Medicinal & Aromatic Plants

Katoch D and Singh B, Med Aromat Plants 2015, 4:4
DOI: 10.4172/2167-0412.1000212

Review Article Open Access

Phytochemistry and Pharmacology of Genus *Zephyranthes*

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Abstract

The genus *Zephyranthes* belongs to family Amaryllidaceae, well known for its ornamental and medicinal values. The species of this genus are bulbous perennials having attractive flowers that generally bloom after heavy rains. The genus had been used traditionally by inhabitants of different countries like India, Peru, China and Africa for various therapeutic purposes like ear and chest ailments, viral infections, tumors, breast cancer, diabetes mellitus. Phytochemically this genus is reported to contain alkaloids, ceramides, phospholipids, sterols, fatty acids, flavonoids and their glycosides. The alkaloids of this genus are broadly classified as Amaryllidaceae alkaloids having different skeleton types. Pharmacological studies have revealed its potential for different activities like anticancer, antifungal, acetylcholinesterase inhibition, antiviral and antibacterial. In the present review the available information on phytochemical and pharmacological studies of *Zephyranthes* genus has been compiled.

Keywords: *Zephyranthes*; Amaryllidaceae alkaloids; Ceramides; Anticancer; Acetylcholinesterase inhibition.

Introduction

Zephyranthes is a genus of bulbous perennials belonging to family Amaryllidaceae. This family is one of the top 20 most widely used plant families well known for its ornamental value. The plants of this family are used by native peoples of different countries for treating various diseases. The genus *Zephyranthes* is one amongst 75 genera under this family [1,2]. It consists of about 90 species and out of which few have been studied for their chemical constituents [3,4]. The phytochemical work on this genus revealed the diversity of compounds especially alkaloids having various pharmacological activities. The name *Zephyranthes* is derived from word '*Zephyrus*' means the Greek God of west wind that reawakened nature each spring and '*anthos*' meaning flower. Common name for the species in this genus are fairy lily, rain flower, zephyr lily, magic lily, rain lily [5]. The present review summarises the phytochemical and pharmacological studies within the genus *Zephyranthes*.

Geographical distribution

The genus *Zephyranthes* is native to western hemisphere and to the higher altitudes like Mexico, Argentina where the species possesses greatest cold hardiness potential. The genus has been naturalised and cultivated as ornamental plant in places like India, Hawaii, Indonesia, Thailand etc. Some species of this genus are widespread whereas some are confined to small geographical area. Broadly these plants are distributed in temperate to tropical areas of the world [6,7].

Morphology and taxonomy

The genus *Zephyranthes* vary in bulb, flower and leaf characteristics i.e. size, color etc. The species belonging to this genus are perennial bulbs which tolerate many natural habitats i.e. from wet soil to dry conditions. Bulbs are covered with dark brown or black tunica and contractile roots. Bulbs size varies from 2.5 to 5cm in diameter [3]. The leaves are deciduous with sheathing basis and have linear blades. The size of leaves varies from tiny to broad. Flowers are funnel shaped having six petals and more often appears in spring and summer. These have general tendency to bloom after a heavy rain therefore named as rain lily. The flowers of this genus are solitary, declinate, point straight upward and have equal stamen length [3,7,8]. Seeds are D-shaped or wedge shaped. *Zephyranthes* bulbs can flower several times during one season and the flower last after one to two days. Leaves may or may not be present during flowering. Beautiful flowers of this genus have increased its ornamental value. Flower color ranges from white, yellow, pink, sometimes contains various tints of yellow to sulphur. Some species have sweet fragrant flowers [9,10].

Zephyranthes genus is scientifically classified under phylum Angiospermae, order Asparagales, family Amaryllidaceae and tribe Hippeastreae. This genus comprises about 90 species according to World checklist of selected plant families out of which few have been studied phytochemically [7,4].

Traditional usage

The genus *Zephyranthes* has been used as folk medicine in many countries. Plant parts like bulbs and leaves have been used for the treating various diseases. In the history of Peru *Z. parulla* had been used for the treatment of tumors, in China *Z. rosea* used for treatment of breast cancer. The leaves of *Z. candida* have been used by indigenous peoples in Africa for treatment of diabetes mellitus. In India bulb extracts of *Z. rosea* and Z. *flava* had been used for variety of therapeutic purposes, e.g. treatment of diabetes, for ear and chest ailments and against viral infections. Traditional usage of this genus from very simple health problems like head ache, cough and cold, boils to very complicated diseases like breast cancer, tuberculosis, rheumatism, tumors shows its importance in treatment of various diseases [2,11,12].

Chemical constituents

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IHBT communication no. 3910

Received September 11, 2015; **Accepted** September 30, 2015; **Published** October 05, 2015

Citation: Katoch D, Singh B (2015) Phytochemistry and Pharmacology of Genus *Zephyranthes*. Med Aromat Plants 4: 212. doi:10.4172/2167-0412.1000212

The family Amaryllidaceae is known to contain characteristic alkaloids known as Amaryllidaceae alkaloids (AAs) mainly responsible for different pharmacological activities [1-2]. Phytochemical investigation on *Zephyranthes* has been initiated in 19th century. Different researchers have reported many compounds from this genus which includes alkaloids, flavonoids, flavans, gibberllins, phospholipids, sterols, lectins, terpenoids and ceramides [13-39] but most of the reports focused on alkaloids. The skeleton types of AAs reported from this genus are lycorine, homolycorine, crinine and haemanthamine, tazettine, pancratistatin, galanthamine types. Table 1 summarize the chemical constituents reported in different species of this genus. Figure 1 shows the chemical structure of the compounds isolated from the genus. To the best of our knowledge about seventy alkaloids have been isolated from this genus.

The initial phytochemical investigation had been done in 1940s by Greathouse, and he reported the presence of an alkaloid 'lycorine' already reported from plants of Amaryllidaceae family, in bulbs and root tissues of *Z. texana* [13]. Later on in 1950s Boit et al., reported AAs from different species of *Zephyranthes* i.e. lycorine, nerinine, haemanthamine, tazettine from *Z. candida*; lycorenine, galanthine, haemanthamine from *Z. citrina*; lycorine, galanthine, tazettine, haemanthamine from *Z. carinata*, lycorine, galanthamine from *Z. rosea*; haemanthamine and galanthamine from *Z. andersoniana* [14-16]. In 1960s, a flavonoids, rutin and alkaloids lycorine, tazettine, nerinine, haemanthidine and zephyranthine were reported from the petals and bulbs of *Z. candida* respectively [17-20]. In the same decade, Dopke et al., reported a new alkaloid tubispacin along with lycorine, powellin, nerispin from the bulbs of *Z. tubispatha* and Maheshwari et al., reported a gibberellin like substance from *Z. lancasteri* during seed development [21-22]. At the end of this decade Rao reported lycorine and haemanthamine from *Z. robusta* [23].Thereafter different groups had investigated this genus and in 1970s the presence of AAs, pretazettine, carinatine, lycorine, galanthine, haemanthamine, maritidine in bulbs of *Z. carinata*, *Z. robusta* and *Z. sulphurea*; a flavonoid glycoside, kaempferol-3-*O*-rhamnoglucoside in flowers of *Z. candida* was reported [24-27].

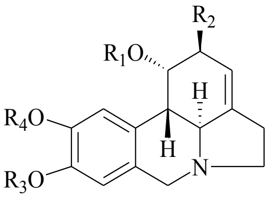
In 1980s Pettit et al., and Ghosal et al., reported alkaloids, pancratistatin, (+)-epimaritidine, crinamine and haemanthamine, maritidine, ungeremine, criasbetaine, zefbetaine, zeflabetaine, alkaloidal phospholipids, two lactam alkaloid, three glucosyloxy alkaloid; flavans, 7-hydroxy-3',4'-methylenedioxyflavan and its glycoside, 7,4'-dihydroxy-3'-methoxyflavan and 7-methoxy-2'-hydroxy-4',5'-methylenedioxyflavan from bulbs and flowers of different species [28-32]. In 1990s, Pettit et al., Kojima et al., reported trans-dihydronarciclasine: an antineoplastic compound, 1-*O*-(3-hydroxybutyryl) pancratistatin and 1-*O*-(3-*O*-β-d-glucopyranosylbutyryl) pancratistatin from *Z. carinata* and *Z. candida* [33,34]. In 2001 Nagatsu et al., Herrera et al., and Mutsuga et al., reported alkaloids oxomaritidine, maritidine, hemanthamine, haemanthidine, vittatine, lycorine, galanthine, narcissidine, 4,5-ethano-2,8-dimethoxy-9-hydroxy-phenantridine, 1-*O*-(3-hydroxybutyryl) pancratistatin , 1-*O*-(3-*O*-β-d-glucopyranosylbutyryl) pancratistatin, pancratistatin, tortuosine, galanthine, carinatine, trispharidine, hamayne from *Z. citrina* and *Z. carinata* [33-37]. In 2006, a novel mannose binding lectin was purified from bulbs of *Z. candida* [38].

In 2009-10, three reports showed the presence of ceramides in the genus. This was the first report of ceramides from this family. The ceramides: zephyranamide A, zephyranamide B, zephyranamide C, zephyranamide D, candidamide A and candidamide B were isolated

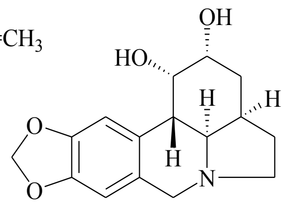
S. No.	Species	Part of plant	Chemical constituents reported	References
1	*Z. candida*	Flowers, bulbs, whole plant, aerial part	Lycorine, nerinine, haemanthamine, tazettine, rutin, haemanthidine, zephyranthine, kaempferol-3-*O*-rhamnoglucoside, trans-dihydronarciclasine, lectin, zephyranamide A, zephyranamide B, zephyranamide C, zephyranamide D, candidamide A, candidamide B, (2S)-3',7-dihydroxy-4'-methoxyflavan, (2S)-4'-hydroxy -7-methoxyflavan, (2S)-4',7-dihydroxyflavan, 7-hydroxy-3',4'-methylene-dioxyflavan, ambrettolide, β-sitosterol, β-daucosterin, pancratistatin, *N*-methylhemeanthidine chloride, *N*-methyl-5,6-dihydroplicane, *O*-methylnerinine, *N*-ethoxycarbonyl ethylcrinasiadine, *N*-isopentylcrinasiadine, 3-epimacronine, *N*-methylcrinasiadine, trisphaeridine, 5,6-dihydrolycorine, nigragillin, 2-hydroxy albomaculine, 6α-hydroxyhippeastidine, 10-deoxy-6α-hydroxyhippeastidine, 6β-hydroxyhippeastidine, 7-hydroxy-3',4'-methylenedioxyflavan	[14,18-20,25,33,38-41,43,45,52]
2	*Z. carinata*	Bulbs	Lycorine, galanthine, tazettine, haemanthamine, pretazetine, carinatine, 1-*O*-(3-hydroxybutyryl) pancratistatin and 1-*O*-(3-*O*-β-d-glucopyranosylbutyryl) pancratistatin, 4,5-ethano-2,8-dimethoxy-9-hydroxy-phenantridine, pancratistatin, tortuosine, trisphaeridine, hamayne	[15,24,34,36]
3	*Z. grandiflora*	Bulbs	Pancratistatin, Zephgrabetaine, lycorine, galanthine, lycoramine, hamayne, hamanthamine, tortuosine, ungeremine	[31,44]
4	*Z. robusta*	Bulbs	Galanthamine, 3-epimacronine, hippeastidine, lycoramine, galanthine, haemanthamine, haemanthidine, hamayne, tazettine, vittatine, lycorine, 11-hydroxy vittatine, 8-*O*-demethylmaritidine	[23,27, 46,51]
5	*Z. citrina*	Whole plant	Lycorine, lycorenine, galanthine, haemanthamine, Oxomaritidine, maritidine, hemanthamine, haemanthidine, vittatine, galanthine, narcissidine	[15,37]
6	*Z. rosea*	Bulbs	Lycorine, galanthamine, Epimaritidine, crinamine, haemanthamine, maritidine	[15,28]
7	*Z. flava*	Bulbs, seeds, flowers	7-hydroxy-3',4'-methylenedioxyflavan and its glycoside, 7,4'-dihydroxy-3'-methoxyflavan and 7-methoxy-2'-hydroxy-4',5'-methylenedioxyflavan, maritidine, 2-*O*-glycerophosphoryllycorine, phosphatidyllycorines, phosphatidylpseudolycorines, phosphatidyllycoriniium methocation, 2-oxy phenanthridinium, zefbetaine, zeflabetaine, crinamine, haemanthamine, lycorine, pseudolycorine, narciclassine, protorimine, kalbreclassine, lycorine-1-*O*-β-D-glucoside, pseudolycorine-1-*O*-β-D-glucoside, criasbetaine, ungeremine	[29,30]
8	*Z. concolor*	Bulbs, aerial part	Chlidanthine, galanthamine, galanthamine *N*-oxide, lycorine, galwesine, epinorgalanthamine	[42]
9	*Z sulphurea*	Bulbs	Tazetine, lycorine, maritidine	[27]
10	*Z. andersoniana*	Bulbs	Haemanthamine, galanthamine	[18]
11	*Z. tubispatha*	Bulbs	Lycorine, powellin, nerispin, tubispacin	[21]
12	*Z. texana*	Bulbs	Lycorine	[13]
13	*Z. lancasteri*	Seeds	Gibberllin like substance	[22]

Table 1: List of chemical constituents reported from different species of genus *Zephyranthes.*

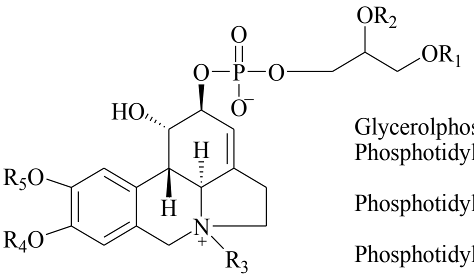
Lycorine type AAs:



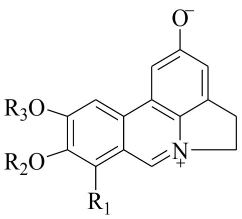
Lycorine, R_1=H,R_2=OH,R_3+R_4= -CH_2-
Lycorine 1-*O*-*β*-D-glucoside, R_1=Glc, R_2=OH, R_3+R_4= -CH_2-
Pseudolycorine,R_1=H,R_2=OH,R_3=H,R_4=CH_3
Pseudolycorine 1-*O*-*β*-D-glucoside, R_1=Glc, R_2=OH, R_3=H, R_4=CH_3
Galanthine,R_1=H,R_2=OCH_3,R_3=CH_3,R_4=CH_3
9-*O*-demethylgalanthine, R_1=H,R_2=OCH_3, R_3=CH_3, R_4=H
Carinatine,R_1=H,R_2=CH_3,R_3=CH_3,R_4=H



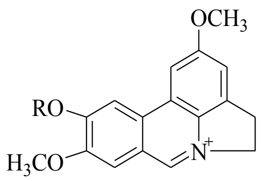
Zephyranthine



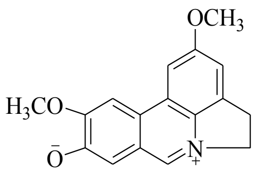
Glycerolphosphorylycorine, R_1=R_2=R_3=H, R_4+R_5=-CH_2-
Phosphotidyllycorines, R_1= -palmitoyl, R_2= -stearoyl, R_3=H, R_4+R_5=-CH_2-
R_1= -palmitoyl, R_2= -oleoyl, R_3=H, R_4+R_5=-CH_2-
Phosphotidylpseudolycorines, R_1= -palmitoyl, R_2= -stearoyl, R_3=R_5=H, R_4=CH_3
R_1= -palmitoyl, R_2= -oleoyl, R_3=R_5=H, R_4=CH_3
Phosphotidylmethyllycorinium cations,R_1= -palmitoyl, R_2= -stearoyl, R_3=CH_3
(α and β , R_4+R_5=-CH_2-



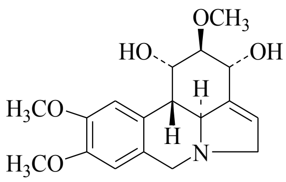
Criasbetaine, R_1=H,R_2=R_3=CH_3
Ungeremine, R_1=H,R_2+R_3=-CH_2-
Zefbetaine, R_1=R_2=H, R_3=CH_3
Zeflabetaine, R_1=OCH_3, R_2+R_3=-CH_2-



Tortuosine, R=CH_3
4,5-ethno-2,8-dimethoxy-9-hydroxyphenanthridine, R=H

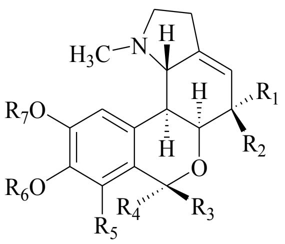


Zephgrabetaine

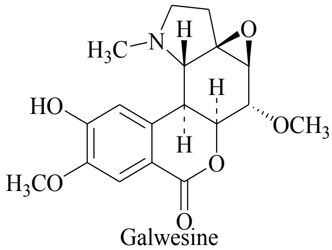


Narcissidine

Homolycorine type AAs:

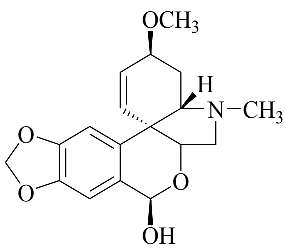


Lycorenine, R_1=R_2=R_3=R_5=H, R_4=OH, R_6=CH_3, R_7=CH_3
Nerinine, R_1=R_2=R_3=H, R_4=OH, R_5=OCH_3, R_6=CH_3, R_7=CH_3
O-methylnerinine, R_1=R_2=R_3=H, R_4=R_5=OCH_3, R_6=CH_3, R_7=CH_3
2-hydroxyalbomaculine, R_1=H, R_2=OH, R_3+R_4=O, R_5=OCH_3, R_6=CH_3, R_7=CH_3

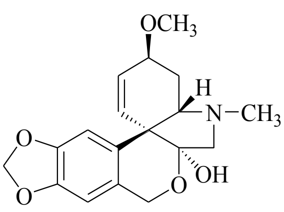


Galwesine

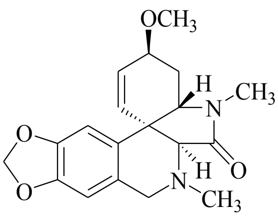
Tazettine type AAs:



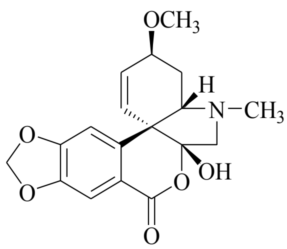
Pretazettine



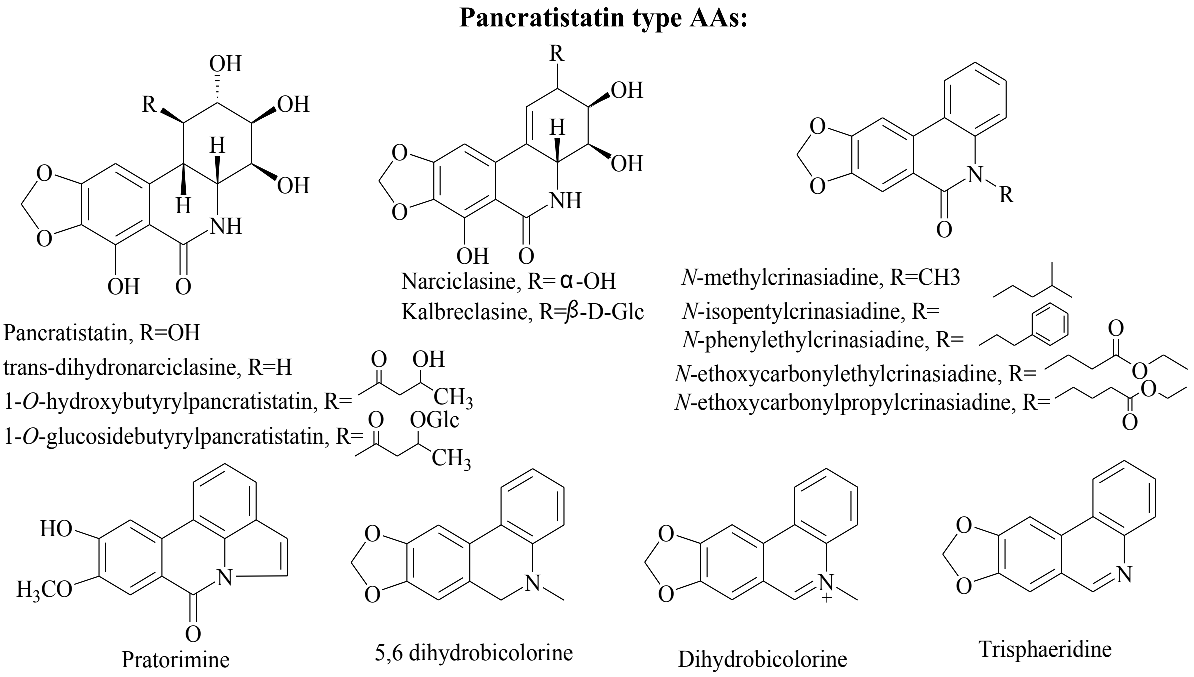
Tazettine

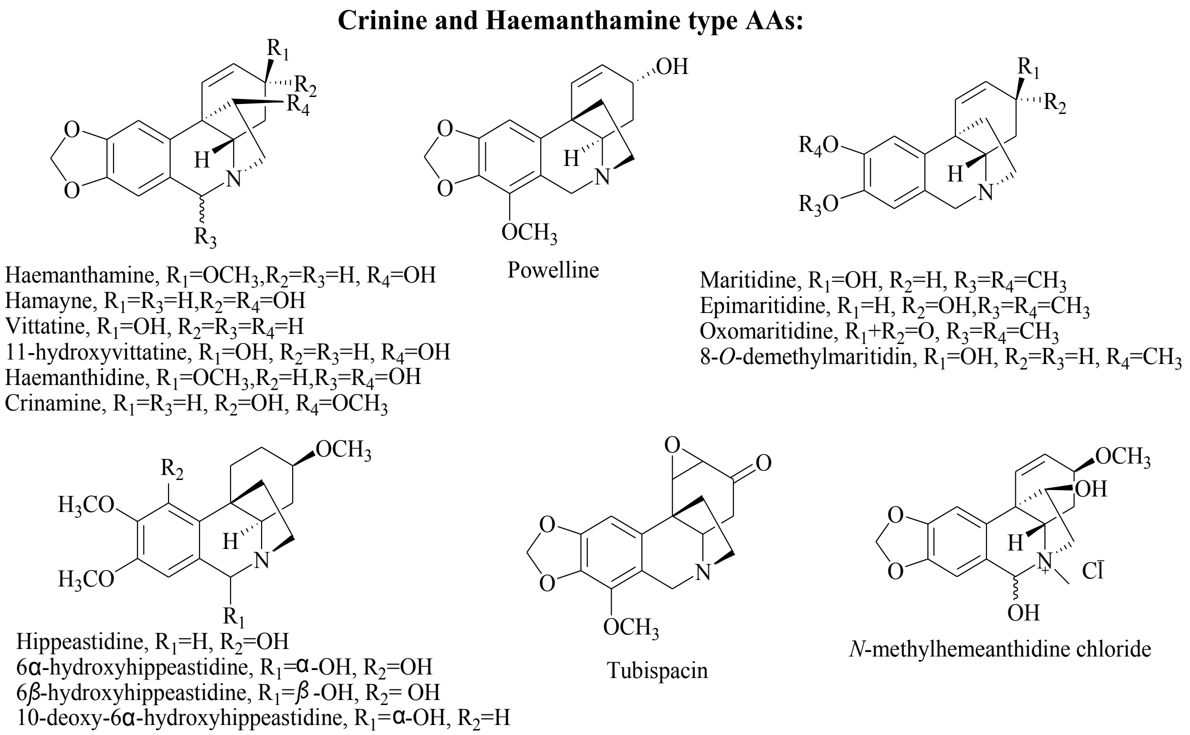


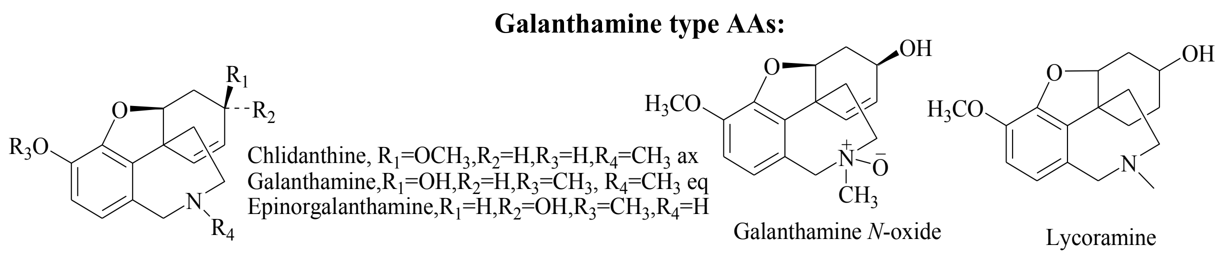
N-methyl-5,6-dihydroplicane



3-epimacronine


Pancratistatin type AAs:
Pancratistatin, R=OH
trans-dihydronarciclasine, R=H
1-*O*-hydroxybutyrylpancratistatin, R=
1-*O*-glucosidebutyrylpancratistatin, R=
Narciclasine, R= α-OH
Kalbreclasine, R=β-D-Glc
N-methylcrinasiadine, R=CH3
N-isopentylcrinasiadine, R=
N-phenylethylcrinasiadine, R=
N-ethoxycarbonylethylcrinasiadine, R=
N-ethoxycarbonylpropylcrinasiadine, R=
Pratorimine
5,6 dihydrobicolorine
Dihydrobicolorine
Trisphaeridine


Crinine and Haemanthamine type AAs:
Haemanthamine, R_1=OCH_3,R_2=R_3=H, R_4=OH
Hamayne, R_1=R_3=H,R_2=R_4=OH
Vittatine, R_1=OH, R_2=R_3=R_4=H
11-hydroxyvittatine, R_1=OH, R_2=R_3=H, R_4=OH
Haemanthidine, R_1=OCH_3,R_2=H,R_3=R_4=OH
Crinamine, R_1=R_3=H, R_2=OH, R_4=OCH_3
Powelline
Maritidine, R_1=OH, R_2=H, R_3=R_4=CH_3
Epimaritidine, R_1=H, R_2=OH,R_3=R_4=CH_3
Oxomaritidine, R_1+R_2=O, R_3=R_4=CH_3
8-*O*-demethylmaritidin, R_1=OH, R_2=R_3=H, R_4=CH_3
Hippeastidine, R_1=H, R_2=OH
6α-hydroxyhippeastidine, R_1=α-OH, R_2=OH
6β-hydroxyhippeastidine, R_1=β -OH, R_2= OH
10-deoxy-6α-hydroxyhippeastidine, R_1=α-OH, R_2=H
Tubispacin
N-methylhemeanthidine chloride


Galanthamine type AAs:
Chlidanthine, R_1=OCH_3,R_2=H,R_3=H,R_4=CH_3 ax
Galanthamine,R_1=OH,R_2=H,R_3=CH_3, R_4=CH_3 eq
Epinorgalanthamine,R_1=H,R_2=OH,R_3=CH_3,R_4=H
Galanthamine *N*-oxide
Lycoramine

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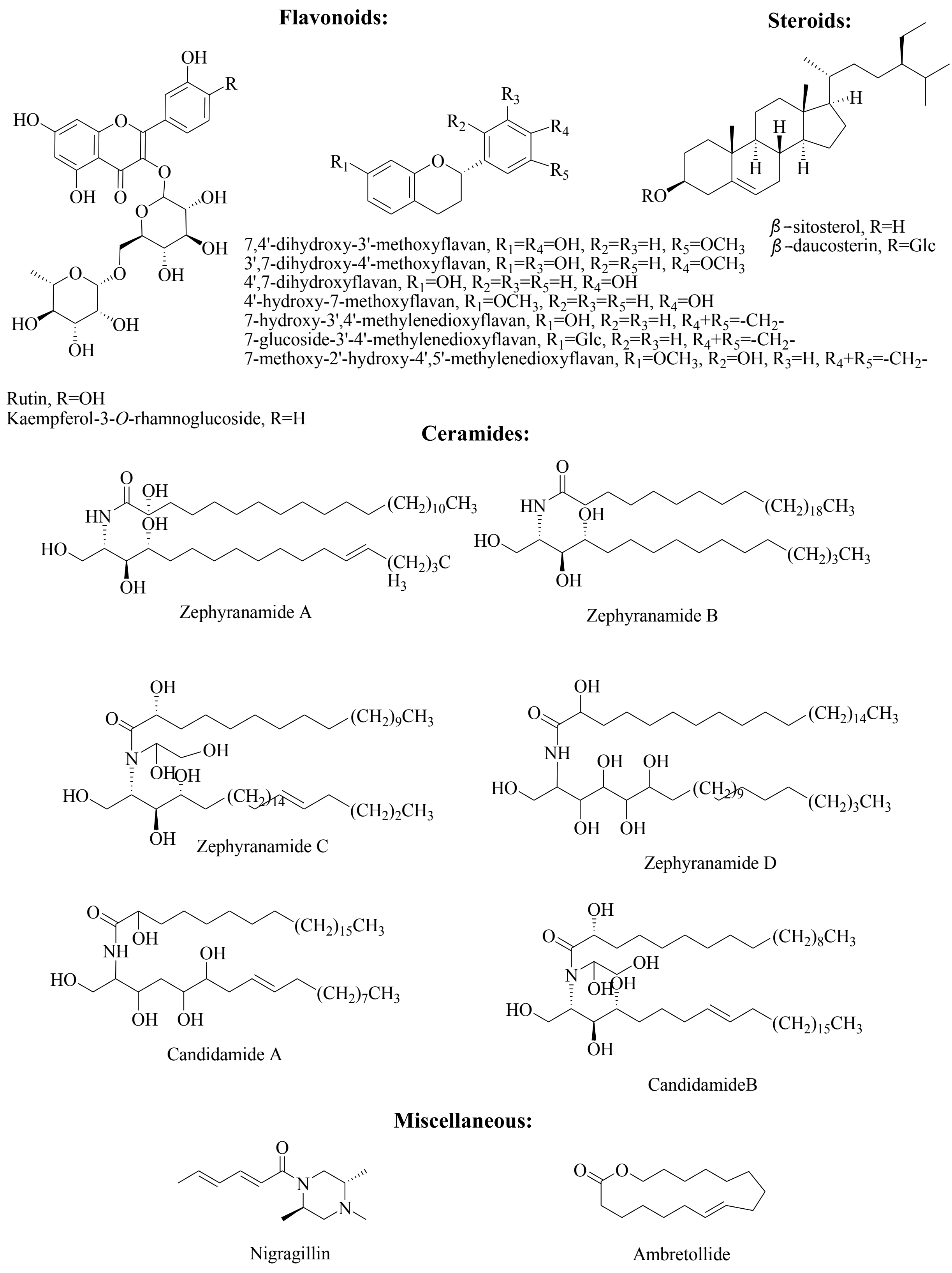

Figure 1: Chemical structure of compounds reported from genus *Zephyranthes.*

from the bulbs of *Z.candida* [39-41]. During this decade flavans, sterols were also reported from the same species [39]. In past five years, the work on this genus was accelerated with isolation of new alkaloids by different researchers, Reyes-chilpa et al., in 2011 reported chlidanthine, galanthamine, galanthamine-*N*-oxide from bulbs of *Z.concolor* [42], Luo et al., in 2012 reported seven new alkaloids, *N*-methylhemeanthidine chloride, *N*-methyl-5,6-dihydroplicane, *O*-methylnerinine, *N*-ethoxycarbonylethylcrinasiadine, *N*-ethoxycarbonyl propylcrinasiadine, *N*-phenethylcrinasiadine, *N*-isopentylcrinasiadine from whole plant of *Z. candida* [43]; in 2013 Katoch et al., reported Zephgrabetaine, a new betaine alkaloid from bulbs of *Z. grandiflora* [44]; in 2014 Shitara et al., reported a new homolycorine type alkaloid 2-hydroxyalbomaculine along with three new crinine type alkaloid 6α-hydroxyhippeastidine, 10-deoxy-6α-hydroxyhippeastidine and 6β-hydroxyhippeastidine from aerial part of *Z. candida* [45] and revised NMR for an alkaloid from *Z. robusta* given by Safratova et al., for 9-*O*-demethylgalanthamine [46]. To the best of our knowledge different compounds reported till August 2015 in this genus are compiled in this review.

Along with isolation of pure compounds different researchers have applied modern hyphenated techniques like GC/MS, LC/MS for chemical profiling of extracts. Compounds mainly alkaloids were identified on the basis of their characteristic mass fragmentation pattern. Reports showing GC/MS based chemical profiling, identified galanthamine, lycoramine, vittatine, nerbowdine, haemanthamine, tazettine, galanthine in bulbs of *Z. robusta* and galanthamine, lycoramine, vittatine, nerbowdine, haemanthamine, tazettine, galanthine in bulbs of *Z. grandiflora* [47-48]. However, chemical profiling of *Z. grandiflora* bulbs by UPLC/MS identified AAs: lycorine, lycoramine, dihydrovittatine, lycoramine-*N*-oxide, galanthine, hamayne, zaiden, ambelline, crinamidine, haemanthamine, vittatine, zefbetaine, ungeremine, 1-*O*-(3-hydroxybutyryl)-pancratistatin, tortuosine [49].

Pharmacological activities

A number of pharmacological studies have been reported from different species of *Zephyranthes.* Pharmacological activities of these species are mainly because of alkaloids present in these plants i.e. AAs. Different activities reported by various research groups are:

Antimicrobial activity

Greathouse in 1941 investigated the resistance to root rot caused by *Phymatotrichum omnivorum* in *Z. texana* and *Cooperia pedunculata* and suggested that the toxicity, quantity and localization of the AAs indicate that alkaloid content of these plants may contribute to the immunity of bulbs from root rot [13]. In 2009 Wu et al., evaluated the antimicrobial activity i.e. antibacterial activities against *Staphylococcus aureus* and *Escherichia coli* and antifungal activities against *Aspergillus niger*, *Candida albicans* and *Trichophyton rubrum* against Penicillin G and ketoconazole as positive control for bacteria and fungi respectively and reported that candidamide A and candidamide B showed moderate activity [40].

In 2010 Singh et al., reported the significant antifungal activity of AAs isolated from *Z. citrina* against *Alternaria solani, A. Triticina, Curvularia lunata, C. Maculans, Cercospora malvacearum, Fusarium udum, Helminthosporium pisi, H. Speciferum, Erysisphe sp.* and *Ustilago cynodontis* [50].

Antiviral activity

In 2014 Oluyemisi et al., reported antiviral activity of lycorine, trisphaeridine and 7-hydroxy-3',4'-methylenedioxyflavan. However lycorine was most active as compared to trisphaeridine and 7-hydroxy-3',4'-methylenedioxyflavan [51,52].

Anticancer activity

In 1964, bulb extract of *Z. candida* displayed activity against human epidermoid carcinoma of the nasopharynx, KB system in the US national cancer Institute research programs [18-20]. In 1966, Fransworth in his review on biological and phytochemical screening of plants reported 19 species of Amaryllidaceae family to be active as tumor inhibitor and *Z. carinata* and *Z. texana* were among these plants [53]. In 1986 Ghosal et al., reported significant antitumour activity of ungeremine, criasbetaine, zefbetaine, zeflabetaine in P-388 and KB systems and caused cytolysis of Sarcoma 180 ascites tumor cells. In 1990 Pettit et al., found the principal cytostatic (P-388) compound *trans*-dihydronarciclasine from bulbs of *Z. candida* using active extract [29].

Antimitotic activity

In 1978, Furmanowa et al., studied the effect of haemanthamine, lycorine and extracts from *Z. robusta* on dividing cells and result suggest that antimitotic activity exhibited by *Z. robusta* may be caused by lycorine and haemanthamine [26].

Antineoplastic activity

In 1984 and 1990 Pettit et al., reported two antineoplastic compounds, pancratistatin from *Z. grandiflora* and trans-dihydronarciclasine from *Z. candida* bulbs using the P-388 lymphocytic leukemia bioassay [31, 33].

Cytotoxicity

In 1998 Kojima et al., compared the cytotoxicity of 1-*O*-(3-hydroxybutyryl) pancratistatin, 1-*O*-(3-*O*-β-d-glucopyranosylbutyryl) pancratistatin and pancratistatin against KB, HeLa and P388-D1 cells and found that cytotoxicity of 1-*O*-(3-hydroxybutyryl) pancratistatin is three times higher than pancratistatin on these cells. Their result indicates significant difference in activity could be related to structure [38]. In 2001 Mutsuga et al., evaluated the cytotoxicity of isolated alkaloids against human epidermoid carcinoma KB cells and showed that pancratistatin and its derivative showed significant activity [36]. In 2012 Luo et al., alkaloids from *Z. candida* were evaluated *in-vitro* cytotoxicity against five human cancer cell lines (HL-60, K562, A549, HepG2, HT-29) and beas-2B immortalized human bronchial epithelial cell line which showed that lycorine, haemanthamine, *N*-methylhemeanthidine chloride, *N*-phenethylcrinasiadine are more potent than positive control (cisplatin) [43]. In 2013 Katoch et al., studied *in-vitro* cytotoxicity of alkaloids from *Z. grandiflora* against C-6 (rat glioma cells) and CHO-K1 (Chinese hamster ovary cells) and reported a dose dependent cytotoxic effect with prominent activity exhibited by lycorine and haemanthamine [44].

Acetylcholinesterase activity

In 2011 Reyes-Chilpa et al., reported acetylcholinesterase activity of Chlidanthine and galanthamine *N*-oxide isolated from bulbs of *Z. concolor* to be five times less active than galanthamine. The alkaloids chlidanthine, galanthamine, galanthamine-*N*-oxide showed poor inhibitory activity of HIV-1 replication and cytotoxicity against human MT-4 cells [42]. In 2011 Cahlikova et al., reported the promising cholinesterase inhibitory activities of alkaloid extract of bulbs of *Z. grandiflora* against human blood acetylcholinesterase and human plasma butyrylcholinesterase [48]. In 2013 Kulhankova et al., reported

8-*O*-demethylmaritidine, alkaloid from *Z. robusta* Baker showed significant acetylcholinesterase inhibition activity and indicates that this activity is mainly related with galanthamine- and lycorine-type skeleton and galanthamine type skeleton are more active inhibitor than other skeletons of AAs. However, crinine alkaloids showed mainly cytotoxicity but not acetylcholinesterase inhibition activity. These alkaloids were also screened for antioxidant activity but were found to be inactive [51].

The different pharmacological activities reported on *Zephyranthes* includes antifungal, antiviral, cytotoxicity, acetylcholinesterase inhibitor, anticancer, antimitotic activities and these were broadly related with isolated AAs and extracts. Among the different skeleton types of AAs lycorine, pancratistatin, haemanthamine and crinine type skeletons were reported to be active against cancer whereas galanthamine type skeletons were reported to be more active inhibitor for acetylcholinesterase.

Conclusion

The genus *Zephyranthes* has immense potential for exploring the chemical compounds for identification as well as isolation for different pharmacological activity. Many species are known but only few are investigated for their phytochemical constituents. The information compiled in this review will help the researchers to use this genus for societal benefit.

Acknowledgements

The authors are grateful to Director, CSIR-IHBT, Palampur for their support during work. A financial support received from Department of Science and Technology, New Delhi is highly acknowledged.

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