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REVIEW

Aporphine Alkaloids: A Kind of Alkaloids' Extract Source, Chemical Constitution and Pharmacological Actions in Different Botany

JIANXIN CHEN†, KUO GAO†, TIEGANG LIU†, HUIHUI ZHAO, JUAN WANG, HAO WU, BING LIU and WEI WANG*

Beijing University of Chinese Medicine, 11 Bei San Huan Dong Lu, ChaoYang District, Beijing 100029, P.R. China

*Corresponding author: Fax: +86 10 64286283; Tel: +86 10 64286508; E-mail: wangwei@bucm.edu.cn
†These authors contributed equally to this work.

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As a kind of common compositions in plants, there are many researches about alkaloids, which was firstly found from *Nelumbo nucifera*. Now more and more aporphine alkaloids appear during the experiments, which belong to isoquinoline type. There are number of pesticide effects about them, which have been revealed in recent years. So comprehensive information about the locality, formation and pesticide effects have been studied and presented in this research in different botany about aporphine alkaloids.

Key Words: Alkaloids' extract, Chemical constitution, Pharmacological actions, Aporphine alkaloids, *Nelumbo nucifera*.

INTRODUCTION

Studies of the alkaloids of *Nelumbo nucifera* began in the 19th century. Since *Nelumbo nucifera* alkali (nuciferine), O-go the methyl nuciferine (O-nornuciferine) and Lin alkali (roemerine) had been found from *Nelumbo nucifera*, so far a number of alkaloid compounds have been isolated from *Nelumbo nucifera*. The *Nelumbo nucifera* alkaloids, based on the nucleus structure, are divided into three categories *i.e.*, single benzyl isoquinoline, aporphine and dehydrogenase aporphine.

Single benzyl isoquinoline *e.g.*, armepavine, N-methyliso-coclaurine, N-methylcoclaurine. Structures of compounds are shown in Fig. 1 and Table-1.

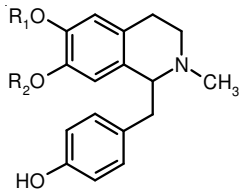

Fig. 1. Nucleus structures of single benzyl isoquinoline

TABLE-1
STRUCTURES OF SUBSTITUENT GROUPS IN SINGLE BENZYL ISOQUINOLINE

Compound	R_1	R_2	Name
Armepavine	CH_3	CH_3	Armepavine
N-Methylisococlaurine	H	CH_3	N-Methylisococlaurine
N-Methylcoclaurine	CH_3	H	N-Methylcoclaurine

Aporphine: Nuciferine, N-nornuciferine, O-nornuciferine, anonaine, roemerine, liriodenine, N-norarmepavine, 2-hydroxy-1-methoxyaporphine. Structures of compounds are shown in Figs. 2 and 3; Table-2.

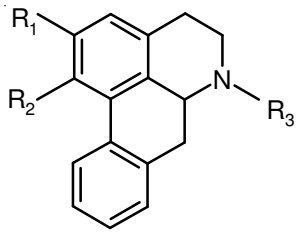

Fig. 2. Nucleus structures of aporphine

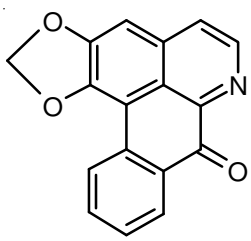

Fig. 3. Structures of liriodenine

Dehydrogenase aporphine: Dehydronuciferinene, dehydroroemerine. Structures of compounds are shown in Fig. 4 and Table-3.

TABLE-2
STRUCTURES OF SUBSTITUENT GROUPS IN APORPHINE

Compound	R_1	R_2	R_3	Name
Nuciferine	OCH_3	OCH_3	CH_3	Nuciferine
N-Nornuciferine	OCH_3	OCH_3	H	N-Nornuciferine
2-Hydroxy-1-methoxyaporphine	OH	OCH_3	CH_3	2-Hydroxy-1-methoxyaporphine
Roemerine	—O—CH_2—O—		CH_3	Roemerine
Anonaine	—O—CH_2—O—		H	Anonaine

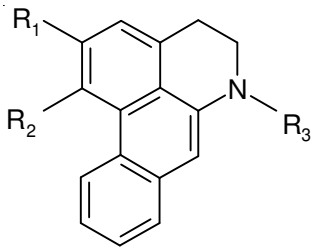

Fig. 4. Nucleus structures of dehydrogenase aporphin

TABLE-3
STRUCTURES OF SUBSTITUENT GROUPS
IN DEHYDROGENASE APORPHIN

Compound	R_1	R_2	R_3	Name
Dehydronuciferinene	OCH_3	OCH_3	CH_3	Dehydronuciferinene
Dehydroroemerine	–O–CH_2–O–		CH_3	Dehydroroemerine

Aporphine alkaloids belong to isoquinoline type alkaloid, including pronuciferine, nuciferine, N-nornuciferine, O-nornuciferine, liriodenine, roemerine, N-norarmepavine, 2-hydroxy-1-methoxyaporphine.

Many researches showed that the alkaloids from *Nelumbo nucifera* had lipid-lowering, weight-losing, antibacterial and antiviral functions. However, review and systemic analysis of distribution, structures and pharmacological activities of aporphine alkaloids have not been reported. The author prompted to provide the currently available information on traditional and local knowledge, ethno biological and ethno medicinal issues and pharmacological studies on these useful plants. The aim of the present review is to introduce aporphine alkaloids as medicinal drugs by highlighting its traditional applications as well as the recent findings for novel pharmacological and clinical applications.

Distribution of aporphine alkaloids in plants

Aporphine alkaloids belong to isoquinoline type alkaloid. The basic structure of which is shown in Fig. 5(A). There are substituent groups at the positions of C_1, C_2 in the native aporphine alkaloids simultaneously and at the same time, substitution reactions may take place at the positions of $C_{3,8,9,10,11}$.

Substituent groups mainly include –OH, –OCH_3,  .

The substituent groups at the position of nitrogen atom are –H, –CH_3, –$COOCH_3$, *etc*. This type of alkaloid mainly includes: alkaloid prototype (Fig. 5A), oxidized aporphine (Fig. 5B) and dehydro-aporphine (Fig. 5C).

Aporphine alkaloids broadly exist in nature and have obvious biological activity, with great content. Now hundreds of aporphine alkaloids have been isolated from more than 20 families and 100 genuses of plants.

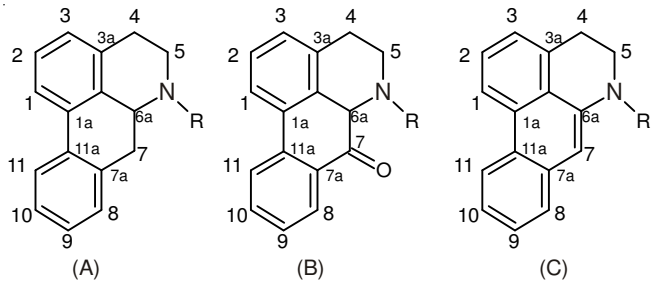

Fig. 5. Three basic structures of aporphine alkaloids

Distribution of aporphine alkaloids[1-61]

Annonaceae: Annonaceae, with original traits, belongs to Magnoliopsida and this so-called "living fossil" is born in American tropics, broadly distributing in tropics and subtropics. Data shows that aporphine alkaloids have the widest distribution in Annonaceae. Aporphine alkaloids have been isolated from 28 genuses of these plants *viz.*, Alphonsea, Anaxagorea, Annona, Artabotrys, Asimina, Cananga, Cheistophlis, Desmos, Duguetia, Enantia, Eupomatia, Fusea, Goniothalamus, Greenwayodendron, Guatteria, Hexalobus, Isolona, Meiocarpidium, Melodorum, Mitrella, Monanthotaxis, Monodora, Pachypodanthium, Polyalthia, Popowia, Pseuduvaria, Schefferomitra, Uvariopsis, Xylopia and Fissistigma.

Menispermaceae: There are about 70 genuses and more than 430 species of plants in Menispermaceae, which mainly distribute in tropics and subtropics. There are about 20 genuses and 60 species in China. Aporphine alkaloids have been isolated from 20 genuses of these plants *e.g.*, Abuta, Anamirta, Cbasmanthera, Cissampelos, Cocculus, Coscinium, Cyclea, Dioscoreophyllum, Fibraurea, Heptacyclum, Kolobopetalum, Legnephora, Meiocarpidium, Menispermum, Pachygone, Pycnarrhena, Rbigiocarya, Sinomenium, Stephania, Telitoxicum, Tiliacora, Tinospora and Triclisia.

Papaveraceae: There are about 23 genuses in Papaveraceae, which broadly distribute in temperate zones and subtropics and most of them are herbs. Aporphine alkaloids have been isolated from 13 genuses of these plants *e.g.*, Argemone, Chelidonium, Corydalis, Dicentra, Dicranostigma, Eschscholtzia, Fumaria, Glaucium, Meconopsis, Papaver, Pteridophyllum, Roemeria and Platycapnos.

Ranunculaceae: Annonaceae, with 50 genuses and more than 2000 species, belongs to Saxifragales, which broadly distributes around the whole world, especially in the north temperate zone and frigid zone and there are 39 genuses and about 750 species of these plants in China. Aporphine alkaloids have been isolated from 9 genuses of these plants *i.e.*, Aconitum, Aquilegia, Caltha, Coptis, Delphinium, Isopyrum, Nigella, Thalictrum and Trollius.

Lauraceae: There are 45 genuses and more than 2000 species in Lauracea, mainly distributing in tropics and subtropic. There are 20 genuses and more than 420 species in China, mainly distributing in areas south of the Qinling mountain/Huaihe river. Aporphine alkaloids have been isolated from 18 genuses of these plants *i.e.*, Actinodaphne, Alseodaphne, Beilschmiedia, Cassytha, Cinnamomum, Cryptocarya, Dehaasia, Laurus, Lindera, Litsea, Machilus, Mezilaurus, Nectandra, Neolitsea, Ocotea, Phoebe, Ravensara and Sassafras.

Monimiceae: There are about 18-25 genuses and 150-220 species in Monimiceae, distributing in the Southern Hemisphere and some of them are shrubs and dungarungas. Aporphine alkaloids have been isolated from 10 genuses of these plants *i.e.*, Atherosperma, Doryphora, Dryadodaphne, Laurelia, Laureliopsis, Monimia, Nemuaron, Palmeria, Peumus and Siparuna.

Magnoliaceae: Magnoliaceae, with original flowers, belongs to dicotyledon and there are 7 genuses and 225 species in it, mainly distributing in tropics and subtropics of Asia, especially in southern China and Indochina, with a few species in America. Aporphine alkaloids have been isolated from 6 genuses of these plants *i.e.*, Elmerrillia, Liriodendron, Magnolia, Michelia, Talauma and Tsoongiodendron.

Berberidaceae: There are 15 genuses and 570 species in Berberidaceae and most of them belong to Berberis. Aporphine alkaloids have been isolated from 4 genuses of these plants *i.e.*, Berberis, Leonitice, Machonia and Nandina.

Aristolochiaceae: Aristolochiaceae, with 7 genuses and 350 species, belongs to dicotyledon, broadly distributing in tropics and temperate zones, especially in southern America. Aporphine alkaloids have been isolated from 2 genuses of these plants *i.e.*, Aristolochia and Bragantia.

Euphorbiaceae: Euphorbiaceae, with 300 genuses and more than 8000 species, belongs to dicotyledon, broadly distributing around the world. Aporphine alkaloids have been isolated from 2 genuses of these plants *i.e.*, Caullophyllum and Croton.

Hernandiaceae: Hernandiaceae, with 3 genuses and 54 species, belongs to dicotyledon, mainly distributing in tropics. Aporphine alkaloids have been isolated from 2 genuses of these plants *i.e.*, Hernandia and Illigera.

Rataceae: Rataceae, with 150 genuses and about 900 species, belongs to dicotyledon, distributing in tropics and temperate zones, mostly in South Africa and Oceania. Aporphine alkaloids have been isolated from 2 genuses of these plants *i.e.*,Fagara and Phellodendron.

Rhamnaceae: Rhamnaceae, with 58 genuses and about 900 species, belongs to dicotyledon, broadly distributing around the world. Aporphine alkaloids have been isolated from 4 genuses of these plants *i.e.*, Colubrina, Ziziphus, Phylica and Retanilla.

Araceae: Araceae, with 115 genuses and more than 2000 species, belongs to monocotyledon, broadly distributing around the world and more than 92% of them are in tropics. Aporphine alkaloids have been isolated from Lysichiton.

Canellaceae: Canellaceae, with 6 genuses, grow in tropics, mainly distributing in South America, West Indies, East Africa and Madagascar. Aporphine alkaloids have been isolated from Cinnamosma.

Leguminoseae: Leguminoseae, with 690 genuses, is the third largest family of spermatophyte, broadly distributing around the world. Aporphine alkaloids have been isolated from 2 genuses of these plants *i.e.*, Erythrina and Euchresta.

Liliaceae: Liliaceae, with 175 genuses and more than 2000 species, broadly distributes around the world and specially in temperate zones and subtropics. Aporphine alkaloids have been isolated from Baeometra.

Nymphaeaceae: Nymphaeaceae, with 8 genuses and about 100 species, belongs to dicotyledon, mainly distributes in temperate zones and tropics. Aporphine alkaloids have been isolated from Nelumbo.

Piperaceae: Piperaceae, with 8 or 9 genuses and about 3100 species, belongs to dicotyledon, mainly distributing in tropics and subtropics. Aporphine alkaloids have been isolated from Piper.

Symplocaceae: Symplocaceae, with 250 species, mainly distributes in tropics and subtropics. Aporphine alkaloids have been isolated from Symplocos.

Sabiaceae: Sabiaceae, with 3 genuses and about 150 species, belongs to dicotyledon, mainly distributing between tropics and temperate zones. Aporphine alkaloids have been isolated from Sabia.

Fumariaceae: Corydalis.

Structures of aporphine alkaloids

The basic structure of aporphine alkaloids is shown in Fig. 6. The names of aporphine compounds, types of substituent groups and botanical sources are shown in Table-4.

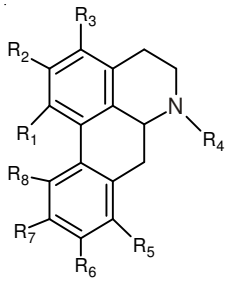

Fig. 6. Basic structure of aporphine alkaloids

Pharmacological activity of aporphine alkaloids

Pharmacological activity on adrenoreceptor: Pharmacological activity on blocking adrenoreceptor is one of the widest and most important bioactivities of aporphine alkaloids, especially in α-adrenoceptor, such as N-methyl-actinodaphnine[182], (+/-)-domesticine[181], corytuberine[92], magnoflorine[92], isothebaine[92], isocorydine[92], Dicentrine [183], S-(+)-boldine[184].

Firstly, most of these alkaloids have effect on blocking α_1-adrenoceptor, such as N-methyl-actinodaphnine[189], (+/-)-domesticine[181], dicentrine[183], while a few aporphine alkaloids, such as (+)-nantenine[185], have the effect of antagonism in α_1-adrenoceptor and α_2-adrenoceptor simultaneously. Different aporphine alkaloids have selectivity for different subtypes of receptor and N-methyl-actinodaphnine [189] has more affinity

TABLE-4
APORPHINE ALKALOIDS

Names of compounds	Structure of compound								Botanical sources
	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	
Caaverine	-OH	-OCH_3	-H	-H	-H	-H	-H	-H	*Ocotea lancifolia*[62] *Celastrinea* Mart[180]
Lirinidine	-OH	-OCH_3	-H	-CH_3	-H	-H	-H	-H	*Annona purpurea*[207] *Nelumbo nucifera*[64] *Papaver armeniacum*[65] *Artabotrys venustus*[67] *Magnolia officinalis* Rehder et W ils[66]
Asimilobine	-OCH_3	-OH	-H	-H	-H	-H	-H	-H	*Diploclisia affinis*[68] *Annona muricata*[69] *Stephania pierrei*[70] *Nelumbo nucifera*[64] *Stephania succifera* -H.S. Lo et -Y-Tsoong[76] *Fissistigma oldhamii*- (Hemsl.) Merr.[72] *Magnolia officinalis*- Rehder etW ils[66]
N-Methyl-asimilobine	-OCH_3	-OH	-H	-CH_3	-H	-H	-H	-H	*Annona purpurea*[125] *Papaver cylindricum*[73] Egyptian Papaver rhoea[74] *Nelumbo lutea* (Wild.) pers.[75]
Nornuciferine	-OCH_3	-OCH_3	-H	-H	-H	-H	-H	-H	*Guatteria* spp.[76] *Annona muricata*[69] *Chasmanthera dependens*[77] *Nelumbo lutea* (Wild.) -pers.[75]
Nuciferine	-OCH_3	-OCH_3	-H	-CH_3	-H	-H	-H	-H	Nelumbinis[78] *Papaver armeniacum*[94] *P. fugax*[94] *P. tauricola*[94] *Nelumbo lutea* (Wild.) -pers[75]
Anonaine	-O-CH_2-O-		-H	-H	-H	-H	-H	-H	*Annona salzmanii* D.C.[79] *Annona squamosa*[80] *Nelumbo lutea* (Wild.) -pers.[77] *D. tiebaghiensis*[225] *Magnolia officinalis*- Rehder etW ils[82]
N-Methylanonaine [1]	-O-CH_2-O-		-H	-CH_3	-H	-H	-H	-H	Annonaceae: Annona, Xylopia Lauraceae: Cryptocarya, Neolitsea Magnoliaceae: Liriodendron Menispermaceae: Stephania Monimiaceae: Laurelia Nympheaceae: Nelumbo Papaverceae: Papaver, Roemeria. Rhamnaceae: Colubrina
Roemrefidine	-O-CH_2-O-		-H	$(-CH_3)_2$	-H	-H	-H	-H	*Sparattanthelium amazonum*[83]
Stephalagine	-O-CH_2-O-		-OCH_3	-CH_3	-H	-H	-H	-H	*Stephania dinklagei*[84]
Stephanine	-O-CH_2-O-		-H	-CH_3	-OCH_3	-H	-H	-H	*Stephania bancroftii* F.M. -Bailey[85] *S. aculeate* F.M. Bailey[85]
Lirinine	-OH	-OCH_3	-H	-CH_3	-H	-OCH_3	-H	-H	*Artabotrys hainanensis*[149]
Lirinine N-oxide[1] (N→O)	-OH	-OCH_3	-H	-CH_3	-H	-OCH_3	-H	-H	Magnoliaceae: Liriodendron
O-methyllirinine[1]	-OCH_3	-OCH_3	-H	-CH_3	-H	-OCH_3	-H	-H	Magnoliaceae: Liriodendron
Anolobine	-O-CH_2-O-		-H	-H	-H	-OH	-H	-H	*Magnolia coco* (Lour.)DC.[86]
Roemerine	-O-CH_2-O-		-H	-CH_3	-H	-OH	-H	-H	*Hornschuchia oblique*[87] *Annona cherimolia*[88] *Annona senegalensis*[89] *Papaver armeniacum*[94] *Nelumbo lutea* (Wild.) pers.[75] *Stephania kwangsiensis*-H.S. Lo[17]
O-Methylanolobine [1]	-O-CH_2-O-		-H	-H	-H	-OCH_3	-H	-H	Annonaceae: Xylopia
Isolaureline	-O-CH_2-O-		-H	-CH_3	-H	-OCH_3	-H	-H	*Fissistigma oldhamii*-(Hemsl.)Merr.[72]
Sparsiflorine[1]	-OH	-OCH_3	-H	-H	-H	-H	-OH	-H	*Croton sparsiflorus*-Morung
Apoglaziovine	-OH	-OCH_3	-H	-CH_3	-H	-H	-OH	-H	*Berberis brandisiana*[90]
Variabiline[1]	-OH	-OCH_3	-H	-CH_3	-H	-H	-N(CH_2-C_6H_6)$_2$	-H	Lauraceae: Coctea
Apocrotonosine[1]	-OCH_3	-OH	-H	-H	-H	-H	-OH	-H	Euphorbiaceae: Croton

Phoebe base II[1]	$-OCH_3$	-OH	-H	$-CH_3$	-H	$-OCH_3$	-H	-H	Lauraceae: Phoebe
Tuduranine	$-OCH_3$	$-OCH_3$	-H	-H	-H	-H	-OH	-H	*S. rotunda, S. sasakii*[91]
Nuciferoline[1]	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	-H	-OH	-H	Papaverceae: Papaver
Mecambroline[1]	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	-OH	-H	Lauraceae: Phoebe Monimiaceae: Laurelia Meconopsis Papaverceae: Meconopsis, Papaver
Michiepressine[195]	$-O-CH_2-O-$		-H	$(-CH_3)_2$	-H	-H	-OH	-H	Magnoliaceae: Michelia
Laureline	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	$-OCH_3$	-H	*Guatteria elata*[98]
Isothebaine	-OH	$-OCH_3$	-H	$-CH_3$	-H	-H	-H	$-OCH_3$	*Mahonia aquifolium*[99] *Papaver bracteatum*[100] *Papaver orientale*[101] *P. pseudo-orientale*[101]
Obovanine[1]	$-O-CH_2-O-$		-H	-H	-H	-H	-H	-OH	Magnoliaceae: Magnolia
Pukateine[1]	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	-H	-OH	*Guatteria elata*
Laurepukine[1](N^+-O^-)	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	-H	-OH	Monimiaceae: Laurelia
O-Methylpukateine [1]	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	-H	$-OCH_3$	Monimiaceae: Laurelia
Crebaine	$-O-CH_2-O-$		-H	$-CH_3$	$-OCH_3$	$-OCH_3$	-H	-H	*S. cepharantha*[95] *S. dielaiana*[95] *S. venosa*[95]
Laurelliptine	-OH	$-OCH_3$	-H	-H	-H	-OH	$-OCH_3$	-H	*Annona salzmanii* D.C.[238] *Nectandra rigida*[96]
Isoboldine	-OH	$-OCH_3$	-H	$-CH_3$	-H	-OH	$-OCH_3$	-H	*Litsea cubeba*[97] *Guatteria dumetorum*[98] *Lindera angustifolia*[99] *Cryptocarya chinensis*-Hemsl[100] *Corydalis bungeana*[101] *Pachygone ovata*[102] *Litsea wightiana*[103] *Corydalis slivenensis*[104] *Neolitsea fuscata*[105] *Corydalis marschalliana*[106]
Laurifoline	-OH	$-OCH_3$	-H	$(-CH_3)_2$	-H	-OH	$-OCH_3$	-H	*Hypserpa nitida*[107]
Bracteoline[1]	-OH	$-OCH_3$	-H	$-CH_3$	-H	$-OCH_3$	-OH	-H	Papaverceae: Papaver
Wilsonirine	-OH	$-OCH_3$	-H	-H	-H	$-OCH_3$	$-OCH_3$	-H	*A. monteiroae*[108]
Thaliporphine	-OH	$-OCH_3$	-H	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	*Croton lechleri*[109] *Neolitsea konishii* K[110] *Corydalis bulbosa*[111] *Mahonia repens*[52] *Corydalis yanhusuo*[112]
Thalicmidine[1](N→O)	-OH	$-OCH_3$	-H	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	Ranuncudaceae: Thalictrum
Fagara base[1]	-OH	$-OCH_3$	-H	$(-CH_3)_2$	-H	$-OCH_3$	$-OCH_3$	-H	Rutaceae: Fagara
Nordomesticine	-OH	$-OCH_3$	-H	-H	-H	$-O-CH_2-O-$		-H	*Nandina domestica*[113] *Corydalis slivenensis*[104]
Domesticine	-OH	$-OCH_3$	-H	$-CH_3$	-H	$-O-CH_2-O-$		-H	*Nandina domestica*[113] *Corydalis slivenensis*[104] *C. susaveolens* Hance[114]
Laurolistsine	$-OCH_3$	-OH	-H	-H	-H	-OH	$-OCH_3$	-H	*Litsea rotundifolia* var. -oblongifolia[115]
Boldine	$-OCH_3$	-OH	-H	$-CH_3$	-H	-OH	$-OCH_3$	-H	*Phoebe grandis*[116] *Lindera aggregate*[117] *Litsea sessilis*[118] *Lindera angustifolia*[46] *Cassytha filiformis*[119] *Peumus boldus* Mol.[120] *Litsea wightiana*[103] *Lindera aggregate*-Kosterm[121]
Norpredicentrine	$-OCH_3$	-OH	-H	-H	-H	$-OCH_3$	$-OCH_3$	-H	*Lindera fragrans* O-liv.[122]
Predicentrine	$-OCH_3$	-OH	-H	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	*Desmos rostrata*[123] *Aromadendron elegans*[124] *Annona purpurea*[258] *Cassytha filiformis* II[125] *Corydalis slivenensis*[104]
Isodomesticine	$-OCH_3$	-OH	-H	$-CH_3$	-H	$-O-CH_2-O-$		-H	*Guatteria dumetorum*[98]
Laurotetanine	$-OCH_3$	$-OCH_3$	-H	-H	-H	-OH	$-OCH_3$	-H	*Lindera angustifolia*[99] *Siparuna pauciflora*[127] *Hernandia nymphaeifolia*[128] *Litsea wightiana*[103]

Lauroscholizine[1]	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	-OH	$-OCH_3$	-H	Hernandiaceae: Hernandia Lauraceae: Actinodaphne, Cassytha, Cryptocarya, Litsea, Neolitsea Magnoliaceae: Liriodendron Monimiaceae: Nemuaron, Palmeria, Peumus Papaverceae: Eschscholtzia Rhamnaceae: Colubrina, Phylica
Xanthoplanine	$-OCH_3$	$-OCH_3$	-H	$(-CH_3)_2$	-H	-OH	$-OCH_3$	-H	*Xylopia parviflora*[129]
Cocsarmine[1]	$-OCH_3$	$-OCH_3$	-H	$(-CH_3)_2$	-H	$-OCH_3$	-OH	-H	Menispermaceae: Cocculus
Norglaucine	$-OCH_3$	$-OCH_3$	-H	-H	-H	$-OCH_3$	$-OCH_3$	-H	*Chasmanthera dependens*[77] *Alphonsea ventricasa*[130]
Glaucine	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	*Annona purpurea*[125] *Corydalis tuber*[131] *Litsea wightiana*[103] *Corydalis bulbosa*[106] *Corydalis yanhusuo*-W.T.Wang[132]
Nornantenine	$-OCH_3$	$-OCH_3$	-H	-H	-H	$-O-CH_2-O-$		-H	*Uvaria chamae* P. Beauv[133]
N-Acetylnornantenine [1]	$-OCH_3$	$-OCH_3$	-H	$-COCH_3$	-H	$-O-CH_2-O-$		-H	Magnoliaceae: Liriodendron
Actinodaphnine	$-O-CH_2-O-$	-H	-H	-H	-OH	$-OCH_3$		-H	*Cassytha filiformis*[134] *Illigera luzonensis*[135]
N-Methylactinodaphnine	$-O-CH_2-O-$	-H	$-CH_3$	-H	-OH	$-OCH_3$		-H	*Illigera luzonensis*[136]
Phanostenine[1]	$-O-CH_2-O-$	-H	-H	-H	$-OCH_3$	-OH		-H	Menispermaceae: Stephania
Dicentrine	$-O-CH_2-O-$	-H	$-CH_3$	-H	$-OCH_3$	$-OCH_3$		-H	*Cassytha filiformis*[137] *Cissampelos capensis*[138] *Glaucium oxylobum*[139] *Lindera megaphylla*[140]
Cryptodorine	$-O-CH_2-O-$		-H	-H	-H	$-O-CH_2-O-$		-H	*Guatteria* spp.[76]
Neolitsine	$-O-CH_2-O-$		-H	$-CH_3$	-H	$-O-CH_2-O-$		-H	*Cassytha filiformis*[134] *Cissampelos capensis*[138]
Corytuberine	-OH	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	-OH	*Annona montana*[141] *Mahonia aquifolium*[99]
Magnoflorine	-OH	$-OCH_3$	-H	$(-CH_3)_2$	-H	-H	$-OCH_3$	-OH	Flos Magnoliae[142] *Hypserpa nitida*[107] *Aristolochia baetica*[143] *Mahonia aquifolium*[144] *Delphinium pentagynum*[145] *Thalictrum angustifolium*[146] *Xylopia parviflora*[129] *Zanthoxylum scandens*[147] *Stephania cepharantha*[148] *Semiaquilegia adoxoide*[149] *Pachygone ovata*[102]
Norcorydine	-OH	$-OCH_3$	-H	-H	-H	-H	$-OCH_3$	$-OCH_3$	*Chelidonium majus*[150] *Litsea wightiana*[103]
Corydine	-OH	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	$-OCH_3$	*Corydalis cava Schweigg. & Kort*[151] *Uvaria chamae* P. Beauv[218] *Glaucium grandiflorum* var.-torquatum[152]
N-Methylcorydine[1]	-OH	$-OCH_3$	-H	$(-CH_3)_2$	-H	-H	$-OCH_3$	$-OCH_3$	Rutaceae: Fagara
Hernovine	$-OCH_3$	-OH	-H	-H	-H	-H	-OH	$-OCH_3$	*Illigera luzonensis*[153] *Hernandia nymphaeifolia*[153]
N-Methylhernovine	$-OCH_3$	-OH	-H	$-CH_3$	-H	-H	-OH	$-OCH_3$	*Hernandia nymphaeifolia*[153]
Lindcarpine	$-OCH_3$	-OH	-H	-H	-H	-H	$-OCH_3$	-OH	*Lindera pipericarpa*-Boerl[154]
N-Methylindcarpine[1]	$-OCH_3$	-OH	-H	$-CH_3$	-H	-H	$-OCH_3$	-OH	Lauraceae: Beilschmiedia, Lindera, Phoebe Magnoliaceae: Magnolia
N,N-Dimethyllind-carpine[1]	$-OCH_3$	-OH	-H	$(-CH_3)_2$	-H	-H	$-OCH_3$	-OH	Magnoliaceae: Magnolia Menispermaceae: *Menis permum*
10-O-Methlhernovine[1]	$-OCH_3$	-OH	-H	-H	-H	-H	$-OCH_3$	$-OCH_3$	Euphorbiaceae: Croton
N,O-Dimethylhernovine[1]	$-OCH_3$	-OH	-H	$-CH_3$	-H	-H	$-OCH_3$	$-OCH_3$	Euphorbiaceae: Croton
Suaveoline	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	-H	-OH	-OH	*Rauvolfia caffra*[155]
Norisocorydine	$-OCH_3$	$-OCH_3$	-H	-H	-H	-H	$-OCH_3$	-OH	*Lindera angustifolia*-Chen[156]

Isocorydine	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	-OH	*Dactylicapnos scandens*[157] *Stephania dinklagei*[84] *Mahonia aquifolium*[92] *Thalictrum fauriei*[158] *Dactylicapnos torulosa*[159] *Glaucium grandiflorum* var.-torquatum[152] *Corydalis slivenensis*[104] *Glaucium flavum*-Crantz[160] *Papaver armeniacum*[65] Egyptian Papaver-rhoeas[74] *Stephania kwangsiensis* H. S.- Lo[17]
Menisperine	$-OCH_3$	$-OCH_3$	-H	$(-CH_3)_2$	-H	-H	$-OCH_3$	-OH	*Xylopia parviflora*[129] *Stephania cepharantha*[148] *Corydalis decumbens*-(Thunb.) Pers.[161] *Tinospora capillipes*[162] *Magnolia grandiflora*[163]
Catalpifoline[2]	$-OCH_3$	$-OCH_3$	-H	-H	-H	-H	$-OCH_3$	$-OCH_3$	Hernandiaceae: Hernandia
O,O-Dimethycory-tuberine[2]	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	$-OCH_3$	Hernandiaceae: Hernandia
Nandigerine[2]	$-O-CH_2-O-$		-H	-H	-H	-H	-OH	$-OCH_3$	Hernandiaceae: Hernandia
N-Methylhernangerine	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	-OH	$-OCH_3$	*Hernandia sonora*[164]
Launobine	$-O-CH_2-O-$		-H	-H	-H	-H	$-OCH_3$	-OH	*Illigera luzonensis*[54]
Bulbocapnine	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	$-OCH_3$	-OH	*Corydalis cava* Schweigg. & Kort[151] *Cassytha filiformis*[119] *Hernandia nymphaeifolia*[128] *Illigera luzonensis*[135] *Corydalis hsuchowensis*[165] *Fumaria par*viflora[166] *Corydalis slivenensis*[104] *Corydalis bulbosa*[106] *Corydalis marschalliana*[111]
O-Methylbulbocapnine	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	$-OCH_3$	$-OCH_3$	*Hernandia nymphaeifolia*[167] *Illigera luzonensis*[54]
Ovigerine	$-O-CH_2-O-$		-H	-H	-H	-H	$-O-CH_2-O-$		*Hernandia nymphaeifolia*[168] *Hernandia sonora*[164]
N-Methylovigerine	$-O-CH_2-O-$		-H	$-CH_3$	-H	-H	$-O-CH_2-O-$		*Hernandia nymphaeifolia*[168]
Preocoteine[2]	-OH	$-OCH_3$	-H	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	Ranuncudaceae: Thalictrum
Preocoteine N-oxid[2] (N→O)	-OH	$-OCH_3$	-H	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	Ranuncudaceae: Thalictrum
O-Demethylpuepareine[2]	$-OCH_3$	$-OCH_3$	-OH	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	Annonaceae: Annona
Norpureine[2]	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	-H	$-OCH_3$	$-OCH_3$	-H	Annonaceae: Annona
Thalicsimidine	$-OCH_3$	$-OCH_3$	$-OCH_3$	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	*Annona purpurea*[125] *Thalictrum flavum* L[169]
Oconovine	$-OCH_3$	$-OCH_3$	$-OCH_3$	$-CH_3$	-H	-H	$-OCH_3$	-OH	*Thalictrum fauriei*[170]
Ocokryptine[2]	$-OCH_3$	$-O-CH_2-O-$		$-CH_3$	-H	-H	$-OCH_3$	-OH	Lauraceae: Coctea
Cassythine	$-O-CH_2-O-$		$-OCH_3$	-H	-H	-OH	$-OCH_3$	-H	*Cassytha filiformis*[137] *Cassytha filiformis*[171] *Cassytha filiformis*[119] *Cassytha filiformis*[134]
O-Methylcassyfiline[2]	$-O-CH_2-O-$		$-OCH_3$	-H	-H	$-OCH_3$	$-OCH_3$	-H	Lauraceae: Cassytha Ranuncudaceae: Thalictrum
Ocoteine	$-O-CH_2-O-$		$-OCH_3$	$-CH_3$	-H	$-OCH_3$	$-OCH_3$	-H	*Cassytha filiformis* II[125] Slavjanka Mountains[172]
Csaaythidine[2]	$-O-CH_2-O-$		$-OCH_3$	-H	-H	$-O-CH_2-O-$		-H	Lauraceae: Cassytha
Ocopodine[2]	$-O-CH_2-O-$		-H	$-CH_3$	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	Lauraceae: Coctea
Bisnorthalphenine [2]	$-CH_2-$	$-OCH_3$	-H	-H	-H	$-O-CH_2-O-$		-O-	Ranuncudaceae: Thalictrum
Thalphenine	$-CH_2-$	$-OCH_3$	-H	$(-CH_3)_2$	-H	$-O-CH_2-O-$		-O-	*Thalictrum przewalskii*[173] *Thalictrum revolutum*[174]
N-Acetylanonaine	$-O-CH_2-O-$		-H	$-COCH_3$	-H	-H	-H	-H	*Aromadendron elegans*-Blume[124] *Magnolia obovata*[175]
Isopiline[2]	-OH	$-OCH_3$	$-OCH_3$	-H	-H	-H	-H	-H	Annonaceae: Isolona
O-Methylisopiline[2]	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	-H	-H	-H	-H	Magnoliaceae: Liriodendron
3-Methoxynuciferine[2]	$-OCH_3$	$-OCH_3$	$-OCH_3$	$-CH_3$	-H	-H	-H	-H	Magnoliaceae: Liriodendron
Tuliferoline[2]	$-OCH_3$	$-OCH_3$	$-OCH_3$	$-COCH_3$	-H	-H	-H	-H	Magnoliaceae: Liriodendron
Norstephalagine[2]	$-O-CH_2-O-$		$-OCH_3$	-H	-H	-H	-H	-H	*Artabotrys maingayi*
Zenkerine	-OH	$-OCH_3$	-H	-H	-H	-H	$-OCH_3$	-H	*Uvaria klaineana*[191]
Pulchine[2]	-OH	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	-H	Lauraceae: Ocotea

Zanthoxyphylline[2]	$-OCH_3$	$-OCH_3$	-H	$(-CH_3)_2$	-H	-H	-H	$-OCH_3$	Rutaceae: Zanthoxylum
Norlaureline[2]	-O-CH_2-O-		-H	-H	-H	-H	-H	$-OCH_3$	*Guatteria elata*
Puterine[2]	-O-CH_2-O-		-H	$-CH_3$	-H	-H	-H	$-OCH_3$	*Guatteria elata*
Buxifoline[2]	-O-CH_2-O-		$-OCH_3$	-H	-H	$-OCH_3$	-H	-H	Annonaceae: Xylopia
Elmerrillicine[2]	-O-CH_2-O-		$-OCH_3$	-H	-H	-H	-H	-OH	Magnoliaceae: Elmerrillia
Liriotulipiferine[2]	$-OCH_3$	-OH	-H	-H	-H	$-OCH_3$	-OH	-H	Magnoliaceae: Liriodendron
Norisodomesticine	$-OCH_3$	-OH	-H	-H	-H	-O-CH_2-O-		-H	*Guatteria dumetorum*[98]
Lirioferine	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	$-OCH_3$	-OH	-H	*Guatteria dumetorum*[98]
N-Methylnantenine	$-OCH_3$	$-OCH_3$	-H	$(-CH_3)_2$	-H	-O-CH_2-O-		-H	*Thalictrum przewalskii*[177]
Litseferine[2]	-O-CH_2-O-		-H	-H	-H	$-OCH_3$	-OH	-H	Lauraceae: Litsea
Nordicentrine	-O-CH_2-O-		-H	-H	-H	$-OCH_3$	$-OCH_3$	-H	*Stephania pierrei*[70]
Litsedine[2]	-O-CH_2-O-		-H	-H	-H	-H	$-OCH_3$	$-OCH_3$	Lauraceae: Litsea
Delporphine[2]	$-OCH_3$	$-OCH_3$	-OH	$-CH_3$	-H	-OH	$-OCH_3$	-H	Ranunculaceae: Delphinium
Noroconovine[2]	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	-H	-H	$-OCH_3$	-OH	Annonaceae: Polyalthia
Polygospermine[2]	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	-H	-H	-O-CH_2-O-		Annonaceae: Polyalthia
Leucoxine[2]	-O-CH_2-O-		-H	$-CH_3$	-OH	$-OCH_3$	$-OCH_3$	-H	*Ocotea minarum* *Ocotea brachybotra*
Ocoxylonine[2]	-O-CH_2-O-		$-OCH_3$	$-CH_3$	-OH	$-OCH_3$	$-OCH_3$	-H	Lauraceae: Ocotea
Leucoxylonine[2]	-O-CH_2-O-		$-OCH_3$	$-CH_3$	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	*Ocotea minarum*
N-Demethylthalphenine[2]	-CH_2-	$-OCH_3$	-H	$-CH_3$	-H	-O-CH_2-O-		-O-	Ranunculaceae: Thalictrum
N-Carbamoyl-asimilobine[3]	$-OCH_3$	-OH	-H	$-CONH_2$	-H	-H	-H	-H	Annonaceae: Hexalobus
Roemerine N-oxide[3] (N→O)	-O-CH_2-O-		-H	$-CH_3$	-H	-H	-H	-H	Papaveraceae: Papaver
N-Formylanonaine	-O-CH_2-O-		-H	-CHO	-H	-H	-H	-H	*Magnolia obovata*[175]
N-Carbamoylanonaine [3]	-O-CH_2-O-		-H	$-CONH_2$	-H	-H	-H	-H	Annonaceae: Hexalobus
Norlirdinine[3]	$-OCH_3$	-OH	$-OCH_3$	-H	-H	-H	-H	-H	Annonaceae: Polyaltbia
3-Hydroxynornuciferine	$-OCH_3$	$-OCH_3$	-OH	-H	-H	-H	-H	-H	*Artabotrys hainanensis*[12]
9-Hydroxy-1,2-dimethoxynoraporphine [3]	$-OCH_3$	$-OCH_3$	-H	-H	-H	-OH	-H	-H	Annonaceae: Monantbotaxis
N-formylxylopine[3]	-O-CH_2-O-		-H	-CHO	-H	$-OCH_3$	-H	-H	Annonaceae: Duguetia
1,2,10-Trimethoxy-aporphine[3]	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	-H	Ranunculaceae: Tbalictrum
Isothebaidine[3]	-OH	$-OCH_3$	-H	$-CH_3$	-H	-H	-H	-OH	Papaveraceae: Papaver
N-Formylputerine[3]	-O-CH_2-O-		-H	-CHO	-H	-H	-H	$-OCH_3$	Annonaceae: Duguetia
N-Methylbuxifoline [3]	-O-CH_2-O-		$-OCH_3$	$-CH_3$	-H	$-OCH_3$	-H	-H	Annonaceae: Duguetia
N-Formylbuxifoline [3]	-O-CH_2-O-		$-OCH_3$	-CHO	-H	$-OCH_3$	-H	-H	Annonaceae: Duguetia
(-)Norannuradhapurine[3]	-O-CH_2-O-		-H	-H	-OH	$-OCH_3$	-H	-H	Annonaceae: Polyaltbia
Stesakine	-O-CH_2-O-		-H	$-CH_3$	$-OCH_3$	-OH	-H	-H	*Stephania cepharantha*[179]
N-Methylboldine[3]	$-OCH_3$	-OH	-H	$(-CH_3)_2$	-H	-OH	$-OCH_3$	-H	Menispermaceae: Cocculus
Laetanine[3]	$-OCH_3$	-OH	-H	-H	-H	-OH	$-OCH_3$	-H	Lauraceae: Litsea
Isocalycinine[3]	-O-CH_2-O-		-H	-H	-H	-OH	-H	$-OCH_3$	Annonaceae: Guatteria
Calycinine	-O-CH_2-O-		-H	-H	-H	$-OCH_3$	-H	-OH	*Daphniphyllum unnanense*[179]
N-Methylcalycinine [3]	-O-CH_2-O-		-H	$-CH_3$	-H	$-OCH_3$	-H	-OH	Annonaceae: Duguetia
Discoguattine[3]	-O-CH_2-O-		-H	-H	-H	$-OCH_3$	-H	$-OCH_3$	Annonaceae: Guatteria
Corydine N-oxide[3] (N→O)	-OH	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	$-OCH_3$	Papaveraceae: Glaucium
Glaufine[3]	$-OCH_3$	-OH	-H	$-CH_3$	-H	-H	-OH	-OH	Papaveraceae: Glaucium
Laetine	$-OCH_3$	-OH	-H	-H	-H	-H	-O-CH_2-O-		*Hernandia nymphaeifolia*[167]
Hernagine[3]	$-OCH_3$	$-OCH_3$	-H	-H	-H	-H	-OH	$-OCH_3$	Hernandiaceae: Hernandia
Isocorydine N-oxide[3] (N→O)	$-OCH_3$	$-OCH_3$	-H	$-CH_3$	-H	-H	$-OCH_3$	-OH	Berberidaceae: Berberis
N,O-Dimethyl-isocorydinw[3]	$-OCH_3$	$-OCH_3$	-H	$(-CH_3)_2$	-H	-H	$-OCH_3$	$-OCH_3$	Menispermaceae: Cocculus,Pacbygone
N-Methylbulbocapnine[3]	-O-CH_2-O-		-H	$(-CH_3)_2$	-H	-H	$-OCH_3$	-OH	Fumariaceae: Corydalis
Isooconovine[3]	-OH	$-OCH_3$	$-OCH_3$	$-CH_3$	-H	-H	$-OCH_3$	$-OCH_3$	Lauraceae: Ocotea
Xyloguyelline[3]	$-OCH_3$	-OH	$-OCH_3$	-H	-H	-O-CH_2-O-		-H	Annonaceae: Xylopia
Danguyelline[3]	$-OCH_3$	-OH	$-OCH_3$	-H	-H	-H	$-OCH_3$	-OH	Annonaceae: Xylopia
Thalisopynine[3]	$-OCH_3$	$-OCH_3$	$-OCH_3$	$-CH_3$	-H	-OH	$-OCH_3$	-H	Ranunculaceae: Tbalictrum
Baicaline[3]	$-OCH_3$	-O-CH_2-O-		-H	-H	$-OCH_3$	$-OCH_3$	-H	Ranunculaceae: Tbalictrum
Duguevanine[3]	-O-CH_2-O-		$-OCH_3$	-H	-H	$-OCH_3$	-H	-OH	Annonaceae: Duguetia
N-Methylduguevanine[3]	-O-CH_2-O-		$-OCH_3$	$-CH_3$	-H	$-OCH_3$	-H	-OH	Annonaceae: Duguetia
N-Formylduguevanine[3]	-O-CH_2-O-		$-OCH_3$	-CHO	-H	$-OCH_3$	-H	-OH	Annonaceae: Duguetia
Ocominarine[3]	-O-CH_2-O-		-H	$-CH_3$	-O-CH_2-O-		$-OCH_3$	-H	*Ocotea minarum*
Norleucoxylonine[3]	-O-CH_2-O-		$-OCH_3$	-H	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	Lauraceae: Ocotea
Ocotominarine[3]	-O-CH_2-O-		$-OCH_3$	$-CH_3$	-O-CH_2-O-		$-OCH_3$	-H	*Ocotea minarum*

with α_1B-receptor. Concentration has great effects on (+/-)-domesticine's[181] selection of receptor and pharmacological effects of (+)-nantenine observed at concentrations lower than 1 μM can be attributed to α_1-adrenergic and 5-HT 2A receptor blocking properties whereas at higher concentrations (> 1 μM) the pharmacological activity of this natural compound may be also due to a decrease of Ca^{2+} influx through transmembrane calcium channels (calcium antagonist activity), to an inhibition of protein kinase C (PKC) actions and/or to an α_2-adrenoceptor blockade[185]. In addition, the substitution of aporphine alkaloids has important effects on pharmacological activity on blocking adrenoreceptor and selectivity for different subtypes. Hydroxy at the C-2 of boldine induces a significant increase in α_1A-subtype selectivity and affinity[186,187]. The replacement of a methoxy moiety at C-1 position of (±)-nantenine with a hydroxyl group increased affinity for the receptor[188]. A hydroxyl group at the C-1 position and a methyl group at the N-6 position in the (±)-nantenine structure are essential for the enhancement of affinity for the α_1-adrenoceptor[189].

Pharmacological activity on serotonin: Nantenine inhibits l-5-HTP plus clorgyline-induced head- twitch response by blocking 5-HT2A receptors in the central nervous system[189]. (+)-Nantenine can inhibit 5-HT(2A) receptor to lower blood pressure and reduce heart rates[191,192]. Results suggest that a methyl group at a nitrogen atom and a methoxy moiety at C-1 in (+)-nantenine play important roles in the development of the antiserotonergic activity[190].

Cytotoxic activity: Cytotoxic activity is another important physiological activity of aporphine alkaloids. Alkaloids with cytotoxic activity have been shown in references[15-22]. Mechanism of this cytotoxic activity is that alkaloids with methylenedioxy ring groups interfere with the catalytic activity of topoisomerases in contrast other aporphines. These interactions with DNA may explain, at least in part, the effects observed on cancer cells and on trypanosomes[119]. The DNA damaging activity of *Stephania dinklagei*[194] and Topoisomerase II inhibition by (+) dicentrine[195] are the mechanism of this cytotoxic activity. (-)-Roemerine, isolated from the leaves of *Annona senegalensis*, was found to enhance the cytotoxic response mediated by vinblastine with multidrug-resistant KB-V1 cells. In the absence of vinblastine, no significant cytotoxicity was observed with KB-3 or KB-V1 cells (ED_{50} > 20 μg/mL) and several other human tumor cell lines were also relatively insensitive. As indicated by its ability to inhibit ATP-dependent [3H]vinblastine binding to multidrug-resistant KB-V1 cell membrane vesicles, (-)-roemerine appears to function by interacting with P-glycoprotein[89]. In addition, different alkaloids have various sensibilities of different cells and substituent groups on alkaloids have effects on the cytotoxic activity.

Pharmacological activity on antioxidation: Boldine has been most widely studied in the pharmacological activity on antioxidation. Boldine inhibits the oxidation of LDL *in vitro* and atherosclerosis *in vivo*[196], prevents human liver microsomal lipid peroxidation and inactivation of cytochrome P4502E1[197] and inhibits oxidative mitochondrial damage to prevent diabetes[198]. Boldine may attenuate the catecholamine oxidation-induced brain mitochondrial dysfunction and decrease the dopamine-induced death of PC12 cells through a scavenging action on reactive oxygen species and inhibition of melanin formation and thiol oxidation[199]. Many other aporphine alkaloids, such as isoboldine, Bulbocapnine, apomorphine, glaucine, magnoflorine and anonaine[200,203], can take effect on antioxidation by removing active oxygen and active free radicles and inhibiting Hypoxanthine-xanthine oxidase system. Antioxidation of aporphine alkaloids is related to their structures[203,204].

Pharmacological activity on antiplatelet effects: Many aporphine alkaloids have this pharmacological activity. The inhibitory effect of dicentrine on platelet aggregation and ATP release was due to the inhibition of thromboxane formation and the elevation of the level of cyclic AMP[205]. The antiplatelet effect of phenanthrene alkaloids is mainly a result of inhibition of thromboxane A2 formation[206]. In addition, sonodione, demethylsonodione, norsonodione, ovigerine, hernangerine, N-methylhernangerine, (+)-malekulatine and isovanillin have obvious effects on antiplatelet effects[125,207,208].

Pharmacological activity on nervous system: (S)-(+)-Boldine was brominated, chlorinated and iodinated using molecular bromine in acetic acid or N-halosuccinimides in trifluoroacetic acid. Initial halogenation occurs at C-3, followed (in the cases of chlorine and bromine) by the less reactive C-8, to afford 3-haloboldines- and 3,8-dihaloboldines. Using a 2:1 ratio of N-iodosuccinimide to boldine, however, only the 3-iodo derivative **6** was obtained. Radioligand binding studies of these products showed that halogenation of boldine at C-3 favours affinity for D(1)- [*vs.* D(2)-] dopaminergic receptors, attaining a low nanomolar IC_{50} value in the case of 3-iodoboldine[209]. Boldine does not display effective central dopaminergic antagonist activities *in vivo* in spite of its good binding affinity at D1- and D2-like receptors and that glaucine, although less effective *in vitro*, does appear to exhibit some antidopaminergic properties *in vivo*[210]. When tested on dopamine (DA) metabolism in the striatum of B6CBA mice, glaucine, 3-bromoboldine, glaucine, 3-bromoboldine, 3-iodoboldine, 8-aminoboldine, 8-nitrosoboldine and 2,9-O,O′-dipivaloylboldine, increased striatal levels of DOPAC and HVA and the HVA/DA ratio, indicating that they cross the blood-brain barrier and that they seem to act as dopamine antagonists *in vivo*[211]. The neuromuscular blockade by boldine on isolated mouse phrenic-nerve diaphragm might be due to its direct interaction with the postsynaptic nicotinic acetylcholine receptor[212]. Corydine, isocorydine and glaucine's possible contributions to activity be preferential binding to blood components or by selective inhibition of acetylcholinesterase. The combined studies indicated that there was a modest preference by the neuromuscular junction of the cat for monoquaternary blockers with the (s)-confirguation[213]. Atherosperminine produced effects associated with dopamine receptor stimulation[214]. Nantenine blocked and rapidly reversed MDMA-induced hyperthermia, attenuated lethality in both housing conditions and reduced MDMA-induced locomotor stimulation and head twitches[215].

Immunoregulatory activity: Boldine concentration-dependently decreased blastogenesis in normal subjects and patients with chronic lymphocytic leukemia (CLL). However,

the decrease in breast cancer patients was significant only at higher concentrations. Natural killer (NK) activity showed no change in healthy controls with normal values, but in cases with low activity treatment with boldine resulted in an increase. In patients with CLL, NK activity was enhanced; in tumor-bearing patients, however, there was no effect. LDCC and NCMC activity did not change significantly in normal controls[216]. The inhibitory effect of 15 semi-synthetic analogues of glaucine on the lipopolysaccharide (LPS)-induced and the concanavalin A (Con A)-induced proliferation of mouse splenocytes was compared *in vitro*. Isoboldine, bracteoline and dehydroglaucine showed a significantly higher potency to suppress LPS-induced proliferation than 1, while 7-hydroxy-4-methylglaucine, 7-formyldehydroglaucine, 7-acetyldehydroglaucine, 7-benzoyldehydroglaucine, oxoglaucine and glaucine-quinol were less inhibitory. Compounds **3**, **4**, boldine, **15** and **16** surpassed significantly the inhibition expressed by **1** on Con A-induced proliferative response[217]. Oxoglaucine has strong effects on immunosuppression[218,219].

Pharmacological activity on antivirus: The pharmacological activity on antivirus of aporphine alkaloids is related to their structures. A series of 18 aporphinoids have been tested *in vitro* against human poliovirus. The aporphines (+)-glaucine fumarate, (+)-N-methyllaurotetanine, (+)-isoboldine and (-)-nuciferine, HCl were found to be active with selectivity indices > 14. The nature of the 1,2-substituents of the isoquinoline moiety appeared to be critical for antipoliovirus activity. An SAR study demonstrated the importance of a methoxyl group at C-2 on the tetrahydroisoquinoline ring for the induction of antipoliovirus activity. Molecular modeling of some compounds in this series revealed the close similarities between the three-dimensional conformational features of the inactive 1,2-substituted derivatives (+)-boldine and (+)-laurolitsine with derivatives containing the 1,2-(methylenedioxy) moiety, which were generally found to be inactive as exemplified by (+)-cassythicine[220]. Hernandonine, laurolistine, 7-oxohernangerine and lindechunine A showed significant anti-human immunodeficiency virus type 1 (HIV-1) integrase activity with IC values of 16.3, 7.7, 18.2 and 21.1 μM, respectively[221].

Pharmacological activity on ion channel: The pharmacological activity on ion channel of aporphine alkaloids mainly means that they can inhibit the calcium ion channels. (+)-Boldine[222], nantenine[185,222,223], glaucine[224] and laurotetanine[43] relaxed the rat thoracic aorta mainly by suppressing the Ca^{2+} influx through both voltage- and receptor-operated calcium channels. Boldine could sensitize the ryanodine receptor and induce Ca^{2+} release from the internal Ca^{2+} storage site of skeletal muscle [2]. Boldine produces a non-parallel shift of the contraction response induced by barium, revealing the occurrence of a non-competitive antagonism. This effect could be the result of interference with intracellular events associated with the barium-induced changes in calcium pools[227]. In addition, some Aporphine alkaloids have effects on the ion channels of K^+, Na^+, Ca^{2+}, for example, isocorydine may interfere with K^+, Na^+ and Ca^{2+} currents in ventricular cells membrane at different concentrations[228] and dicentrine has blocking effects on ion channels of K^+ and Na^+ currents in ventricular cells[229,230].

Others: Aporphine alkaloids have other less common pharmacological activities. (S)-dicentrine and (S)-neolitsine have anthelmintic activity[231]. From the leaves of *Nelumbonucifera* (an aquatic plant), one new compound, 24(*R*)-ethylcholest-6-ene-5α-ol-3-*O*-β-D-glucopyranoside, along with 11 known metabolites, were isolated and identified by spectroscopic methods including 1D- and 2D NMR. Antifungalactivity for (*R*)-roemerine (IC_{50}/MIC = 4.5/10 μg/mL against *Candida albicans*) and antimalarialactivity for (*R*)-roemerine and *N*-methylasimilobine (IC_{50} = 0.2 and 4.8 μg/mL for the D6 clone, respectively and 0.4 and 4.8 μg/mL for the W2 clone, respectively) was observed. An analysis of the structure-activity relationship shows that the substituents in position C-1 and C-2 of aporphine alkaloids are crucial for the antimalarialactivity[232]. The alkaloids boldine, glaucine, predicentrine, apomorphine, coclaurine, norarmepavine and codeine may act by blocking mitochondrial electron transport. The trypanocidal effects of these alkaloids appear to be correlated with their antioxidative activities[233]. Boldine has antileishmanial, antiinflammatory, antipyretic, cytoprotective effects[234,235]. (+)-Actinodaphnine, (+)-N-Me-actinodaphnine, (+)-anonaine, (-)-xylopine and (-)-N-Me-xylopine MeI, had the strongest inhibitory activities against three G(+) bacteria (*Bacillus cereus*, *Micrococcus* sp. and *Staphylococcus aureus*). (+)-Actinodaphnine, (+)-N-Me-actinodaphnine, (+)-anonaine, anhydroushinsunine, anhydroushinsunine MeI, ushinsunine isomethine, O-Me-armepavine methine and O,O-di-Et-N-Me-coclaurine methine had potent antifungal activities against *Candida albicans*, *Cryptococcus neoformans* and other *Candida* species[237,238].

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