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A comprehensive review on ethnomedicinal and pharmaceutical properties of *Aerides*, a medicinally important genus of orchids

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Abstract

The genus Aerides consists of only a few species and these species are highly valuable for their ornamental flowers and therapeutic potential. Several orchids in this genus are used as traditional medicines in various cultures and areas based on their natural populations. Many bioactive substances, such as phenanthrenes, phenolic compounds, stilbenoids, and phenylpropanoids have been reported in Aerides orchids. A wide range of pharmacological activities, including anti-inflammatory, anticancer, antioxidant, neuroprotective, antimicrobial, and α-glucosidase inhibitory characteristics, are attributed to the presence of these secondary metabolites. The native populations of Aerides orchids are threatened by overexploitation due to extensive commercial demand for their ornamental and therapeutic properties. This review highlights numerous pharmacological and medicinal properties of Aerides orchids with an emphasis on their conservation and sustainable utilization.

Keywords: *Aerides,* Ethnomedicine, Phytochemistry, Pharmacology.

Introduction

Orchids belong to the family Orchideaceae, which comprises one of the largest and most diverse groups amongst the flowering plants, with over 750 genera and 28,000 species dispersed all over the world except Antarctica (Zhang *et al*. 2022; Castillo-Perez *et al*. 2024). Orchids' richness and distribution differ from place to place and severely rely on climatic conditions. In terms of orchid distribution, the Indo-Malaysian region and Colombia are the richest in the world (Paul and Kumaria 2017; Vibha *et al*. 2019). Because of their amazing variety of forms, colours and

shapes, both cut flowers and potted plants of orchids are highly demanded in the world's floriculture industry (Bhattacharyya *et al*. 2014; Sarmah *et al*. 2024). Even though orchids are typically planted for their aesthetic qualities, they are also utilized as food and traditional medicines in many countries around the world (Hossain 2011; Ahmed *et al*. 2024). The populations of orchids in the wild are rapidly declining due to anthropogenic activities like massive deforestation and urbanization as well as overexploitation due to illegal trade triggered by the high commercial demand for attractive flowers and medicinal properties (Bhattacharyya *et al*. 2014; Debnath and Kumaria 2023). The IUCN Red List currently classified a total of 955 orchid species as threatened, 259 as critically endangered, 456 as endangered, 240 as vulnerable, 105 as nearly threatened, and 6 species as extinct (IUCN 2022; Monica *et al*. 2024).

Genus *Aerides* Lour

The genus *Aerides* Lour is a small genus of the family Orchidaceae, which includes 31 species distributed in tropical and subtropical regions of Asia, such as India, Nepal, Bhutan, China to Philippines, Sulawesi and Papua New Guinea (POWO 2024; Metusala 2024). This genus is epiphytic in nature, except for *Aerides krabiensis*, which grows in a boletus-like manner on the surface of limestone (Teoh 2021). The genus was established in 1790 by Loureiro. Since its initial classification**,** it has undergone several taxonomic modifications. Dozens of species once described in this genus have been assigned to other related genera (Chen *et al*. 2023; Tao *et al*. 2024).

The phytomorphology of the genus is described as monopodial, erect, freely branching, trunk surrounded by the base of bipartite, elongated and coriaceous leaves. Flowering is seasonal with several inflorescences bearing many fragrant pink flowers that open at the same time **(Fig.1A-C)**. Sepals and petals are free and widespread and the lip is three-lobed with a spur characteristic of the genus (Teoh 2021). Due to the fragrant nature of the flowers, many species of this genus are considered as a highly valuable source for creating artificial hybrids and variants (Kocyan *et al*. 2008). According to POWO (2024), *Aerides agasthiyamalaiana, A. crassifolia, A. crispa, A. emericii, A. maculosa, A. mcmorlandii, A. multiflora, A. odorata, A. ringens, and A. rosea* are among the 31 species that have been identified as existing in India.

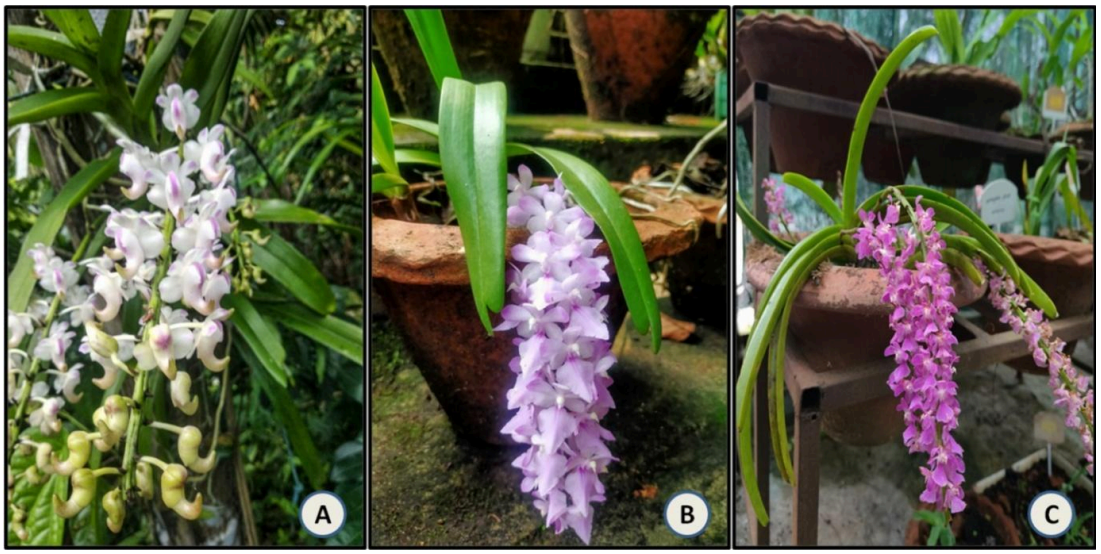

Fig.1. Aerides orchids in the greenhouse of Plant Biotechnology Laboratory, Botany Department, NEHU (A) *A. odorata* (B) *A. rosea* (C) *A. multiflora*

Ethnomedicinal Uses

Plants have been used as traditional medicines for thousands of years; and have evolved over the centuries among many different communities (Thapa *et al*. 2022). There is a long history of using orchids as traditional medicines around the world. Although orchids originated on earth 120 million years ago, the Chinese were the first to cultivate, describe and use orchids as a source of herbal remedies since 2800 B.C. **(**Jalal *et al*. 2008; Hossain 2011; Pant 2013). Apart from China, in many countries like America and some parts of Europe, Australia and Africa, orchids have been used as traditional drugs for a very long time (Bulpitt *et al*. 2007; Tsering *et al*. 2017). The oldest references to the Indian system of traditional medicine found in the ancient Sanskrit literature known as '*Veda*'. '*Ashtavarga*', known as the 'herb of immortality,' is an important ingredient of various classical Ayurvedic formulations like '*Chavyanprasa*', a combination of 8 herbs containing 4 species of orchids, namely**,** *Malaxis muscifera* (Jivaka), *Malaxis acuminate* (Rishbhaka), *Habenaria intermedia* (Riddhi), and *Habenaria edgeworthi* (Vriddhi) **(**Singh and Duggal 2009**;** Hossain 2011; Tsering *et al*. 2017; Choudhary *et al*. 2023; De 2023). In '*Sushrutasamhita*', one of the ancient Sanskrit literature sources, the use of orchid drugs under the name "*Rasna*" (*Acampe praemorsa* and *Vanda tessellata*) is mentioned. The *"Rasna Panchaka Quatha"* is an Ayurvedic formulation used to treat arthritis and rheumatism. The root of *Vanda tessellata* is an antidote against scorpion sting and a

remedy for bronchitis. **'***Rasna'* plant *Acampe praemorsa* belongs to the Aeridinae subtribe, which is very close to the *Aerides* genus (Hossain 2011; Bindiya Prakash and Bais 2016; Khan *et al*. 2019). Orchid species under the genera *Aerides, Coelogyne, Dendrobium* and *Vanda* possess both medicinal and ornamental properties and are the most commonly used medicinal orchids which have both high medicinal and ornamental values (Hegde 2005; Subedi *et al*. 2013; De and Medhi 2014).

Depending on the region it grows, the genus *Aerides* has various uses in traditional medicine in different parts of the world**.** *Aerides falcata* is commonly used as a tonic for weak infants in Vietnam, while leaf powder of *A. multiflora* is used in tonic preparations in Nepal. It has been reported that some species of *Aerides* are used traditionally as medicine for skin diseases. For e.g., in South Asian countries, the seeds of *A. falcata* are sprinkled on boils and used to promote healing of skin diseases. The traditional healers from Sikkim have used the stem powder of *A. odorata* to cure skin diseases (Panda and Mandal 2013; Teoh 2016; Rivai *et al*. 2023). Studies have shown that the hill tribes of Odisha, India used fresh roots of *A. odorata* mixed with *Saraca asoca* root powder, *Azadirachta indica* bark and regular salt to cure painful inflamed joints (Dash *et al*. 2008; Teoh 2016). The species, *A. maculosa* and *A. odorata* are used as herbal remedies for tuberculosis. The leaf juice of *A. odorata* has been used for the treatment of tuberculosis and among the *Bhilla* tribe of Maharashtra, India the use of infusion made from the roots of *A. maculosa* are used (Dash *et al*. 2008; Kamble *et al*. 2010). The use of orchid species belonging to the genus *Aerides* in the treatment of follems related to the ear and nose has been reported. For e.g., the leaf juice of *A. multiflora* is used in Sikkim to treat nasal congestion and otitis media. Also, boils in ears and nose are reported to have been treated with the juice obtained from leaves of *A. odorata* (Rao 2004; Panda and Mandal 2013; Teoh 2016). In southern parts of India, powder of *A. crispa* along with neem oil is used to cure pain and deafness (Rajendran *et al*. 1997). Leaves and mature capsules of *A. odorata* and leaf paste of *A. rosea*, *A. multiflora* are used for cuts and wounds in India and Nepal (Rao 2004; Joshi *et al*. 2009; Subedi *et al*. 2013; Teoh 2016; Ninawe and Swapna 2017; Gupta *et al*. 2024).

Phytochemical and Pharmacological Activities

Secondary metabolites which are low molecular weight organic compounds, are produced under stress conditions and play a critical role in medicinal orchids. Their

diverse biological activities, high specificity and diversity make them a promising source of highly specialized active ingredients for the treatment of incurable diseases (Thakur *et al*. 2019; Gantait *et al*. 2021; Li *et al*. 2023). Alkaloids, flavonoids, tannins, phenanthrenes, steroids, stilbenoids and bibenzyls are some of the secondary metabolites which are responsible for imparting medicinal properties to the orchids (Raskoti and Ale 2021; Targu *et al*. 2024). Due to the presence of these phytochemicals, the tissue extracts of orchids have been found to have anti-inflammatory, antimicrobial, anti-aging, anti-HIV, anti-helminthic, anti-dandruff, analgesic, anti-rheumatic, diuretic, hypoglycemic, antibacterial, antiviral, antispasmodic, anticarcinogenic, relaxing and neuroprotective properties (Gutierrez 2010; Pant *et al*. 2022; Shukla *et al*. 2022; Bazzicalupo *et al*. 2023; Targu *et al*. 2023, 2024). Different types of compounds have been reported to be present in the species of *Aerides* (Table 1).

Further, medicinal orchids often contain phenanthrenes, a kind of substance with three-benzene rings, categorized as simple, dihydrophenanthrene, phenanthraquinone, phenanthrenefuran and phenanthrene dimer, found only in the subfamilies of orchids, Orchidoideae and Epidendroideae (Niu *et al*. 2017; Thant *et al*. 2021; Li *et al*. 2023). The genus *Aerides* has been reported as a source of novel phenanthrene compounds. Aeridin, also known as 2,7-dihydroxy-l,3-dimethoxy-9, 10-dihydrophenanthropyran, is a phenanthropyran derivative found in *Aerides crispa* **(Fig.2)**. It is known for its significant anti-inflammatory activities (Anuradha and Parkasa Rao 1998; Mridula *et al*. 2009). *Aerides rosea* is the source of two new phenanthrene derivatives: aerosin (3-methoxy-9,10-dihydro-2,5,7-phenanthrenetriol) and aerosanthrene (5-methoxyphenanthrene-2,3,7-triol) The species, *A. rosea* also yields 3,5-dimethoxyphenanthrene-2,7-diol and 3-methoxy-2,7-dihydroxy-5H-phenanthro[4,5-bcd]pyran (Cakova *et al*. 2015). Three unique phenanthrene compounds have been identified from ***A. multiflora***, viz., aerimultins A, B, and C. All three have been found to exhibit α-glucosidase inhibitory activity, wherein aerimultins C shows the highest level of this activity (Thant *et al*. 2021). Rivai *et al*. (2023) have reported that two biphenanthrene derivatives, 2,7-dihydroxy-3,4,6-trimethoxyphenanthrene and aerifalcatin isolated from *A. falcata* show anti-neuroinflammatory and anticancer properties and can extensively reduce

the release of IL-6 and TNF-α, two pro-inflammatory cytokines in the cell lines. Aerifalcatin has also shown a decrease in the glioblastoma and neuroblastoma cell migration and proliferation in *in-vitro* cell lines. Both the reported compounds hold promise for further exploration as therapeutic agents for central nervous system (CNS) diseases.

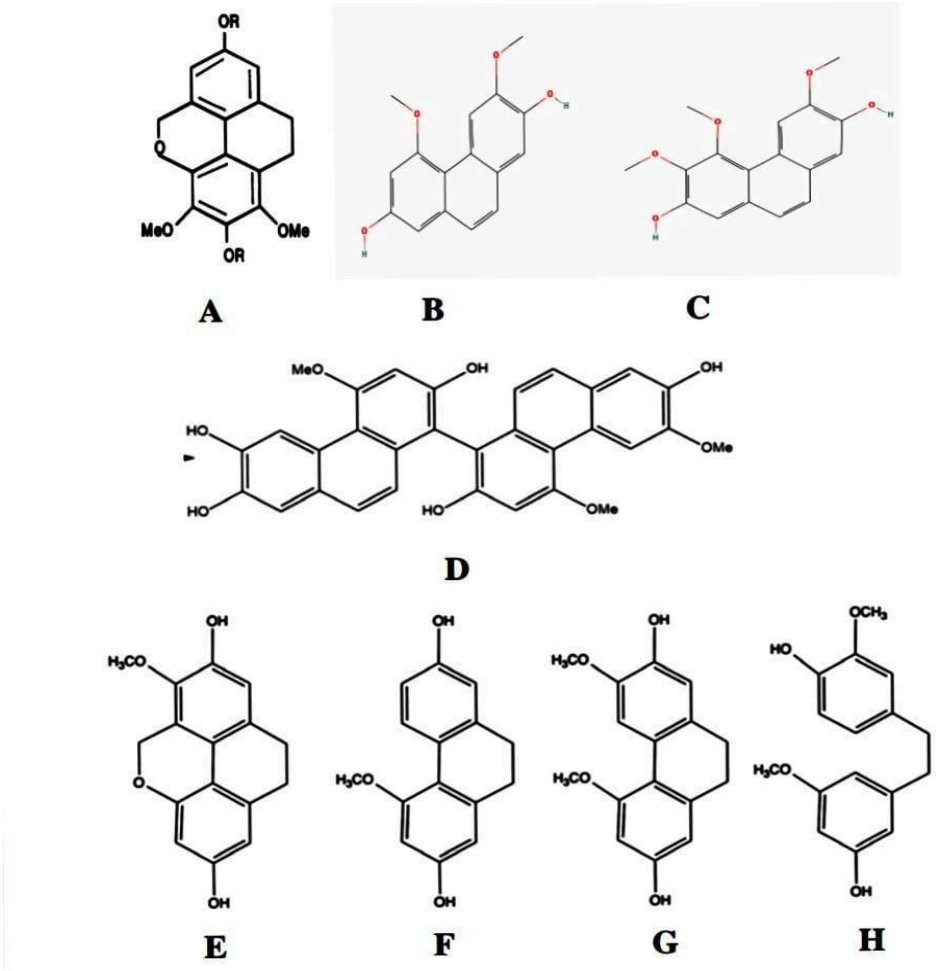

Fig.2. Some bioactive compounds identified from *Aerides* genus

(A) Aeriden; (B) 3,5-dimethoxyphenanthrene-2,7-diol; (C) 2,7-dihydroxy-3,4,6 trimethoxyphenanthrene; (D) Aerifalcatin; (E) Imbricatin; (F) Coelonin; (G) Methoxycoelonine; (H) Gigantol

Another group of compounds, the phenolics include hydroxyl groups. These phenolic compounds are classified into two groups according to the number of phenol units in their structure: simple phenols and polyphenols. The phenolic compounds namely 2-methyl-5(1,2,2-trimethycyclopentyl) phenol and phenyl(piperidin-3-yl) methanone reported in the species *A. odorata* showing anticancer properties

(Oon *et al*. 2015). Also stilbenoids such as gigantol, coelonin, methoxycoelonin and imbricatin which are one of the important secondary metabolites found in orchids. Out of these compounds, imbricatin has been reported to show antioxidant activity, whereas gigantol shows anti-inflammatory and anticancer effects. Both these compounds are reported to be present in *A. multiflora* and *A. rosea* (Simmler *et al*. 2010; Charoenrungruang *et al*. 2014; Cakova *et al*. 2015; Thant *et al*. 2021; Chowdhury *et al*. 2024).

Some other secondary metabolites such as the phenylpropanoid compound, dihydroconiferyl dihydro-p-coumarate, are also reported to show antioxidant activities and anti-inflammatory effects (Ahammed *et al*. 2021, 2023). This compound is found to be produced from the phenylpropanoid that is present in *A. multiflora* (Thant *et al.* 2021). Using cell lines, studies have shown that agrostonin reported from *A. multiflora* and *A. falcata* and syringaresinol from *A. falcata*, show significant anti-neuroinflammatory effects and strong cytotoxic activities in C6 glioblastoma and SH-SY5Y *in-vitro* cells, indicating a suppressive role of the compounds in brain cancer cells. Additionally, syringaresinol extracted from *A. falcata* is reported to exhibit anti-cancerous properties in leukaemia, breast cancer and prostate cancer (Rivai *et al*. 2023).

Conclusion and Future Perspectives

The medicinal species under the orchid genus *Aerides* contain bioactive compounds that may have antioxidant, anticancer and anti-inflammatory effects. However, *Aerides* orchids are still relatively unknown due to their small populations. There is a significant potential to discover novel compounds within this genus, which can be scientifically validated and used in pharmaceutical industries. To achieve this, further studies are needed to be carried out on the conservation of *Aerides* spp. and identification of bioactive compounds present in these orchids. This could involve the use of biotechnological approaches of conservation and sustainable utilization of the species under the genus *Aerides* so as to avoid the pressures on their natural populations.

Table 1. Bioactive compounds of *Aerides* genus with molecular structures and their biological activities.

Sl. no.	*Aerides* species	Compound name	Molecular formula	Phytochemical class	Biological activity	References
1	*A. crispa*	Aeridin	$C_{17}H_{16}O_5$	Phenanthropyran	Anti-inflammatory activity	Mridula *et al*. (2009)
2	*A. falcata*	Aerifalcatin	$C_{31}H_{24}O_8$	Biphenanthrene derivatives	Anti-neuroinflammatory and anticancer activity	Rivai *et al*. (2023)
3	*A. falcata*	2,7-Dihydroxy-3,4,6-tri methoxyphenanthrene	$C_{17}H_{16}O_5$	Biphenanthrene derivatives		
4	*A. falcata*	Syringaresinol	$C_{22}H_{26}O_8$	Polyphenol		
5	*A. falcata* *A. multiflora*	Agrostonin		Others		
6	*A. falcata*	Paprazine	$C_{17}H_{17}NO_3$	Phenylpropanoid	Anti-inflammatory and antioxidant activity	Rivai *et al*. (2023); Bakrim *et al*. (2024)
7	*A. falcata*	n-Trans-feruloyl tyramine	$C_{18}H_{19}NO_4$	Alkaloid	Antioxidant and α-glucosidase inhibitory activity	Soi-Ampornkul *et al*. (2022); Rivai *et al*. (2023)
8	*A. multiflora*	Aerimultin A		Phenanthrene	α-Glucosidase inhibitory activity	Thant *et al*. (2021)
9	*A. multiflora*	Aerimultin B				
10	*A. multiflora*	Aerimultin C				
11	*A. multiflora* *A. rosea*	Gigantol	$C_6H_{18}O_4$	Stilbenoid	Anti-inflammatory and anticancer activity	Charoenrungruang *et al*. (2014); Thant *et al*. (2021); Chowdhury *et al*. (2024)
12	*A. multiflora* *A. rosea*	Imbricatin	$C_{16}H_{14}O_4$	Stilbenoid	Antioxidant activity	Simmler *et al*. (2010); Cakova *et al*. (2015); Thant *et al*. (2021)
13	*A. multiflora*	Dihydroconiferyl dihydro-p-coumarate	$C_{19}H_{22}O_5$	Phenylpropanoid	Antioxidant and anti-inflammatory activity	Ahammed *et al*. (2021); Thant *et al*. (2021); Ahammed *et al*. (2023).

14	*A. odorata*	2-Methyl-5-(1,2,2-Trime thycyclopentyl) phenol	$C_{15}H_{22}O$	Phenol	Anticancer activity	Oon *et al*. (2015)
15	*A. odorata*	Phenyl(piperidin-3-yl) methanone	$C_{12}H_{15}NO$	Phenylpiperidines		
16	*A. odorata*	β-Selinene	$C_{15}H_{24}$	Sesquiterpenoid	Antioxidant and anti-inflammatory activity	
17	*A. odorata*	Squalene	$C_{30}H_{50}$	Triterpene	Antibacterial, antioxidant, anti-tumour, anticancer, immunostimulent, lipoxygenase inhibitory activity	
18	*A. rosea*	Coelonin	$C_{15}H_{14}O_3$	Stilbenoid	Anti-inflammatory activity	Jiang *et al.* (2019)

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