

Review

Phytochemical and Biological Aspects of *Zephyranthes citrina* Baker: A Mini-Review

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Abstract: *Zephyranthes citrina* Baker is a bulbous herb, commonly known as yellow rain lily belongs to the family Amaryllidaceae. It is a native of tropical and subtropical America but nowadays it is cultivated as a popular ornamental herb in several parts of the world including India. This herb represents one of the richest sources of phytochemicals, especially alkaloids and possesses great potential for pharmaceutical applications. It shows remarkable antiprotozoal, antimicrobial, anti-Alzheimer, cytotoxic, antioxidant, anti-inflammatory, analgesic, and dye removal activities. This review is an effort to give a detailed study of the literature on the biological activities of *Zephyranthes citrina*. This review concludes that *Zephyranthes citrina* has a great potential to treat various diseases and could be used as a source for novel healthcare products in the near future, which requires further experimentation.

Keywords: Amaryllidaceae alkaloids; Biological activities; Traditional medicines; Yellow rain lily; *Zephyranthes citrina*

1. Introduction

Since the beginning of human farming practices, the role of plants in medicine has been of immense importance (Pastorino *et al.* 2018). Plants have always been a well-known source of food, drug, and recent statistic show that more than 45% of all approved drugs from 1981 to 2019 are of natural origin or mimics thereof (Newman and Cragg 2020). According to the World Health Organization, medicinal plants would be the prime source for procuring a variety of drugs (Rates 2001). Almost 80% who live in developed countries are said to be dependent on the use of traditional medicine or traditional medicinal plants. The practice of traditional medicinal plants is extensively spread in India, China, Japan, Pakistan, Sri Lanka, and Thailand (Abdala *et al.* 2012; Singh *et al.* 2020). Presently, there is a hike in medicinal plant utilization in the world, due to the proven efficacy of medicinal plants, in healing several diseases and claims that show it is safe to be used (Perez Gutierrez and Baez 2009; Michel *et al.* 2020). Many plant species have been recorded to exert pharmacological properties due to their phytoconstituents such as alkaloids, flavonoids, glycosides, saponins, steroids, tannins, and terpenoids (Paul *et al.* 2015; Paul 2016; Paul and Sinha 2016).

Plants of the family Amaryllidaceae, a group of monocotyledonous species consisting of about 85 genera and 1100 species, are one of the most significant alkaloid-containing plant taxa (Bastida *et al.* 2006; Jin and Yao 2019). The genus *Zephyranthes* is naturally occurring in the Western hemisphere up to the higher altitudes like Mexico and Argentina, in tropical and subtropical areas of the Americas. Species of the genus have been naturalized and cultivated as ornamental plants in places like India, Hawaii, and Indonesia (Meerow *et al.* 1999; Katoch and Singh 2015). These group of plants are commonly known as "rain lilies" owing to their

tendency to bloom after a period of rain (Fernández-Alonso and Groenendijk 2004). Genus *Zephyranthes* consists of economically important plant species due to their high ornamental value and presence of valuable bioactive compounds. The chemical structures of these alkaloids are very variable as well as their pharmacological properties (Cahlíková *et al.* 2011; Syeed *et al.* 2021). *Zephyranthes citrina* Baker commonly known as yellow rain lily or yellow little witch inhabits humid places and appears immediately after the start of the rainy season. It is a native of tropical and subtropical America (León 1946; Müller-Doblies 1996; Singh *et al.* 2010). To date, however, the knowledge of the chemical compositions of *Z. citrina* is still limited.

However, to the best of our knowledge, and as per the extensive literature survey, no attempt has been reported to cumulatively compile the information in the form of a review that covers all the significant aspects of *Zephyranthes citrina*. Thus, the current review aimed at documenting and critically assessing the up-to-date information of *Zephyranthes citrina* based on botanical description, traditional uses, phytochemical constituents, and biological activities.

2. Taxonomic Classification

Domain: Eukaryota

Kingdom: Plantae

Phylum: Tracheophyta

Class: Liliopsida

Order: Asperagales

Family: Amaryllidaceae

Genus: *Zephyranthes*

Species: *Zephyranthes citrina*

Binomial name: *Zephyranthes citrina* Baker

Common names: citron zephyr lily, yellow rain lily

3. Botanical Description

Zephyranthes citrina is a perennial, bulbous herb with green leaves dull 4 mm wide (Bobby *et al.* 2003). The one-inch lemon yellow flowers of *Z. citrina* spring forth in late summer. It blooms luxuriantly in natural grasslands and as well as in gardens after rain fall (Prakash and Vedanayaki 2019a; Prakash and Vedanayaki 2019b). Flowers are erect, funnel-shaped, 3.1–5 cm. Stamens are 1.2–2 cm long, diverged in 2 distinctly sub-equal sets. Anthers are 5–7 mm long; style longer than perianth tube; stigma capitate, usually among or below anthers (Parmar 2016) (Fig. 1).



Figure 1. Different parts of *Zephyranthes citrina*. a. flowers, b. fruit, c. seeds, and d. bulb

4. Traditional Uses

The genus *Zephyranthes* is scattered over the world's tropical and warm regions and has been cultivated as ornamental plants for their colorful flowers and for their extensive use as traditional or folk medicines against various diseases in many countries and areas (Jin 2016). The bulbs, leaves, or whole plants of closely related species are used in traditional medicine for the treatment of various diseases (Katoch and Singh 2015). The decoction of leaves of *Zephyranthes candida* has been used in South Africa and tribes of Andhra Pradesh in India as a remedy for diabetes mellitus and in mainland China to treat infantile convulsions, epilepsy, and tetanus (Watt and Breyer-Brandwijk 1962; Agarwal 1997; Zhan *et al.* 2017a). *Zephyranthes parulla* has been employed in Peru as a treatment for tumors (Pettit *et al.* 1984; Trimiño Ayllón *et al.* 1989). In China, *Zephyranthes rosea* has been used in breast cancer treatment (Konrath *et al.* 2013; Kulhánková *et al.* 2013). *Zephyranthes flava* and *Zephyranthes rosea* are used for a variety of therapeutic purposes including viral infections in India (Ghosal *et al.* 1985; Ghosal *et al.* 1986; Kornienko and Evidente 2008). In Argentina, bulbs of *Zephyranthes carinata* are used for skin diseases and parasitosis in traditional Toba medicine (Martínez and Barboza 2010). The whole plants of *Z. carinata* are also used as a traditional Chinese medicine to treat swelling, snake bites, and stomach bleeding in China (Zhan *et al.* 2017b).

5. Phytochemical Constituents

The preliminary phytochemical studies showed that the bulb extract of *Zephyranthes citrina* contains alkaloids, flavonoids, phenolic compounds, saponins, tannin, and terpenoids in different quantities (Prakash and Vedanayaki 2019a). So far, phytochemical constituents of *Zephyranthes citrina* have not been intensively studied, and only a few alkaloids have been isolated from it. The species of *Zephyranthes* are known for producing a structurally exclusive

group of alkaloids, named Amaryllidaceae alkaloids (AAs). Boit *et al.* (1957) analyzed phytochemicals of *Zephyranthes citrina* and isolated four alkaloids, viz, galanthine, haemanthamine, lycorine, and lycorenone. Herrera *et al.* (2001) isolated eight crinane and lycorane type alkaloids from whole plants of *Zephyranthes citrina*, namely, lycorine, haemanthamine, haemanthidine, vittatine, maritidine, galanthamine, narcissidine, and a new alkaloid oxomaritidine. Oxomaritidine alkaloid was reported for the first time from a natural source. Zephyramine, a new alkaloid also isolated from the bulbs of *Zephyranthes citrina* (Iraida *et al.* 2001). Recently, twenty known AAs of various structural types, and one new alkaloid of narcikachnine type, named narciliine, have been isolated from fresh bulbs of *Zephyranthes citrina*. The isolated known alkaloids belong to the crinine, homolycorine, lycorine, tazettine, haemanthamine, and galanthamine structural types, namely buphanisine, nerinine, galanthine, tazettine, haemanthamine, 1-O-acetylcaranine, methylpseudolycorine, lycorine, 6-hydroxyhippeastidine, 10-deoxy-6-hydroxyhippeastidine, narcissidine, haemanthidine, vittatine, maritidine, dihydromaritidine, 9-O-demethylgalanthine, 9-O-demethylhomolycorine, lycoramine, 8-O-demethylmaritidine, and tortuosine (Kohelová *et al.* 2021) (Table 1 and Fig. 2).

Table 1. List of isolated Amaryllidaceae alkaloids (AAs) from *Zephyranthes citrina*

AAs types	Alkaloid names	Plant parts	References
Haemanthamine	Haemanthamine	Aerial part and bulbs	Boit <i>et al.</i> , 1957; Herrera <i>et al.</i> , 2001; Kohelová <i>et al.</i> , 2021
	Haemanthidine	Aerial part and bulbs	Herrera <i>et al.</i> , 2001; Kohelová <i>et al.</i> , 2021
	Vittatine	Aerial part and bulbs	Herrera <i>et al.</i> , 2001; Kohelová <i>et al.</i> , 2021
	Maritidine	Aerial part and bulbs	Herrera <i>et al.</i> , 2001; Kohelová <i>et al.</i> , 2021
	Oxomaritidine	Aerial part and bulbs	Herrera <i>et al.</i> , 2001
	Dihydromaritidine	Bulbs	Kohelová <i>et al.</i> , 2021
	8-O-demethylmaritidine	Bulbs	Kohelová <i>et al.</i> , 2021
Lycorine	Lycorine	Aerial part and bulbs	Boit <i>et al.</i> , 1957; Herrera <i>et al.</i> , 2001; Kohelová <i>et al.</i> , 2021
	Galanthine	Aerial part and bulbs	Boit <i>et al.</i> , 1957; Herrera <i>et al.</i> , 2001; Kohelová <i>et al.</i> , 2021
	Narcissidine	Aerial part and bulbs	Herrera <i>et al.</i> , 2001; Kohelová <i>et al.</i> , 2021
	1-O-acetylcaranine	Bulbs	Kohelová <i>et al.</i> , 2021
	Methylpseudolycorine	Bulbs	Kohelová <i>et al.</i> , 2021
	9-O-demethylgalanthine	Bulbs	Kohelová <i>et al.</i> , 2021
	Tortuosine	Bulbs	Kohelová <i>et al.</i> , 2021
Crinine	Buphanisine	Bulbs	Kohelová <i>et al.</i> , 2021
	6-hydroxyhippeastidine	Bulbs	Kohelová <i>et al.</i> , 2021
	10-deoxy-6-hydroxyhippeastidine	Bulbs	Kohelová <i>et al.</i> , 2021
	Zephyramine	Bulbs	Iraida <i>et al.</i> , 2001
Homolycorine	Lycorenine	Bulbs	Boit <i>et al.</i> , 1957
	Nerinine	Bulbs	Kohelová <i>et al.</i> , 2021
	9-O-demethylhomolycorine	Bulbs	Kohelová <i>et al.</i> , 2021
Tazettine	Tazettine	Bulbs	Kohelová <i>et al.</i> , 2021
Galanthamine	Lycoramine	Bulbs	Kohelová <i>et al.</i> , 2021
Narcikachnine	Narciliine	Bulbs	Kohelová <i>et al.</i> , 2021

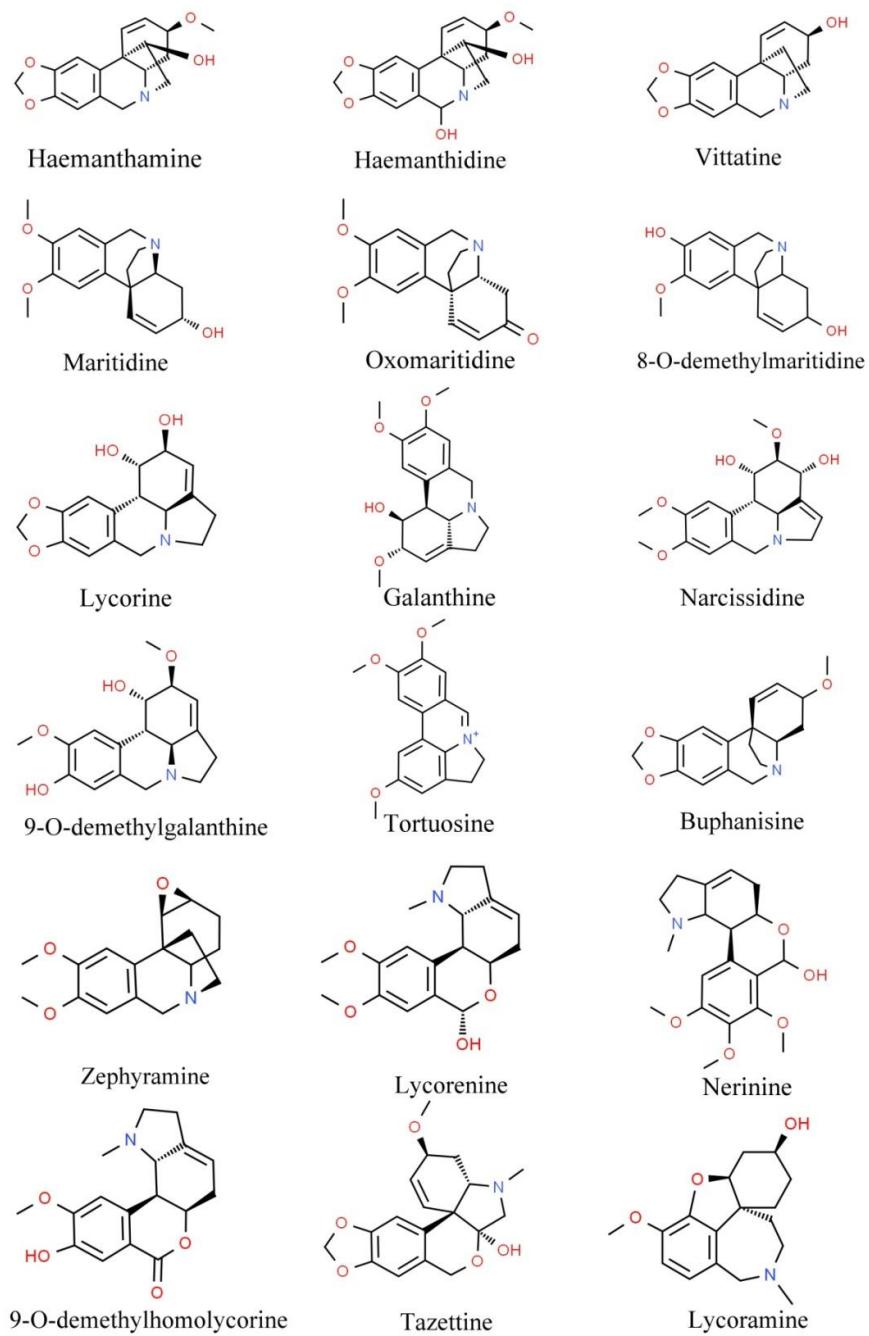


Figure 2. Structure of isolated alkaloids isolated from *Zephyranthes citrina*

6. Biological Activities

Zephyranthes citrina is a bulbous, monocotyledonous herb that has folkloric applications against several ailments and diseases. Only a very few biological as well as pharmacological investigations have been carried out based on the constituents mainly alkaloids present in it, a lot more can still be explored and utilized therapeutically. A summary of the findings of some of these studies is presented below (Fig. 3).

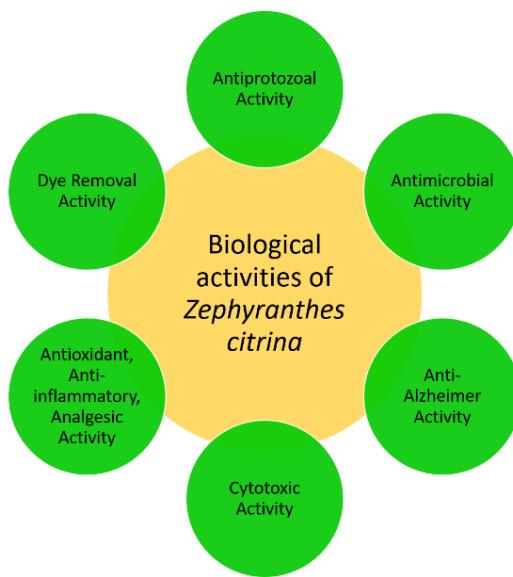


Figure 3. Different biological activities of *Zephyranthes citrina*

6.1. Antiprotozoal Activity

Antiprotozoal activity of a few isolated AAs was investigated using *in vitro* assay against *Trypanosoma brucei*, *Trypanosoma cruzi*, and *Plasmodium falciparum* (Herrera *et al.* 2001). According to their study haemanthidine showed some activity against *Trypanosoma brucei rhodesiense* (strain STIB900, stage trypomastigotes) with an IC₅₀ of 1.1 mg/ml. Alkaloid galanthine and oxomaritidine showed mild activity with IC₅₀ values of 3.1 mg/ml and 2.8 mg/ml, respectively. Haemanthidine also exhibited some activity against *Trypanosoma cruzi* (strain Tulahuen C4, stage trypomastigotes) with an IC₅₀ of 1.4 mg/ml. A mild activity was observed in galanthine against *Plasmodium falciparum* (strain K1, stage IEF) with an IC₅₀ of 0.2 mg/ml (Herrera *et al.* 2001).

6.2. Antimicrobial Activity

The antifungal activity of two isolated alkaloids (alkaloid A and alkaloid B) from bulbs of *Zephyranthes citrina* was observed against 10 phytopathogenic and saprophytic fungi, viz, *Aternaria solani*, *Aternaria triticina*, *Curvularia lunata*, *Curvularia maculans*, *Cercospora malvacearum*, *Erysiphe* sp., *Fusarium udum*, *Helminthosporium pisi*, *Helminthosporium speciferum*, and *Ustilago cynodontis*. Both alkaloids A and B were effective in inhibiting spore germination. In alkaloid B the maximum effect was observed against *Ustilago cynodontis* where 100% inhibition was seen at 400 mg/ml followed by *Curvularia lunata*, *Cercospora malvacearum* and *Helminthosporium pisi* which showed 100% spore germination inhibition at 600 mg/ml concentrations. Similar results were observed with alkaloid A, where 100% spore germination inhibition was seen at 800 mg/ml against *Curvularia lunata*, *Cercospora malvacearum* and *Helminthosporium pisi*. Alkaloid B was also used against *Erysiphe* sp. causing powdery mildew in *Impatiens balsamina* in the field as pre-and post-inoculation treatments. The alkaloid extract was effective in both pre-and post-inoculation treatments (Singh *et al.* 2010). Prakash and Vedanayaki (2020) were synthesized silver nanoparticles by using a methanolic extract of bulb of *Zephyranthes citrina*. Synthesized silver nanoparticles were investigated for antimicrobial activity against both bacterial (*Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Salmonella typhi*) and fungal strains (*Aspergillus niger*, *Candida albicans*, and *Fusarium oxysporum*). The results revealed that synthesized silver nanoparticles exhibit good inhibition efficiency against representative microorganisms.

6.3. Anti-Alzheimer Activity

Kohelová *et al.* (2021) were evaluated *in vitro* acetylcholinesterase (AChE), butyrylcholinesterase (BuChE), and prolyl oligopeptidase (POP) inhibition activities of twenty-one Amaryllidaceae alkaloids of various structural types isolated from fresh bulbs of *Zephyranthes citrina*. Significant human AChE/BuChE (hAChE/hBuChE) inhibitory activity was exhibited by the newly described narcikachnine-type alkaloid narciliine, with IC_{50} values of $18.7 \pm 2.3 \mu M$ and $1.34 \pm 0.31 \mu M$, respectively. The newly isolated heterodimeric narcikachnine-type alkaloid narciliine displayed promising biological activities connected with the potential treatment of neurodegenerative diseases like Alzheimer (Kohelová *et al.* 2021).

6.4. Cytotoxic Activity

Methanolic extract of *Zephyranthes citrina* bulb was studied for *in-vitro* cytotoxic activity through MTT assay against three different human cancer cell lines such as cervical cancer (HeLa), breast cancer (MCF-7), and oral squamous carcinoma cancer (SCC-9). The results revealed that increase in the concentration of the extract, the percentage of inhibition become increases. The changes in the cell lines after exposure to the extract were observed in various dose-dependent manners. The results showed that methanolic bulb extract of *Zephyranthes citrina* exhibited significant cytotoxic effects on SCC-9 cell lines having an IC_{50} value of 88.79 $\mu g/ml$. In accordance with the findings from the report, the phytochemical constituents such as flavonoids, alkaloids, phenolics, and terpenoids are the major components that are responsible for the potential cytotoxic activity (Prakash and Vedanayaki 2019b). Aslam *et al.* (2016) tested acute toxicity of methanolic plant extract on Wister albino rats which was found to be 1000 mg/kg of body weight.

6.5. Antioxidant, Anti-inflammatory, and Analgesic Activity

Zephyranthes citrina dried whole plant methanolic extract was assessed for its antioxidant potential and showed marked activity. The methanolic extract of *Zephyranthes citrina* was also tested for its anti-inflammatory and analgesic activities at the dose of 100 mg/kg and 200 mg/kg. These activities were found to be dose-dependent, and the analgesic effect lasts for 120 minutes at the dose of 100 mg/kg and 200 mg/kg (Aslam *et al.* 2016).

6.6. Dye Removal Activity

The adsorption of methylene blue dye from an aqueous solution using carbon derived from the bulb of *Zephyranthes citrina* bulb has been successfully investigated by Prakash *et al.* (2020). According to them, it can be used as a low-cost material and environmentally benign for the recovery of dyes from an aqueous solution and the possibility of reusing carbon. Vedanayaki and Prakash (2021) also investigated removal of the methylene blue dye from wastewater samples using carbon derived from *Zephyranthes citrina* bulb by kinetics and isotherm studies.

7. Conclusions

Zephyranthes citrina, a bulbous herb, is well known as yellow rain lily, which has been used for ornamental and folk medicinal purposes. This review has summarized a comprehensive understanding of the phytochemical and biological properties of *Z. citrina* reported to date. The majority of the investigations are focused on the isolation and structural elucidation of Amaryllidaceae alkaloids from the bulb of *Z. citrina*. Extensive research has been reported the presence of approximately 24 Amaryllidaceae alkaloids from this plant. *Z. citrina* extracts and

its constituents exert various biological activities, such as antiprotozoal, antimicrobial, anti-Alzheimer, cytotoxic, antioxidant, anti-inflammatory, analgesic, and dye removal activities. However, there are still some scientific gaps in the reported literature on the phytochemistry of *Z. citrina*. This review contributes a constructive base for further scientific studies on this herb and its favorable clinical application. This compilation would certainly intensify the opportunity for future research on its potential medicinal properties and assist in developing practical strategies for its sustainable application.

Authors' Contributions

Conceptualization: IB, DP; Writing original draft: IB, DP; Writing-review and editing: IB, DP. All authors read and approved the final manuscript.

Acknowledgements

IB is grateful to the management, Kalyani Mahavidyalaya, Kalyani for providing necessary facilities and encouragement.

Conflict of Interests

The authors declare that there are no conflicts of interest related to this article.

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