves	*E. Variegate*	[104]
(181)	Cristadine			
(182)	Protosinomenine			
(183)	*N*-nor protosinomenine	Leaves	*E. Crista galli*	[105]
(184)	Orientaline			
(185)	*N*-nor Orientaline	Leaves	*E. Speciosa*	[106]
(186)	Reticuline	Flowers	*E. corallodendron* L.	[43]
(187)	Nor-reticuline	Leaves and stems	*E. stricta*	[40]
(188)	Norisoorientaline	Flowers	*E. corallodendron* L.	[43]
(189)	Abrine	Bark	*E. caffra*	[107]
(190)	Hypaphorine	Flowers	*E. corallodendron* L.	[43]
		Leaves and stems	*E. stricta*	[40]
		Flowers	*E. mulungu*	[82]
		Seeds	*E. crista-galli*	[15]
		Fruits	*E. vespertilio*	[45]
		Barks	*E. crista-galli*	[72]
		Barks	*E. caffra*	[107]
		Seeds	*E. velutina*	[100,108]
(191)	Hypaphorine methyl ester	Bark, leaves & seeds	*E. variegate*	[109]
(192)	*N*,*N*-Dimethyltryptophan methyl ester			
(193)	1H-Indole-3-propanamide	Seeds	*E. addisonae*	[110]
(194)	*S*-1-(4-Hydroxy-3-methoxyphenethyl)-5-hydroxypyrrolidin-2-one	Barks	*E. stricta*	[42]
(195)	*N*-(3-Hydroxy-4-methoxyphenethyl)-4-hydroxylbutanamide			
(196)	Isoboldine		*E. abyssinica*	[105]
			E. poeppigiana	
(197)	Scoulerine		*E. orientalis*	[111]
(198)	Coreximine			



	R_1	R_2	R_3	R_4	R_5	R_6
1.	OCH_3	OCH_3	OCH_3	H	H	O
2.	OCH_3	OCH_3	OCH_3	=O	=O	O
3.	OCH_3	OCH_3	OCH_3	OH	H	O
4.	OCH_3	OCH_3	OCH_3	H	β-OH	O
5.	OCH_3	OCH_3	OCH_3	=O	β-OCH3	O
6.	OCH_3	OCH_3	OCH_3	=O	α-OCH3	O
7.	OCH_3	OCH_3	OCH_3	H	β-OCH3	O
8.	OCH_3	OCH_3	OCH_3	β-OH	β- OCH3	O
9.	OCH_3	OCH_3	OCH_3	H	H	H
10.	OCH_3	OCH_3	OCH_3	H	H	CH_2COOH
11.	OCH_3	OCH_3	OCH_3	=O	=O	H
12.	OCH_3	OCH_3	OCH_3	OH	=O	H
13.	OCH_3	OCH_3	OCH_3	H	α-OH	H
14.	OCH_3	OCH_3	OCH_3	H	β-OH	H
15.	OCH_3	OCH_3	OCH_3	H	H	CH_2COCH_3
16.	OCH_3	OCH_3	OCH_3	H	β-Glu	H
17.	OCH_3	OCH_3	OCH_3	=O	β-Glu	H
18.	OH	OCH_3	OCH_3	H	H	H
19.	OH	OCH_3	OCH_3	H	α-OH	H
20.	OH	OCH_3	OCH_3	H	β-OH	H
21.	OH	OCH_3	OCH_3	H	=O	H
22.	O-Glu	OCH_3	OCH_3	H	β-OH	H
23.	OH	OCH_3	OCH_3	H	OCH_3	H
24.	OH	OCH_3	OCH_3	H	H	O
25.	O-Glu	OCH_3	OCH_3	H	β- OCH_3	H
26.	O-Glu	OCH_3	OCH_3	H	H	H
27.	O-Glu	OCH_3	OCH_3	H	H	O
28.	O-Glu	OCH_3	OCH_3	10,11-Double Bond		O
29.	O-Rham	OCH_3	OCH_3	H	H	H
30.	OCH_3	OH	OH	H	H	H
31.	OH	OCH_3	OH	H	H	H
32.	OH	OH	OCH_3	H	H	H
33.	OH	OH	OCH_3	H	=O	H
34.	OH	OH	OCH_3	H	OCH3	H
35.	OH	SO_3H	OCH_3	H	H	H
36.	OH	O-β-D-Glu	OCH_3	H	H	H
37.	O-β-D-Glu	OH	OCH_3	H	H	H
38.	SO_3CH_2COOH	OH	OCH_3	H	H	H
39.	OCH_3	SO_3CH_2COOH	OCH_3	H	H	H
40.	OCH_3	OCH_3	OH	H	H	H
41.	OCH_3	OCH_3	OH	H	α-OH	H
42.	OCH_3	OH	OCH_3	H	H	H
43.	OCH_3	OH	OCH_3	H	β-OH	H
44.	OCH_3	OH	OCH_3	H	=O	H
45.	OCH_3	OH	OCH_3	H	β-OCH3	H
46.	OCH_3	SO_3Na	OCH_3	H	H	H
47.	OCH_3	O-glu	OCH_3	H	β-OCH3	H
48.	OCH_3	OCH_3	OCH_3	H	β-OCH_3	H
49.	OCH_3	OCH_3	OCH_3	H	OCH_3	CH_2COCH_3
50.	H	OCH_3	H_2	H	H	=O
51.	OCH_3	OCH_3	OCH_3	10,11-Double Bond		=O
52.	OCH_3	OCH_3	OCH_3	=O	OH	H
53.	OCH_3	OCH_3	OCH_3	-N(C(CH₃)₂) N-		H
54.	-OCH_2O-		OCH_3	=O	=O	H
55.	-OCH_2O-		OCH_3	H	H	O
56.	-OCH_2O-		OCH_3	H	OH	O
57.	-OCH_2O-		OCH_3	=O	OH	H
58.	-OCH_2O-		OCH_3	OH	=O	O
59.	-OCH_2O-		OCH_3	H	H	H
60.	-OCH_2O-		OCH_3	H	H	CH_2COOH
61.	-OCH_2O-		OCH_3	H	=O	H
62.	-OCH_2O-		OCH_3	H	OCH_3	H
63.	-OCH_2O-		OCH_3	H	OCH_3	O
64.	-OCH_2O-		OCH_3	H	O-Glu	H
65.	-OCH_2O-		OCH_3	=O	O-Glu	H
66.	-OCH_2O-		OCH_3	H	OH	H
67.	-OCH_2O-		H_2	H	H	O
68.	-OCH_2O-		OCH_3	-N(C(CH₃)₂) N-		H
69.	-OCH_2O-		OCH_3	10,11-Double Bond		O
70.	X	OCH_3	OCH_3	H	H	H
71.	X	OH	OCH_3	H	H	H
72.	OCH_3	Y	OCH_3	H	H	H
73.	OH	X	OCH_3	H	H	H

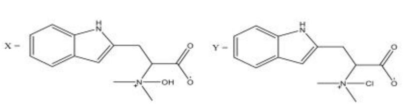
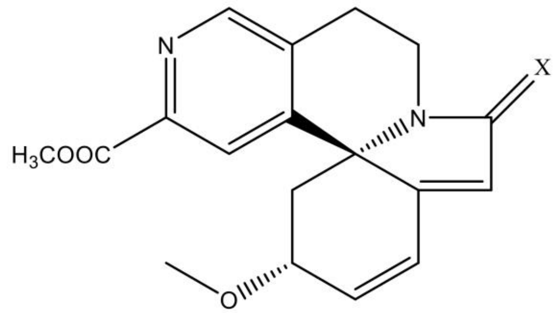


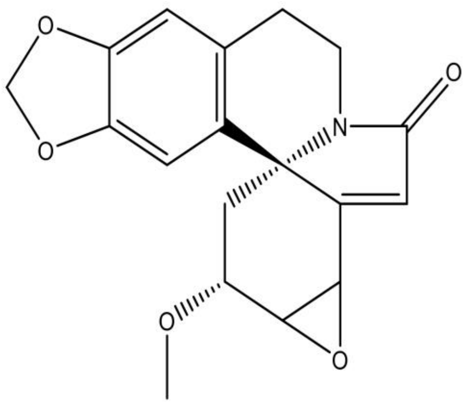
Fig. 2. Dienoid erythrinan alkaloids with benzene ring D (1-73)



(74) X= H
(75) X= O

Fig. 3. Dienoid erythrinan alkaloids with Aza ring D (74-75)

About 198 alkaloids were reported from different *Erythrina* sp. including ninety-one dienoid alkaloids **1-91**, forty-three alkenoid alkaloids **92-134**, thirty-four dimeric **140-156, 160-176,** and three trimeric **157-159** erythrinan alkaloids (**Fig. 10 &11**), five lactonic erythrinan alkaloids **135-139**, and one homoerythrinan alkaloid **177**, in addition to several alkaloids from different classes (**Fig. 12**). When compared to the most recent review by (Fahmy et al, 2019) **[34]**, the last years have witnessed an increase in the number of isolated dimeric alkaloids, where thirty new dimeric alkaloids **141-153**, **160-176** were isolated from the late 2019 till early 2023, in addition to seven dienoid alkaloids **8, 10, 49, 60, 77, 79, 80**, six dienoid alkaloid glycosides **16, 17, 28, 65, 86, 90**, four alkenoid alkaloids **122, 123, 127, 134** and one homoerythrinan alkaloid **177.**



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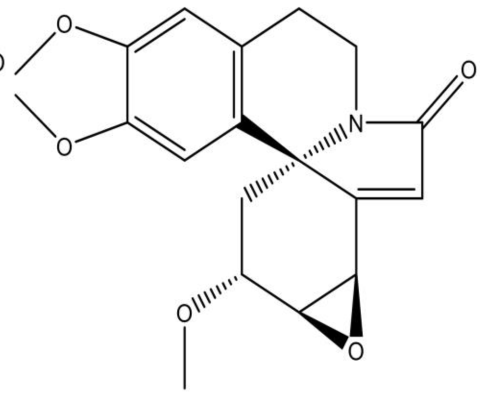

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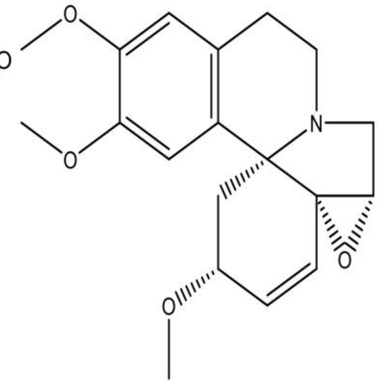

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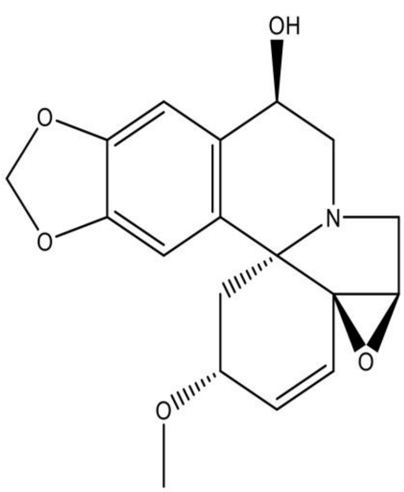

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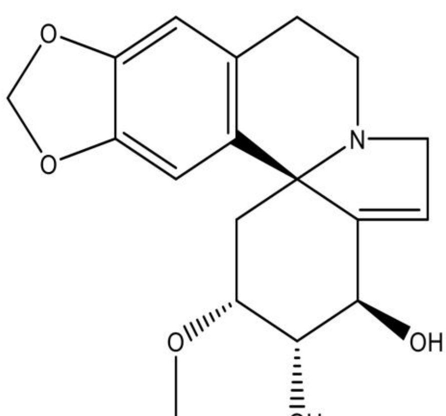
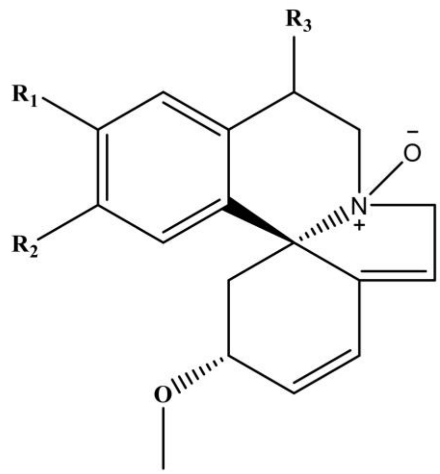


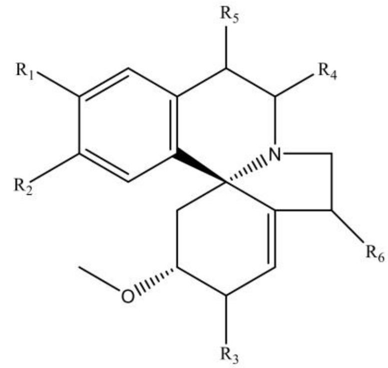
(80)

Fig. 4. Dienoid erythrinan alkaloids with modified structure (76-80)



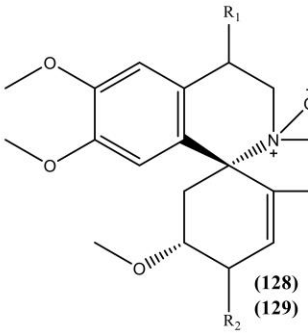
	R_1	R_2	R_3
81.	OCH_3	OCH_3	α-OH
82.	OCH_3	OCH_3	β -OH
83.	OCH_3	OCH_3	β -OCH_3
84.	OH	OCH_3	H
85.	OCH_3	OCH_3	H
86.	O-Glu	OCH_3	H
87.	OCH_3	OH	H
88.	OCH_3	OSO_3Na	H
89.	-OCH_2O-		H
90.	-OCH_2O-		O-β-Glu
91.	-OCH_2O-		OH

Fig. 5. Dienoid erythrinan *N*-oxide alkaloids (81-91)

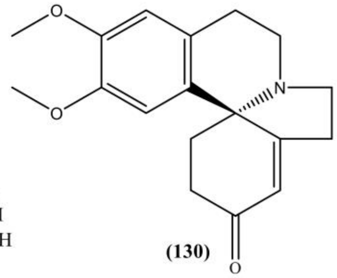


	R_1	R_2	R_3	R_4	R_5	R_6
92.	OCH_3	OCH_3	β-OH	=O	=O	H
93.	OCH_3	OCH_3	=O	=O	=O	H
94.	O-Rham	OCH_3	=O	H	OH	H
95.	OCH_3	OCH_3	=O	H	OH	H
96.	OCH_3	OCH_3	β-OH	H	H	H
97.	OCH_3	OCH_3	β-OH	H	OH	H
98.	OCH_3	OCH_3	=O	H	H	H
99.	OCH_3	OH	OH	H	H	H
100.	OCH_3	OH	=O	H	H	H
101.	OCH_3	OH	=O	H	OH	H
102.	OH	OH	OH	H	H	H
103.	OH	OCH_3	β-OH	H	H	H
104.	OH	OCH_3	=O	H	H	H
105.	OH	OCH_3	=O	H	OH	H
106.	OH	OH	=O	H	H	H
107.	OH	OCH_3	β-OH	H	OH	H
108.	OCH_3	OCH_3	α-OH	H	H	H
109.	OCH_3	OCH_3	α-OH	H	OH	H
110.	OCH_3	OCH_3	α-OH	H	OCH_3	H
111.	OCH_3	OCH_3	=O	H	H	H
112.	-OCH_2O-		β-OH	=O	=O	H
113.	-OCH_2O-		β-OH	β-OH	H	H
114.	-OCH_2O-		β-OH	H	OH	H
115.	-OCH_2O-		β-OH	H	OCH_3	H
116.	-OCH_2O-		H_2	H	H	H
117.	-OCH_2O-		β-OH	H	H	H
118.	-OCH_2O-		α-OH	H	H	H
119.	-OCH_2O-		α-OH	H	OH	H
120.	-OCH_2O-		=O	H	H	H
121.	-OCH_2O-		β-OH	H	H	α-OH
122.	-OCH_2O-		α -OH	H	H	α-OH
123.	-OCH_2O-		α -OH	H	H	β-OH
124.	OCH_3	OCH_3	β-OH	=O	=O	β-OH
125.	OCH_3	OCH_3	NHOH	H	H	$CHCl_2$
126.	OCH_3	OCH_3	H_2	H	H	$CHCl_2$
127.	OCH_3	OCH_3	α -OH	H	H	α-OH

Fig. 6. Alkenoid erythrinan alkaloids (92-127)



	R_1	R_2
(128)	H	β-OH
(129)	β-OH	α-OH



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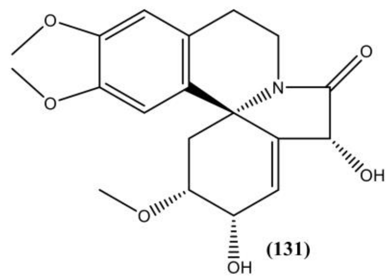
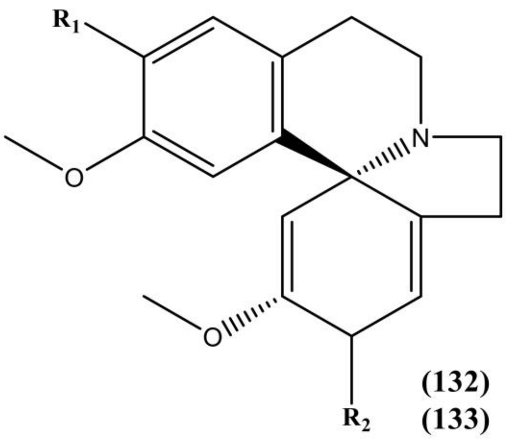
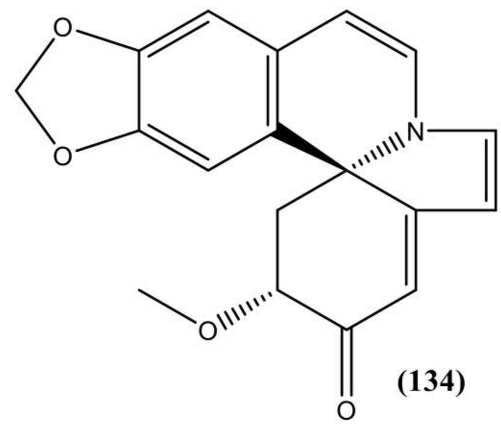


(131)

Fig. 7. Alkenoid erythrinan alkaloids (128-131)

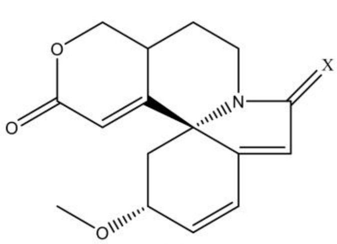


	R_1	R_2
(132)	OH	=O
(133)	OCH_3	OH

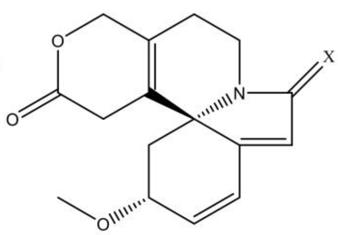


(134)

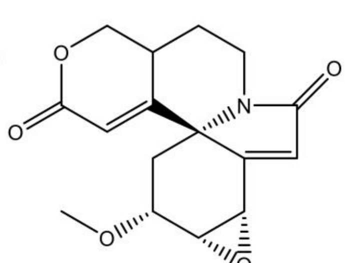
Fig. 8. Alkenoid erythrinan alkaloids with modified structure (132-134)



(135) X= H
(136) X= O



(137) X= H
(138) X= O



(139)

Fig. 9. Lactonic erythrinan alkaloids (135-139).

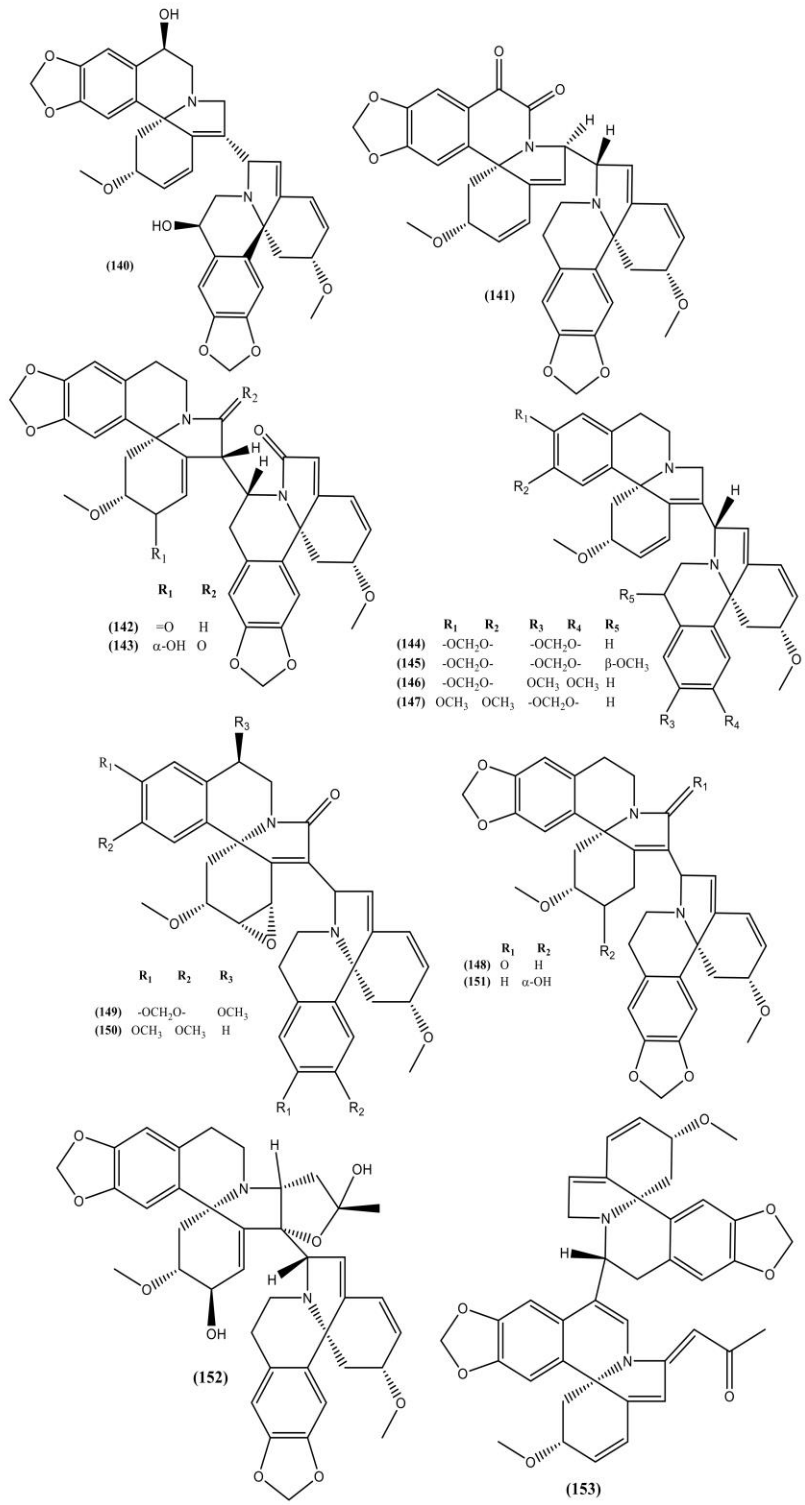


Fig. 10. Dimeric erythrinan alkaloids (140-153)

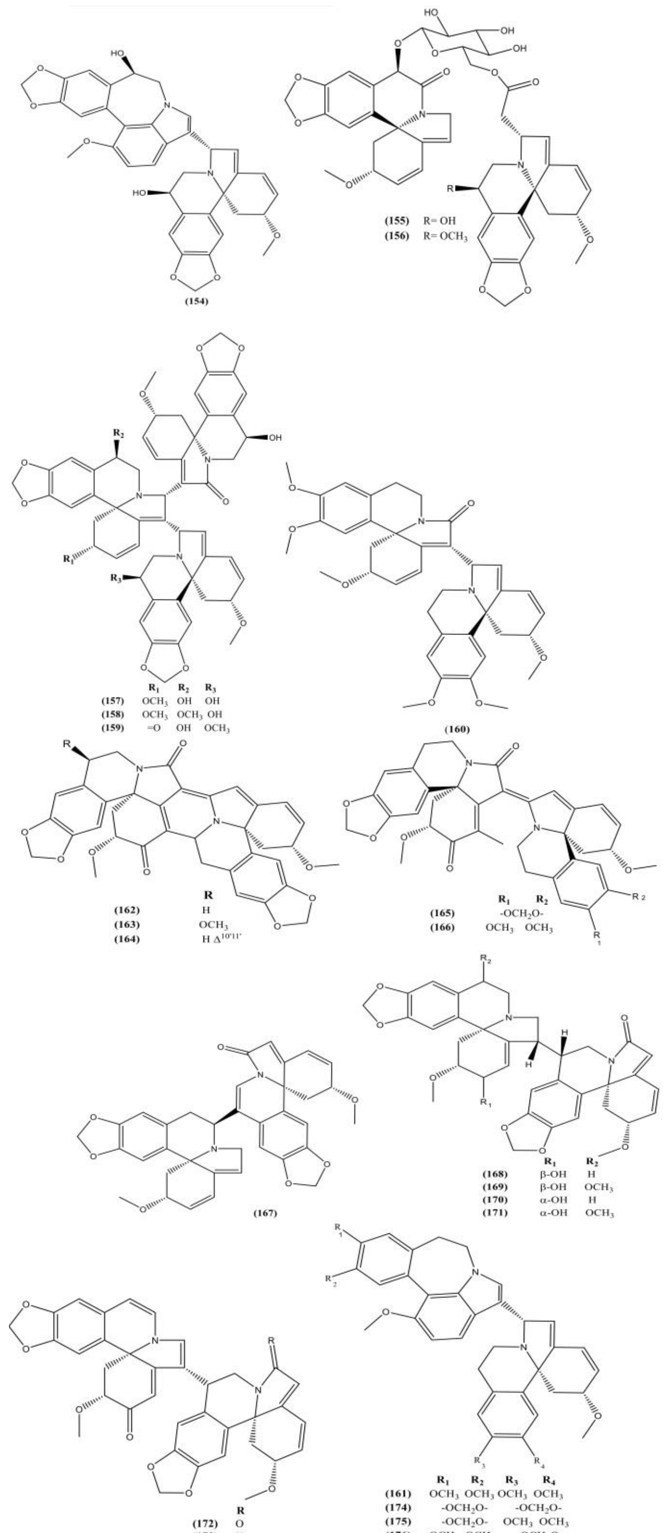


Fig. 11. Dimeric (154-156, 160-176) and trimeric erythrinan alkaloids (157-159)

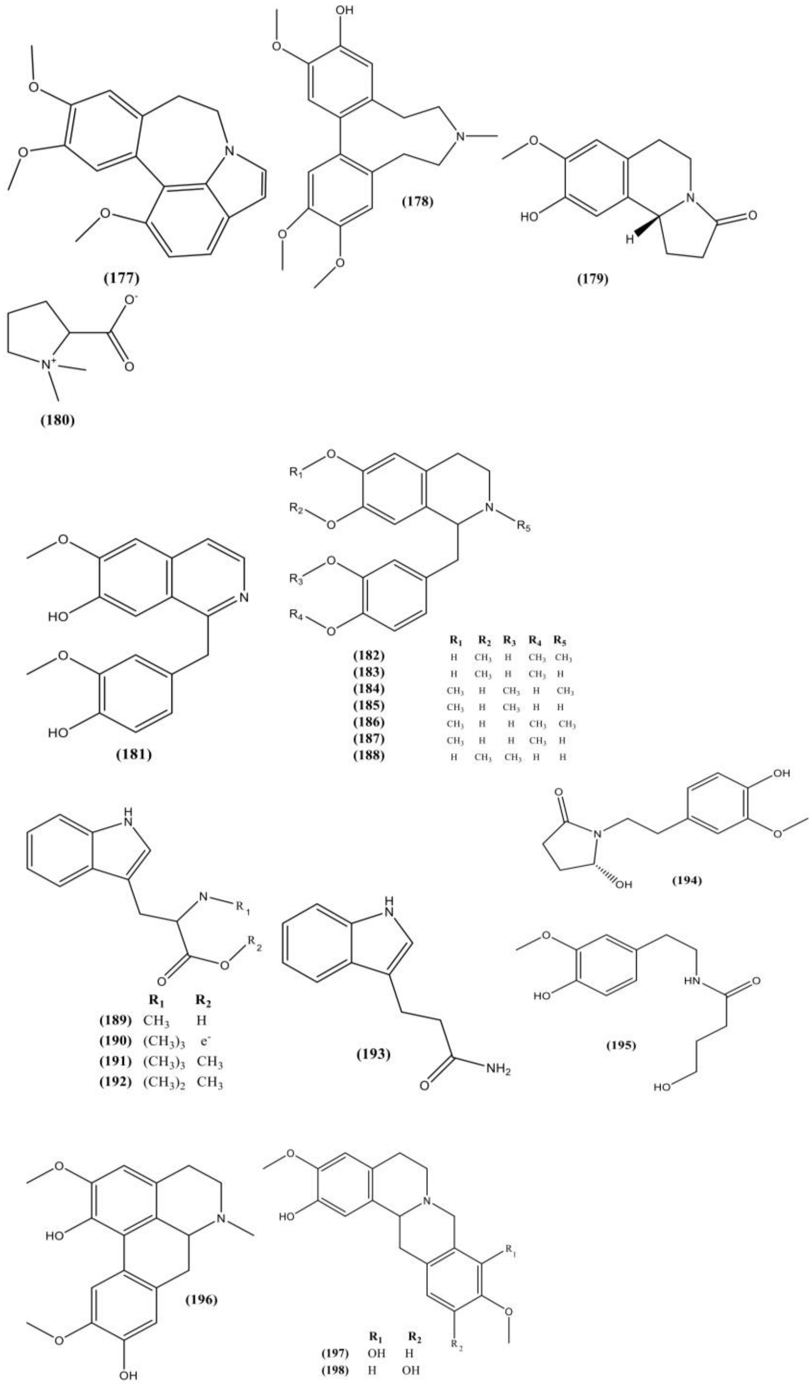


Fig. 12. Other reported classes of alkaloids from genus *Erythrina*. (177-198)

3.2 Neurological Activities of *Erythrina* Alkaloids

Despite the large number of isolated *Erythrina* alkaloids reaching 198 alkaloids to date, only a few studies evaluated the neurological activities of the pure isolated *Erythrina* alkaloids (**Table. 2-4**). Among the reviewed studies, it was found that only nine alkaloids were evaluated namely: erysotrine **9** and its derivatives hydroxyerysotrine (in *α* **13** and *β* **14** forms) and erythravine **40** with its derivative hydroxyerthravine **41** which were evaluated for both anxiolytic and antiepileptic activity. As for erysodine **18**, it was evaluated for anxiolytic and anti-Alzheimer's activity. Erythraline **59**, erythrinine **66,** and crystalline A **89** were only evaluated for anti-Alzheimer's activity.

Table.2. Reported anxiolytic activities of previously isolated erythrinan alkaloids.

Compound name	Plant source	Assay results	Ref.
(+)-11R-Hydroxyerythravine **41**	Flowers of *E. mulumgu*	A dose of 10 mg/kg given orally decreased the latency period needed to leave the enclosed arm in Elevated T-maze (ETM) test.	**[112]**
(+)-Erythravine **40**		Doses of 3 and 10 mg/kg given orally decreased the latency period needed to leave the enclosed arm in ETM test.	
(+)11α -Hydroxyerysotrine **13**		Doses of 3 and 10 mg/kg given orally impaired the inhibitory avoidance task in the ETM test	
Erysotrine **9**	Flowers of *E. mulungu*	A dose of 0.5 μg/μL given through the intracerebroventricular (i.c.v) route increased the number of entries to the open arms in Elevated plus maze (EPM) test.	**[21]**
	Flowers of *E. suberosa*	A dose of 3 mg/kg given orally increased the number of transitions between the light and dark chambers and the time spent in the lightened chamber in the light/dark transition model (LDTM)	**[24]**
Erysodine **18**	Flowers of *E. suberosa*	A dose of 10 mg/kg given orally increased the percentage of open arm entries in the EPM test.	**[24]**

Table.3. Reported anticonvulsant activities of previously isolated erythrinan alkaloids.

Compound name	Plant species	Assay results	Ref.
11*β*-Hydroxyerysotrine (Erythrartine) **14**	Inflorescences of *E. verna*	Pretreatment with a 3 μg/μl dose via i.c.v route prevented picrotoxin or kainic acid, pilocarpine and pentylenetetrazol (PTZ) induced seizures in the rats by 100, 72 and 85%, respectively.	**[23]**
(+)-erythravine **40**	Flowers from *E. mulungu*	Pretreatment with 1, 2, and 3 μg/μL doses via i.c.v route prevented bicuculline-induced seizures in the rats by 40, 60, and 80%, respectively. Pretreatment with 2 or 3 μg/μL doses via i.c.v route inhibited kainic acid and PTZ-induced seizures in all treated rats. Pretreatment with 3 μg/μL dose via i.c.v route inhibited NMDA-induced seizures in the rats by 20%.	**[22]**
(+)-11-α-hydroxy erythravine **41**	Flowers from *E. mulungu*	Pretreatment with 0.5, 1, and 2 μg/μL doses via i.c.v route inhibited bicuculline-induced seizures in rats by 60, 100 and 100%, respectively. Pretreatment with 2 and 3 μg/μL doses via i.c.v route inhibited PTZ-induced seizures in rats by 40 and 60%, respectively. Pretreatment with 1 and 2 μg/μL doses via i.c.v route inhibited kainic acid – induced seizures in rats by 40 and 100%, respectively. Pretreatment with 0.5, 1 and 2 μg/μL doses via i.c.v route inhibited NMDA-induced seizures in the rats by 80, 100 and 100%, respectively.	**[22]**
Erysotrine **9**	Flowers from *E. mulungu*	Pretreatment with 2 and 3 μg/μL doses via i.c.v route inhibited bicuculline-induced seizures in rats by 20 and 100%, respectively. The same doses protected 40, 100 and 60, 100% of the rats against PTZ and NMDA-induced seizures respectively, while 0.25 and 0.5 μg/μL doses prevented kainic acid-induced seizures in 40 and 100% of the rats, respectively.	**[21]**

Table.4. Reported anti Alzheimer's activities of previously isolated erythrinan alkaloids.

Compound name	Plant species	Assay results	Ref.
Erythraline **59**	Seeds of *E. velutina*	Treatment with a concentration of 10 μmol increased the mean paralysis time of the $A\beta_{1\text{–}42}$ transgenic *Caenorhabditis elegans (C. elegans)* worms by 35.9% compared to the same concentration of memantine that caused 23.5% increase.	**[27]**
	Flowers of *E. caffra*	It inhibited acetylcholinesterase (AChE) activity with an IC_{50} value of 119.35 μg/ml	**[26]**
Erysodine **18**	Seeds of *E. velutina*	Treatment with a concentration of 10 μmol increased the mean paralysis time of the $A\beta_{1\text{–}42}$ transgenic *C. elegans* worms by 40.2% compared to the same concentration of memantine that caused 12.8% increase	**[27]**
Erythrinine **66**	Flowers of *E. caffra*	It inhibited AChE activity with an IC_{50} value of 714.6 μg/ml	**[26]**
Cristanine A **89**		It inhibited AChE activity with an IC_{50} value of 3246.4 μg/ml	**[26]**

Conclusion

Genus *Erythrina* is rich in alkaloids with a characteristic nucleus. Among *Erythrina* alkaloids reported between 2008 to 2023, erysotrine was the most reported from different *Erythrina* species. Over the past years, advances in structure elucidation techniques enabled the identification of more complex dimeric erythrinan alkaloids. Most studies focused on investigating the biological activities of *Erythrina* plant crude extracts and/or fractions rather than the isolated pure compounds. Based on the reported data, some of the investigated *Erythrina* alkaloids displayed promising anticonvulsant and anxiolytic activities in contrast to their weak anti-Alzheimer, more specifically anti-AChE, activities.

Recommendations

Future studies should focus on evaluating the activities of the isolated pure *Erythrina* compounds rather than the crude plant extracts and/or fractions as this enables other scientists to evaluate the possible mechanisms of action of these compounds and to identify specific pharmacophores.

Declarations

Ethics approval and consent to participate
Not applicable

Consent to publish
Not applicable

Availability of data and materials
All the data are provided within the manuscript file and the attached figures.

Competing interests
The authors declare that there were no competing interests.

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Authors' contributions

Data collection, analysis, and manuscript preparation were performed by Ahmed M. Salem, and designing the whole work and reviewing the written manuscript was performed by Abdel Nasser B. Singab, Eman Al-Sayed, and Nada M. Mostafa

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