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Phytochemistry and biological health promoting properties of *Cymbidium* orchids

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ABSTRACT

Cymbidiums are scientifically intriguing owing to their wide range of bioactive compounds and diverse range of biological activities. The genus *Cymbidium* is reported to be socially important in numerous social cultures, including religious, protective, ornamental, cosmetic, and medicinal purposes. Furthermore, the members of the genus *Cymbidium* contain numerous phytoconstituents with diverse health-promoting properties such as anti-cancerous, anti-inflammatory, anti-oxidant, anti-microbial, and neuroprotective effects. Due to its high ornamental value and usage in traditional medicines, the genus has been over-exploited and it is under threat. Therefore, it is crucial to study this genus of high medicinal importance so as to harness its bioactive compounds without over-exploiting the natural populations. The current review aims to provide a concise overview of the biologically active compounds present in the *Cymbidium* orchids. To validate the use of plants in traditional medicines, it is essential to conduct comprehensive research for the confirmation of their biological activities.

Keywords: *Cymbidium*, Ethnopharmacology, Phytochemistry, Pharmacology, Bioactive compounds

INTRODUCTION

Orchids are one of the most exotic and exquisite groups of flowering plants comprising of nearly 35,828 species with over 736 genera (Kim et al. 2020; Govaerts, 2022). Although orchids are distributed widely across the globe, their population is diminishing to a great extent due to over exploitation, habitat fragmentation, indiscriminate collection and climate change (Fonge et al. 2019). Currently, 955 orchid species are categorized as threatened, 259 as critically endangered, 456 as endangered, 240 as vulnerable, 105 as nearly threatened, and 6 species have been recorded as extinct according to the IUCN Red List (IUCN, 2022). Cymbidiums are commonly known as 'boat orchids' and comprises 75-80 species with different growth habits such as epiphytes (around 70%), lithophytes and terrestrial. Some species of

Cymbidium are shown in **Fig.1**. *Cymbidium* orchids are reported to be predominantly found in tropical and subtropical regions of northeast India, Japan, eastern Asia and northern Australia (Zotz, 2013; Yang et al. 2021; Zhang et al. 2021; Balilashaki et al. 2023). They hold a remarkable position in the floriculture industry due to their highly priced ornamental and economical values (Pal et al. 2019; Zhang et al. 2021). In addition to their commercial importance, the species of *Cymbidium* are found to produce many bioactive substances belonging to different phytochemical classes. The present review article gives a concise view on the researches in ethnopharmacology, phytochemistry, pharmacological properties and biological activities of the *Cymbidium* orchids.

Fig.1. (a) *C. aloifolium* **(b)** *C. eburneum* **(c)** *C. hookerianum* **(d)** *C. lancifolium* **(e)** *C. iridioides* **(f)** *C. devonianum*

ETHNOPHARMACOLOGY

Orchids have been used in Ayurvedic or herbal medicines throughout the world. The earliest descriptions of orchids in therapeutic utilizations have been reported from China since 2800 B.C. (Bulpitt, 2005). However, in India orchids such as *Habenaria edgeworthii, Habenaria intermedia, Crepidium acuminatum* and *Malaxis muscifera* have been used in ancient Ayurvedic preparation 'Ashtavarga' (Hossain, 2011; Teoh, 2016; Pant et al. 2013; Arora et al. 2017). Orchids are often used for the treatment of various ailments and diseases such as allergies, arthritis, chest pains, rheumatism, muscular pains, menstrual disorders, paralysis, spermatorrhea, gastrointestinal problems, cholera, piles, boils, diarrhoea, leucorrhoea, tuberculosis, syphilis, hepatitis, wounds, sores, cancers. It is therefore, remarkably specified that orchids have high medicinal potential for pharmaceutical drugs, which has eventually drawn immense attention to explore their medicinal properties and bioactive compounds (Hossain, 2011; Teoh, 2016; Arora et al. 2017; Badalamenti et al. 2021). The genus *Cymbidium* holds a significant importance in ornamental, cosmetic, and medicinal

fields. Leaves, roots, and flowers of *Cymbidium* orchids have traditional herbal importance and are used for various ailments by tribal people. The traditional uses of different species of the genus are summarized in **Table 1**. Various plant parts of the *Cymbidium* orchids are reported to be of medicinal values. For e.g., root paste of *C. aloifolium* is used to cure tumours, nervous system disorders, bone fractures and kidney disorders. Also, paste made of the roots of the same species is used to cure vomiting, diarrhoea, vertigo, weakness of eyes and paralysis when consume with ginger. Further, the root powder of *C. bicolor* is used to cure epilepsy and depression; root paste of *C. devonianum* is used to treat boils. The roots of *C. ensifolium* have been used to ease liver dysfunction, nephropathy and to treat gonorrhoea and that of *C. faberi* are used for relieving cough. The leaf extracts of *C. aloifolium* and *C. finlaysonianum* are reported to cure boils, fever, otitis and epilepsy. The leaf juice of *C. iridioides* and *C. elegans* is used as haemostatic for wounds and treatment of diarrhoea. Studies have shown that the whole plant of *C. hookerianum* can be used for treatment of fractures and injuries on soft tissues. And, the whole plant of *C. goeringii* is used as hypotensive and diuretic cures.

TABLE 1 Ethnopharmacology of *Cymbidium* orchids

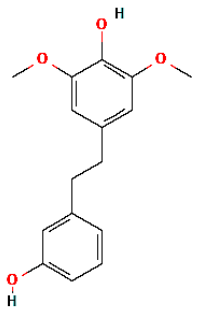
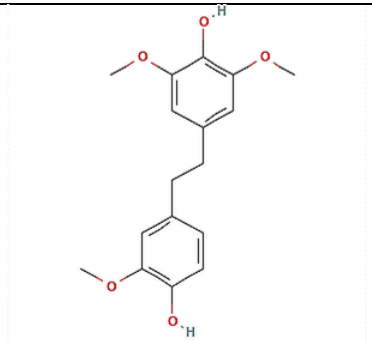
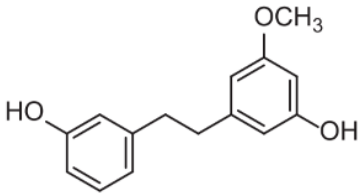
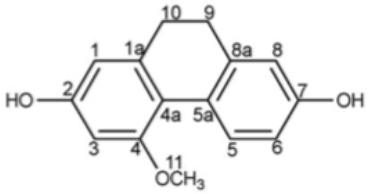
Sl. No.	*Cymbidium* species	Country	Plant parts used	Medicinal use	References
1.	*C. aloifolium* (L.) Sw.	Bangladesh	Leaf, root and whole plant	Boils, fever, fractures, earaches, burns, sores, chronic illnesses, weak eyes, vertigo, and paralysis	Pant (2013); Teoh (2016); Ninawe and Swapna (2017); Teoh, (2019); Hossain and Sharma (2019)
		India	Fruit, leaf and root	Tumours, nervous disorders and bone fractures, heal wounds, boils, cure vomiting, diarrhoea, vertigo, weakness of eyes, paralysis, otitis and epilepsy	
		Myanmar	Flower, leaf and rhizome	Gonorrhoea, conjunctivitis and cure fractures	
		Nepal	Rhizome, whole plant	Emetic, purgative, demulcent, bone fractures, dislocated bones and tonic	
		Thailand	Leaf and root	Ear infections and kidney disorders	
2.	*C. bicolor* Lindl.	China	Leaf	Fractures	Teoh (2016, 2019)
		India	Flower, leaf and root	Epilepsy, depression, skin pigmentation, joint pain and inflamed skin	
3.	*C. devo nianum* Paxton	Nepal	Root and whole plant	Boils, cough and cold	Pant (2013); Teoh (2016)
4.	*C. elegans* Lindl.	India, Nepal	Flower, leaf, tuber and whole plant	Coagulation, demulcent and emetic	Jalal et al. (2010); Pant (2013); Teoh (2016); Singh (2022)
5.	*C. ensifolium* (L.) Sw.	India	Flower and Rhizome	Decoction for eye sores and gonorrhoea	Chuakul, (2002); (Sood) 2006; Yonzone et al. (2011) Jimoh et al. (2022)
		Thailand	Root	Ease liver dysfunction and nephropathy	
6.	*C. faberi* Rolfe	China	Root	Resolving phlegm and cough	Wang (2014); Lv et al. (2020)
7.	*Cymbidium finlaysonianum*	Thailand	Leaf	Otitis	Chuakul (2002; Lertnitikul et al.

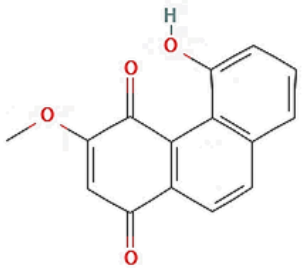
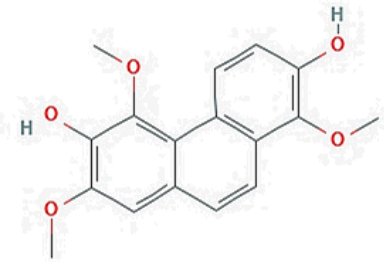
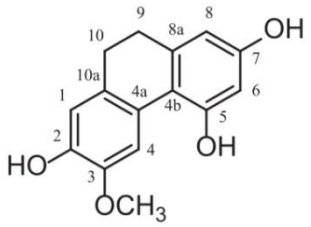
	Lindl.				(2018)
8.	*C. goeringii* (Rchb. f.) Rchb. f.	China, India, Japan, Korea, Thailand, Vietnam	Whole Plant	Hypotensive and diuretic activities	Watanabe et al. (2007); Gutiérrez, (2010)
9.	*C. hookerianum* Rchb. f.	China	Whole plant	Fractures and injuries to soft tissues	Rao (2004); Teoh (2016)
		India	Seed	Haemostatic	
10.	*C. iridioides* D. Don	India, Nepal	Leaf	Haemostatic and diarrhoea	Jalal et al. (2010); Pant and Raskoti (2013); Teoh (2016)
11.	*C. kanran* Makino	China	Root and whole plant	Cough, asthma, gastroenteritis and ascariasis	Teoh (2016); Jeong et al. (2017)
12.	*C. lancifolium* Hook.	China	Whole Plant	Rheumatism and improve blood circulation	Teoh (2016); Mudoi et al. (2023)
13.	*C. macrorhizon* Lindl.	India	Rhizome	Diaphoretic, febrifuge, boils and rheumatism	Teoh (2016)
14.	*C. sinense* (Jacks.) Willd.	China	Whole plant	Purification of heart and lungs, cough and asthma	Teoh (2016); Mudoi et al. (2023)
15.	*C. wilsonii* (Rolfe ex De Cock) Rolfe	China	Root	Weak lungs, cough, bronchitis, tonsilitis and body ache	Teoh (2016)

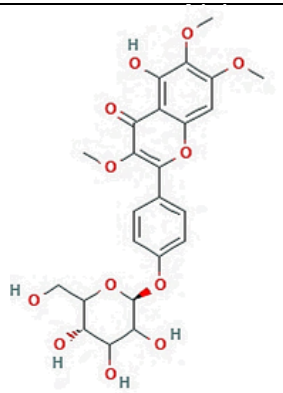
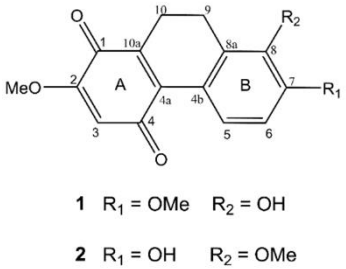
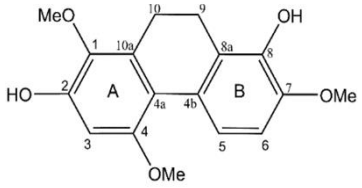
PHYTOCHEMISTRY

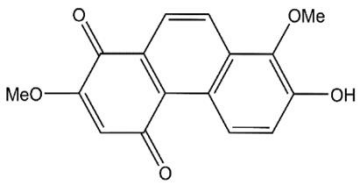
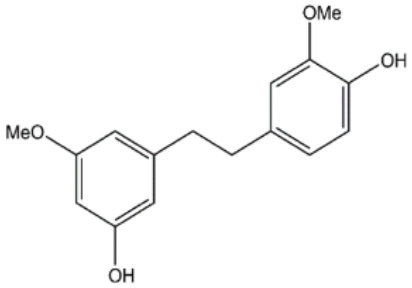
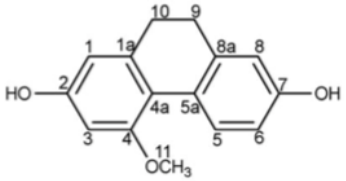
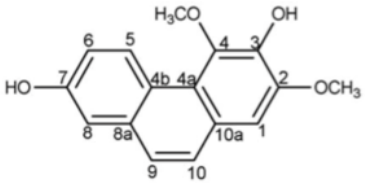
The spectroscopic analyses carried out by several workers have highlighted the presence of phytochemicals in the *Cymbidium* orchids. Although only a few reports are available, a notable richness in the important bioactive compounds has been found in the genus *Cymbidium*. The active compounds found in the species of *Cymbidium* along with their chemical structures reported by various researchers are shown in **Table 2**. The different bioactive compounds found in *C. aloifolium* belong to chemical families such as monomeric stilbenes, bibenzyl, phenanthrene, flavonols and dihydrophenanthrene which have anti-bacterial, anti-nociceptive, anti-oxidant, anti-inflammatory, analgesic and haemostatic effects (Juneja et al. 1987; Barua et al. 1990; Howlader et al. 2011; Teoh, 2016). Phytochemicals such as cymensifin, cypripedin and gigantol which show anti-cancerous and cytotoxic effects are reported in *C. ensifolium* (Jimoh et al. 2022). The active compounds found in *C. faberi* belong to phenanthrenes which have anti-oxidant, anti-inflammatory and cytotoxic effects against human cancer cell lines (Lv et al. 2020). Phytochemical class of compounds such as dihydrophenanthrene, monomeric stilbenes, bibenzyl and phenanthrenes are reported in *C. finlaysonianum* which have anti-oxidant properties and cytotoxic effects against human lung cancer cell lines. The species, *C. goeringii* has a monomeric peptidoglycan-related compound and bibenzyl phytochemical class which aid in hypotensive and diuretic problems. They also exhibit inhibitory effects against Lipopolysacharride-induced nitric oxide, Prostaglandin E2, Tumour Necrosis Factor-alpha, Interleukin-1 beta and Interleukin-6 (Won et al. 2006; Watanabe et al. 2007). Sterols and triterpenoids which have spasmolytic activity are reported in *C. iridioides*. Also, in *C. kanran*, flavone C-glycosides are found to be reported which have anti-cancer, anti-inflammatory and anti-oxidant effects (Jeong et al. 2017).

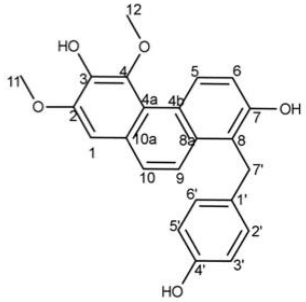
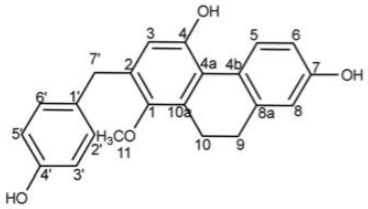
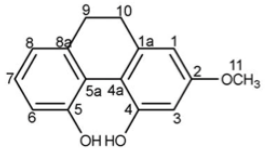
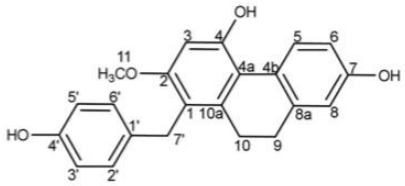
TABLE 2 Identified active compounds with molecular structures and their biological activities

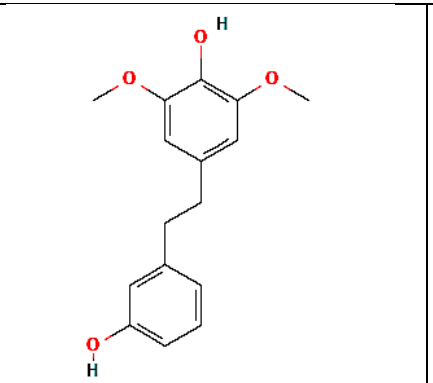
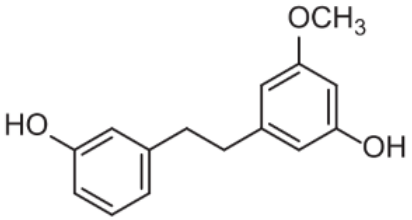
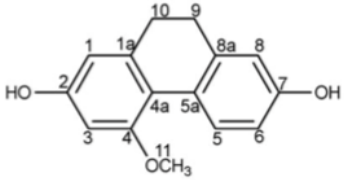
Sl. no.	Name of the plant	Name of active compound	Molecular formula	Structure	Phytochemical class	Biological activity	References
1.	*Cymbidium aloifolium* (L.) Sw.	(4-[2-(3-hydroxyphenyl)ethyl]-2,6-dimethoxyphenol)	$C_{16}H_{18}O_4$		Monomeric stilbenes	Antifungal, antinociceptive, anti-inflammatory, anti-oxidant, CNS depressant activity and cytotoxic effects against human small cell lung cancer (NCI-H187) cell line.	Juneja et al. (1987); Barua et al. (1990); Howlader et al. (2011); Howlader and Alam, (2011); Teoh (2016); Lertnitikul et al. (2018); Lv et al. (2020); Kim et al. (2023)
		Aloifol II (4,4'-dihydroxy-3,3',5-trimethoxybibenzyl)	$C_{17}H_{20}O_5$		Monomeric stilbenes		
		Batatasin III (3-[2-(3-hydroxyphenyl) ethyl]-5-methoxyphenol)	$C_{15}H_{16}O_3$		Bibenzyl		
		Coelonin (9,10-dihydro-4-methoxy-2,7-phenanthrenediol)	$C_{15}H_{14}O_3$		Phenanthrene		

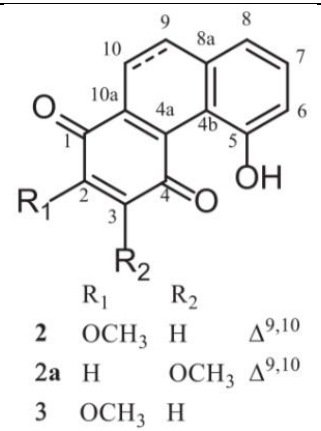
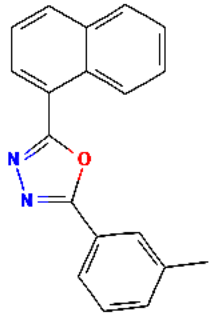
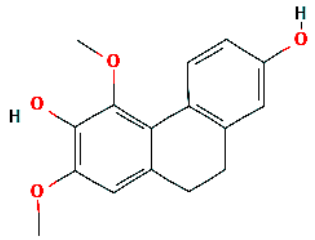
		Cymbinodin-A (5-hydroxy-3-methoxyphenanthrene-1,4-dione)	$C_{15}H_{10}O_4$		Phenanthrene		
		Denthyrsinin (1,5,7-trimethoxyphenanthrene-2,6-diol)	$C_{17}H_{16}O_5$		Phenanthrene		
		6-methoxycoelonin (3,5-dimethoxy-9,10-dihydrophenanthrene-2,7-diol)	$C_{16}H_{16}O_4$		Phenant hrene		

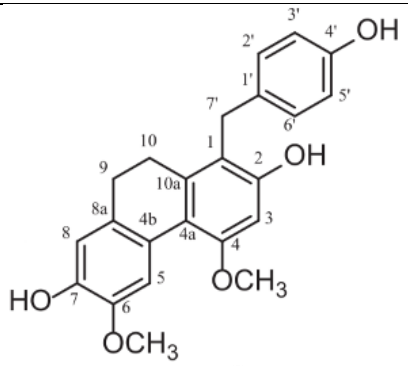
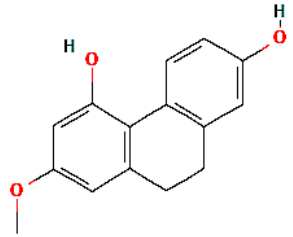
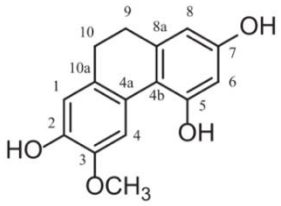
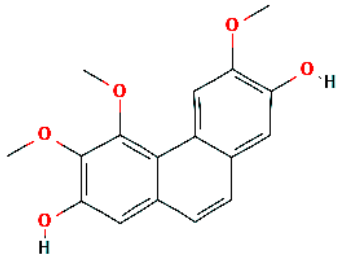
		Pendulin (3-hydroxy-2,4,6,7,8-pentamethoxyphenanthrene)	$C_{24}H_{26}O_{12}$		Flavonols		
2.	*Cymbidium ensifolium* (L.) Sw.	Cymensifin A (1) (8-hydroxy-2,7-dimethoxy-9,10-dihydrophenanthrene-1,4-dione) Cymensifin B (2) (7-hydroxy-2,8-dimethoxy-9,10-dihydrophenanthrene-1,4-dione)	$C_{16}H_{14}O_5$ $C_{16}H_{14}O_5$	 **1** R_1 = OMe R_2 = OH **2** R_1 = OH R_2 = OMe	Dihydrophenanthrene	Anti-cancerous; cytotoxic effects against various cancer cells	Jimoh et al. (2022)
		Cymensifin C (2,8-dihydroxy-1,4,7-trimethoxydihydrophananthrene)	$C_{17}H_{18}O_5$		Dihydrophenanthrene		

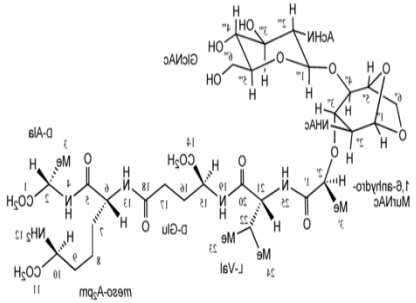
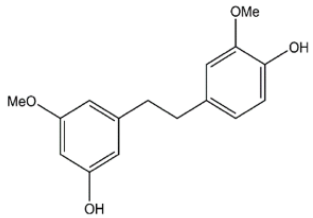
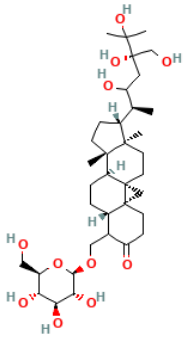
		Cypripedin (7-Hydroxy-2,8-dimethoxy-1,4-phenanthrenedione)	$C_{16}H_{14}O_5$		Phenanthrenequinone		
		Gigantol (3',4-dihydroxy-3,5'-dimethoxybibenzyl)	$C_{16}H_{18}O_4$		Bibenzyl		
3.	*Cymbidium faberi* Rolfe	Coelonin 9,10-Dihydro-4-methoxy-2,7-phenanthrenediol	$C_{15}H_{14}O_3$		Phenanthrene	Anti-oxidant, anti-inflammatory and cytotoxic activities against human cancer cell lines (HL-60, MCF-7, HCT-8)	Lv et al. (2020)
		5,7-dimethoxyphenanthrene-2,6-diol (DD)	$C_{16}H_{14}O_4$		Phenanthrene		

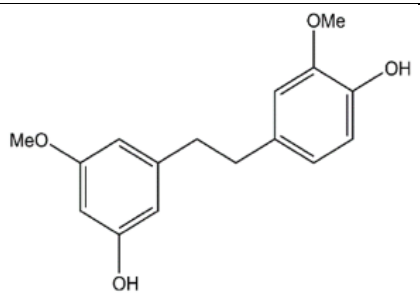
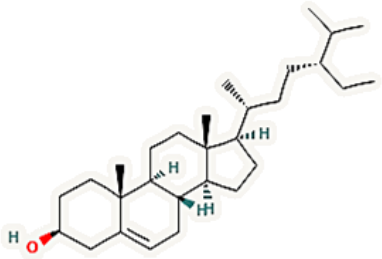
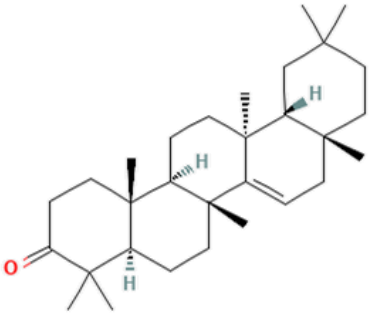
		1-(4-hydroxybenzyl)-5,7-dimethoxy-phenanthrene-2,6diol (HDP)	$C_{23}H_{20}O_5$		Phenanthrene		
		7-(4-hydroxybenzyl)-8-methoxy-9,10-dihydrophenanthrene-2,5-diol (HMD)			Phenanthrene		
		2-methoxy-9,10-dihydro- phenanthrene-4,5-diol (MDD)	$C_{15}H_{14}O_3$		Phenanthrene		
		Shancidin 8-[(4-hydroxyphenyl)methyl]-9,10-dihydrophenanthrene-2,5-diol	$C_{21}H_{18}O_3$		Phenanthrene		

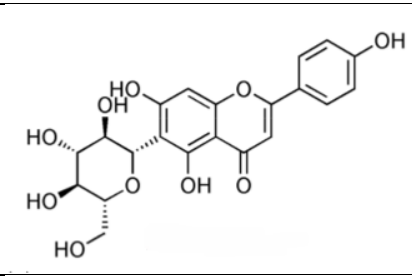
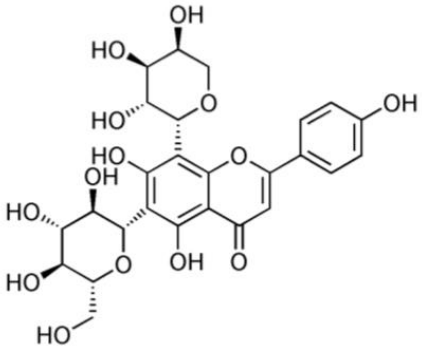
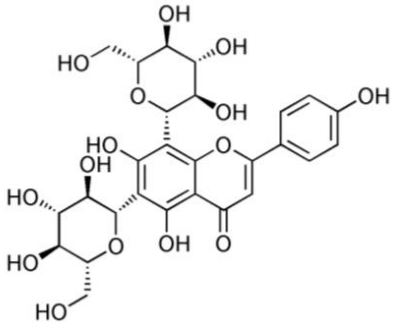
4.	*Cymbidium finlaysonianum* Lindl.	Aloifol I 4-[2-(3-hydroxyphenyl) ethyl]-2,6-dimethoxyphenol	$C_{16}H_{18}O_4$		Monomeric stilbenes	Anti-oxidant and cytotoxic effect against human small cell lung cancer (NCI-H187) cell line.	Lertnitikul et al. (2018); Kim et al. (2023)
		Batatasin III 3-[2-(3-hydroxyphenyl) ethyl]-5-methoxyphenol	$C_{15}H_{16}O_3$		Bibenzyl		
		Coelonin 4-methoxy-9,10-dihydrophenanthrene-2,7-diol	$C_{15}H_{14}O_3$		Phenanthrene		

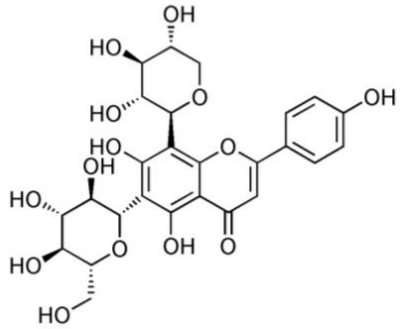
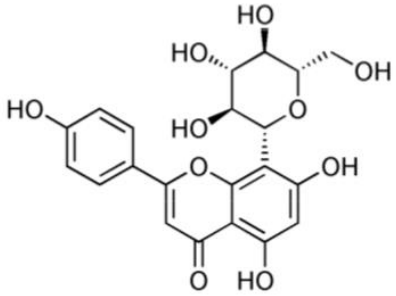
		Cymbinodin-A (2) 5-hydroxy-3-methoxyphenanthrene-1,4-dione Ephemeranthoquinone B (3) 5-hydroxy-2-methoxy-1,4-dihydrophenanthrene-1,4-dione	$C_{15}H_{10}O_4$	 **2** R_1 = OCH_3, R_2 = H, $\Delta^{9,10}$ **2a** R_1 = H, R_2 = OCH_3, $\Delta^{9,10}$ **3** R_1 = OCH_3, R_2 = H	Phenanthrene		
		3,3'-dihydroxy-4,5-dimethoxybibenzyl	$C_{19}N_{14}N_2O$		Bibenzyl		
		Flavanthridin 3,7-dihydroxy-2,4-dimethoxy-9,10-dihydrophenanthrene	$C_{16}H_{16}O_4$		Phenanthrene		

		1-(4-hydroxybenzyl)4,6-dimethoxy-9,10-dihydrophenanthrene-2,7-diol.	$C_{23}H_{22}O_5$		Dihydrophenanthrene		
		Lusianthridin 7-methoxy-9,10-dihydrophenanthrene-2,5-diol	$C_{15}H_{14}O_3$		Phenanthrene		
		6-methoxycoelonin 3,5-Dimethoxy-9,10-dihydrophenanthrene-2,7-diol	$C_{16}H_{16}O_4$		Phenanthrene		
		3,4,6-trimethoxyphenanthrene-2,7-diol	$C_{17}H_{16}O_5$		Phenanthrene		

5.	*Cymbidium goeringii* Rchb.f.	Cymbidine A	$C_{39}H_{63}N_7O_{20}$		monomeric peptidoglycan-related compound	Hypotensive and diuretic activities; exhibit inhibitory effects against LPS-induced nitric oxide, PGE2, TNF-alpha, IL-1beta and IL-6	Won et al. (2006); Watanabe et al. (2007)
		Gigantol 3',4-dihydroxy-3,5'-dimethoxybibenzyl	$C_{16}H_{18}O_4$		Bibenzyl		
6.	*Cymbidium iridioides* D. Don	Cymbidoside	$C_{36}H_{60}O_{11}$		Triterpene glucoside	Spasmolytic activity	Dahmen and Leander, (1978); Juneja et al. (1985); Kim et al. (2023)
		Gigantol 3',4-dihydroxy-3,5'-dimethoxybibenzyl	$C_{16}H_{18}O_4$		Bibenzyl		

							
		Sitosterol	$C_{29}H_{50}O$		Sterols		
		Taraxerone	$C_{30}H_{48}O$		Triterpenoid		
7.	*Cymbidium kanran* Makino	Isovitexin	$C_{21}H_{20}O_{10}$		Flavone C-Glycosides	Anticancer anti-inflammatory and anti-oxidant effects	Jeong et al. (2017)

							
		Schaftoside	$C_{26}H_{28}O_{14}$		Flavone C-Glycosides		
		Vicenin-2	$C_{27}H_{30}O_{15}$		Flavone C-Glycosides		
		Vicenin-3	$C_{26}H_{28}O_{14}$		Flavone C-Glycosides		

							
		Vitexin	$C_{21}H_{20}O_{10}$		Flavone C-Glycosides		

BIOLOGICAL ACTIVITIES

Owing to bioactive compounds present in *Cymbidium* orchids, they have immense role in biological and health promoting activities **(Fig. 2)**. Cymbidiums are broadly known for their use in traditional medicines and have broad spectrum in their biological activities. They are reported to be anti-inflammatory, anti-fungal, anti-oxidant and anti-cancer. Additionally, they are also found to have analgesic activity, central nervous system depressant effects, hypotensive, diuretic and spasmolytic activities. Studies on *C. aloifolium* have reported its anti-fungal activity wherein it was found that its chloroform fraction was inhibitory to the growth of *Trichophyton melangrophytes* at 250 μg/ml. Additionally, it is also reported to have analgesic, anti-inflammatory and anti-oxidant properties (Howlader et al. 2011). Studies by Howlader and Alam (2011) reported that the ethanolic leaf extract of *C. aloifolium* possess depressant activity in neuropharmacological experimental models in mice. Also, *C. ensifolium* has been found to possess anti-cancerous activity. In a study conducted by Jimoh et al. (2022), three distinct dihydrophenanthrene derivatives *viz*., cymensifins A, B, C, together with two known compounds, cypripedin and gigantol were isolated from the plant parts and when evaluated for their efficacy against on human lung cancer H460, breast cancer MCF7, and colon cancer CaCo 2 cells showed cytotoxic effects (Charoenrungruang et al. 2014; Wattanathamsan et al. 2018; Jimoh et al. 2022). The phenanthrenes reported from *C. faberi* such as coelonin, dihydrophenanthrene, shancidin and phenanthrene, 1-(4'-hydroxybenzyl)-4,8-dimethoxyphenanthrene-2,7-diol (HDP) showed inhibitory activities against cancer cell lines, but intriguingly shancidin displayed a remarkable effect (Lv et al. 2020). Lertnitikul (2018) isolated fourteen bioactive compounds mostly bibenzyls and phenanthrene derivatives from the whole plant parts of *C. finlaysonianum.* Using Resazurin microplate assay to evaluate the *in vitro* cytotoxicity against NCI-H187 cell lines of the phenanthrene derivatives, it was found that all the compounds exhibited varying degrees of cytotoxicity against cancer cells (Sut *et al*., 2017). An active compound, cymbidine A isolated from *C. goeringii* has hypotensive and diuretic activities when tested on mice models (Watanabe et al. 2007). On the other hand, Juneja et al. (1985) have reported that ethanolic extract of *C. iridioides* possesses spasmolytic activity.

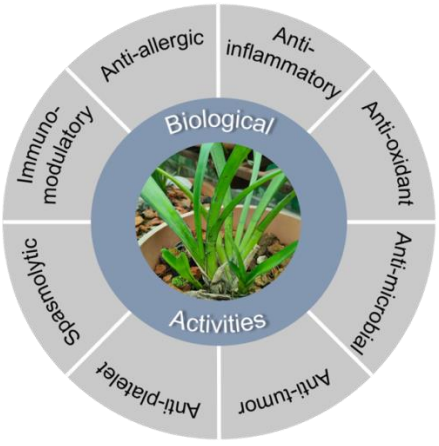


Fig. 2. Biological activities of genus *Cymbidium*

CONCLUSION AND FUTURE PERSPECTIVES

The *Cymbidium* genus is a significant source of medicinal plants, containing a diverse range of bioactive compounds from various phytochemical classes. A variety of biological activities, including anti-microbial, anti-cancerous, anti-inflammatory, spasmolytic, and analgesic have been reported from the extracts of *Cymbidium* orchids. There is a vast potential for discovering new bioactive compounds in the genus *Cymbidium* for drug discovery but scientific validation for its herbal usage is confined to only some species. Therefore, more in-depth studies have to be carried out so as to identify important bioactive compounds and harness potential drugs from the genus.

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