Genetic Diversity and Its Relationship of *Dendrobium* (Orchidaceae) Based on Bioactive Compounds and Their Biological Activities: A Meta-Analysis

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Abstract: Information on genetic diversity and its relationship is fundamental for the conservation and breeding programs of orchid germplasm. The study aimed to assess the genetic diversity and relationships of *Dendrobium* germplasm based on bioactive compounds, their biological activities, and plant organ by a meta-analysis approach. A total of 51 species of *Dendrobium* have been collected and identified as producing bioactive compounds, including their biological activities and plant organs (parts). In this case, the highest genetic diversity had shown by polyphenols (H' index = 0.90) as substances, neuroprotective (H' = 0.80) for activity, and the leaf organ with an H' index of 0.89. The UPGMA analysis showed that *Dendrobium* grouped into seven clusters, where the furthest relationship had presented by *D. moschatum* and *D. catenatum*. However, the closest related was by *D. scabrilingue* with *D. delacourii*, including *D. snowflake* and *D. ovatum*. Based on these parameters, *Dendrobium* shows unique genetic diversity and relationships. Thus, this information is valuable for future conservation and breeding programs of *Dendrobium*.

1. Introduction

Orchid is the second largest flowering plant (Angiospermae), with more than 28,000 species recorded worldwide (Zhang et al., 2022). This genetic resource is essential for edible, ornamental plants, and as a raw material for medicinal and pharmaceutical purposes (Wang et al., 2018). For example, *Dendrobium*, with more than 1500 species present and spread across the tropics and subtropics (Wang, 2021; Zheng et al., 2018), is one of the orchid genera with the second-highest export value worldwide, with transactions reaching US$ 5.6 million (De et al., 2014). Furthermore, *Dendrobium* has been used for a thousand years by traditional Asian communities, especially in China and India, as a tonic or herbal to treat various diseases, such as inflammation, pyretic, and cancer (Cakova et al., 2017; Zhao et al., 2019). Consequently, on the one hand, many bioactive compounds have been explored massively from these *Dendrobium* species. On the other hand, breeding efforts to assemble new *Dendrobium* cultivars are also being carried out.

For years, three colorful flowers of *Dendrobium*, i.e., yellow, yellow-white, and purple-white, including sweet smell characteristics, have been modified to make novel hybrids or cultivars (Sawettalake et al., 2017; Li et al., 2021). In this case, over 8,000 *Dendrobium* hybrids or cultivars have been developed by inter-specific hybridization related to flower morphological characteristics (Pongsrila et al., 2014). However, this success is not directly proportional to its existence in the wild. Most wild *Dendrobium* species are susceptible and decrease due to deforestation, natural fragmentation of habitats, and other factors (Hinsley et al., 2018). Further, some are listed as endangered status in the CITES (Convention on International Trade in Endangered Species) Appendix II, e.g., *Dendrobium aberrans* (from Papua New Guinea), *D. acutimentum* (Indonesia), *D. acutilingue* (Philippines), and *D. alabense* (Malaysia) (CITES, 2023). The International Union for Conservation of Nature and Natural Resources also reported some endangered *Dendrobium*, for example, *D. whistleri*, *D. flexicaule*, and *D. leptocladum* (IUCN, 2023).

Thus, assessment and evaluation of these genetic resources are urgent. Conventionally, comparative morphology and anatomy are familiar in determining or assessing the diversity and relationships of *Dendrobium* (Adams, 2011). However, these two approaches have certain limitations due to the high variability of these orchids. Sometimes, the results are confusing due to environmental factors. Hence, further study needs to be employed by more strong characteristics than morphological and anatomical ones. One of which is biochemical marker application. While this marker is less effective than molecular, the data are beneficial for ensuring quality, efficacy, and safety in the herbal medicine sector (Gahlawat et al., 2017). Besides, analysis of diversity and genetic relationships of *Dendrobium* using biochemical markers is rarely reported or carried out.

This study aimed to assess the genetic diversity and the relationships of *Dendrobium* germplasm based on bioactive compounds, their biological activities, and the type of plant organs, by a meta-analysis approach. According to Deshmukh (2021), meta-analysis is a statistical combination of results from two or more separate studies extracted from aggregate data of published articles. Then, in addition to being easy, simple, and low-cost, it can overcome the constraints of formal statistical techniques by aggregating the results of individual experiments to draw general conclusions (van de Wouw et al., 2010). Following Simske (2019), this approach shows high efficiency and is comprehensible to the entire gamut of data science. Several studies using this technique, such as van de Wouw et al. (2010), in evaluating genetic diversity trends in crop cultivars from the twentieth century, and Saputra et al. (2021) for swamp and river buffalo haplotype diversity based on the *cytochrome b* gene.

2. Material and Methods

2.1. Data collection

This study was conducted using a meta-analysis approach, initially by collecting, tabulating, and analyzing various data based on literature searching. A total of 51 species of *Dendrobium* have been collected and identified as producing bioactive compounds, including their biological activities (Table S1, Supplementary).

2.2. Data analysis

The data obtained were then analyzed in a multivariate manner using a numerical taxonomy approach with the help of MVSP ver. 3.1 (Kovach, 2007). The genetic diversity of *Dendrobium* was determined using the Shannon-Weaver index (H') by the following equation:

$$\boldsymbol{H' = -\sum pi(\log_2 pi)/\log_2 N}$$

In this case, *pi* was the ratio of the frequency of observed characters, while *N* was the sum of all observed characters. The level of genetic diversity was determined by criteria: maximum, H = 1.00; high, H = 0.76–0.99; moderate, H = 0.46–0.75; and low, H = 0.01–0.45 (Mursyidin and Khairullah, 2020). Reconstruction of genetic relationship using cluster analysis with UPGMA (unweighted pair group of arithmetic means) method and MVSP ver. 3.1 (Kovach, 2007). The principal component analysis (PCA) was employed to evaluate the orchid grouping (Das et al., 2017).

3. Results and Discussion

Bioactive compounds are necessary as raw drug materials for pharmaceutical and medicinal purposes (Atanasov et al., 2021). Most of such materials are obtained from nature today (Atanasov et al., 2021). According to Srivastava et al. (2014), the primary source of drugs comes from medicinal plants and has been explored for the foundation of systematic conventional medicinal products worldwide. In this study, *Dendrobium* was identified as containing dominant compounds, i.e., flavonoid and bibenzyl (Figure 1), as reported similarly by Wang (2021).

According to Hostetler et al. (2017), flavonoids are secondary metabolites belonging to the phenolic class (because they have polyphenolic groups) and are present in various plants, including food sources such as fruits and vegetables. In general, secondary metabolites are involved in the interaction of plants with their environment, and hence they are particularly substantial for ecological functions, e.g., allelopathy, animal attractants, seed distribution, and biochemical defense against bacteria, bugs, and herbivores (Srivastava et al., 2014).

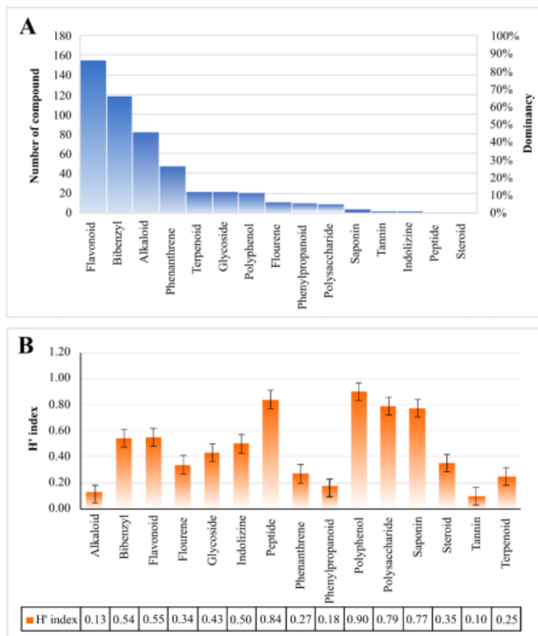

Figure 1. Bioactive compounds found in *Dendrobium*: dominancy (A) and its genetic diversity (B)

In particular, flavonoids have essential biological roles in diverse organisms (Kumar and Pandey, 2013). In plants, for example, this compound is synthesized by the phenylpropanoid pathway and has urgent responsibilities in pigmentation and fragrance in flowers, including attracting pollinators in seed or spore germination and fruit dispersion (Kumar and Pandey, 2013). Furthermore, flavonoids protect plants from many abiotic and biotic stressors, including frost hardiness, drought tolerance (Panche et al., 2016), and microbial infection (Kumar and Pandey, 2013). Recently, these compounds have been responsible for many pharmacological activities (Kumar and Pandey, 2013).

Meanwhile, bibenzyls are a secondary metabolite distinguished structurally by the absence and presence of two phenyls connected with ethane (C_6-C_2-C_6) (Nandy and Dey, 2020). Bibenzyls are fragrant chemicals found in plants and bryophytes (Nandy and Dey, 2020). It is generated from the phenylpropanoid biosynthesis pathway and belongs to the polyketide family. This pathway comprises numerous secondary metabolites (Chen et al., 2022). Furthermore, bibenzyls are the synthetic precursors of dihydrophenanthrenes. He et al. (2017) reported twenty-three bibenzyls with flexible structures. For *Dendrobium*, 89 bibenzyl derivatives were present (He et al., 2020).

Interestingly, bibenzyl and flavonoids are interrelated in the biosynthetic pathway (Ahmad et al., 2022). In this case, the difference lies in the enzyme binding to substrates. For example, as a member of the polyketide synthase, chalcone synthase catalyzes the Claisen cyclization to create chalcones and dihydrochalcones (bibenzyl derivates), which are required for flavonoid biosynthesis (Chen et al., 2022). According to Lei et al. (2018), 31 unigenes annotated by the Kyoto Encyclopedia of Genes and Genomes (KEGG) database were engaged in flavonoid pathways by bio-modification, accumulation, transportation, and controlling process.

However, recent interest in the substances of bioactive compounds has shown the potential health benefits. In this study, the bioactive compounds of *Dendrobium* show the highest antioxidant, anticancer, and anti-inflammatory activities (Figure 2). According to Kumar and Pandey (2013), flavonoids' functional hydroxyl groups, for example, can mediate antioxidant actions by scavenging free radicals and chelating metal ions. Furthermore, these chemicals are linked to a broad spectrum of health-promoting effects and are essential for nutraceutical, pharmacological, medical, and cosmetic applications (Panche et al., 2016). Beneficial biochemical and antioxidant effects have even been linked to many diseases, such as cancer, Alzheimer's, atherosclerosis, and others (Panche et al., 2016).

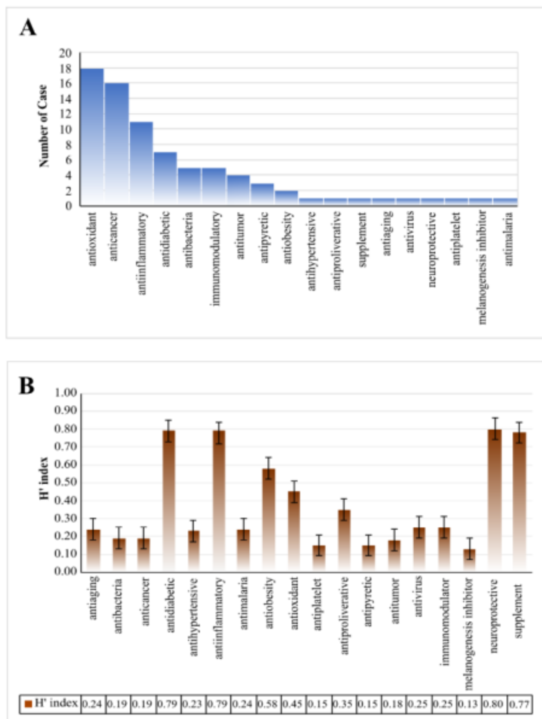

Figure 2. The activity of bioactive compounds found in *Dendrobium*: dominancy (A) and its genetic diversity (B)

Regarding the plant parts used, although the leaf has the highest H index of diversity, i.e., 0.89, the stem is the most widely used with dominance of 90%, followed by the whole part of the plant (Figure 3). In traditional medicine, several organs or parts of plants are common, such as leaves, roots, stems (barks), flowers, fruits, or seeds (Khan and Ahmad, 2019; Srivastava et al., 2014). However, as the need for bioactive substances has grown, so has the exploitation of medicinal plants. As a result, alternative technologies for producing metabolites from plants on a big scale without damaging their natural population are urgent (Cragg and Newman, 2013).

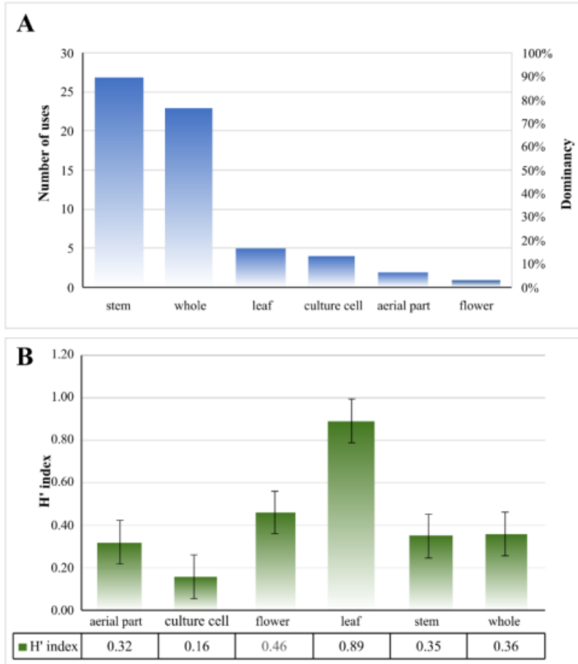

Figure 3. Plant organ and related source of *Dendrobium* which is widely used as a producer of bioactive compounds: dominancy (A) and its genetic diversity (B)

Initially, researchers tried to domesticate or cultivate medicinal plants to support conservation efforts (Phondani et al., 2016). However, due to rapid changes or replacement market demand, the cultivator finds it difficult to choose and decide which plant species to plant (Chen et al., 2016). In addition, most of the medicinal plants come from natural seeds (wild populations) (Hilonga et al., 2019). Generally, these seedlings have low germination rates or specific ecological requirements, making them hard to plant. For example, *Cymbidium* and *Phalaenopsis* are famous orchids that bloom after 2–3 years of vegetative phase (Ahmad et al., 2022).

Another issue is the lack of knowledge about pollination, seed germination, and growth in medicinal plant production (Febjislami et al., 2019). Domestic production of medicinal plants is a potential conservation method that lowers misidentification, genetic and phenotypic diversity, extract variability and instability, hazardous components, and contamination in herbal extracts (Chen et al., 2016; Guo et al., 2009). In this case, biotechnology allows for plant cells, tissues, organs, or entire organisms by cultivating them in vitro to obtain desired substances (Alamgir, 2018; Panche et al., 2016).

Many biotechnological procedures, such as embryogenesis, organogenesis, cell line screening, media modification, and elicitation, have recently been developed to improve the production of secondary metabolites from medicinal plants (Mohaddab et al., 2022). Cell cultures containing bioactive compounds are collected at a specified period (typically during the stationary phase of their development cycle), dried, extracted, identified, and quantified (Twaij and Hasan, 2022). The core notion of plant cell suspension is biosynthetic totipotency, in which each cell in the culture preserves the complete genetic information for the range of chemical creation (Fazili et al., 2022).

Then, apart from the essential value of the bioactive and the activities, information on the genetic diversity of *Dendrobium* is also urgent and needed. According to Govindaraj et al. (2015), genetic diversity is necessary to develop a new line population for future evolutionary processes and adaptive environmental changes. Hence, this parameter is critical for future conservation and breeding programs (Lloyd et al., 2016). For conservation, assessing genetic diversity has a beneficial impact on increasing the effectiveness and efficiency of that program (Salgotra and Chauhan, 2023).

Similarly, this parameter becomes more valuable in the context of climate change for plant breeding efforts (Govindaraj et al., 2015). In this case, high levels of genetic diversity are beneficial in promoting population survival and adaptive potential guarantee in the face of rapidly changing environmental factors (Teixeira and Huber, 2021). In other words, preserving genetic diversity is urgent in retaining their capability for the current and future crop breeding programs (Swarup et al., 2021).

Besides genetic diversity, analysis of genetic relationships is also a valuable parameter for plant conservation and breeding programs. In this study, the UPGMA analysis showed that *Dendrobium* grouped into seven clusters (Figure 4), where the furthest relationship had presented by *D. moschatum* and *D. catenatum*. Meanwhile, the closest relation was by *D. scabrilingue* with *D. delacourii*, including *D. snowflake* and *D. ovatum* (Figure 5). The PCA showing a different grouping with the UPGMA, where Dendrobium were separated into six clusters (Figure 6).

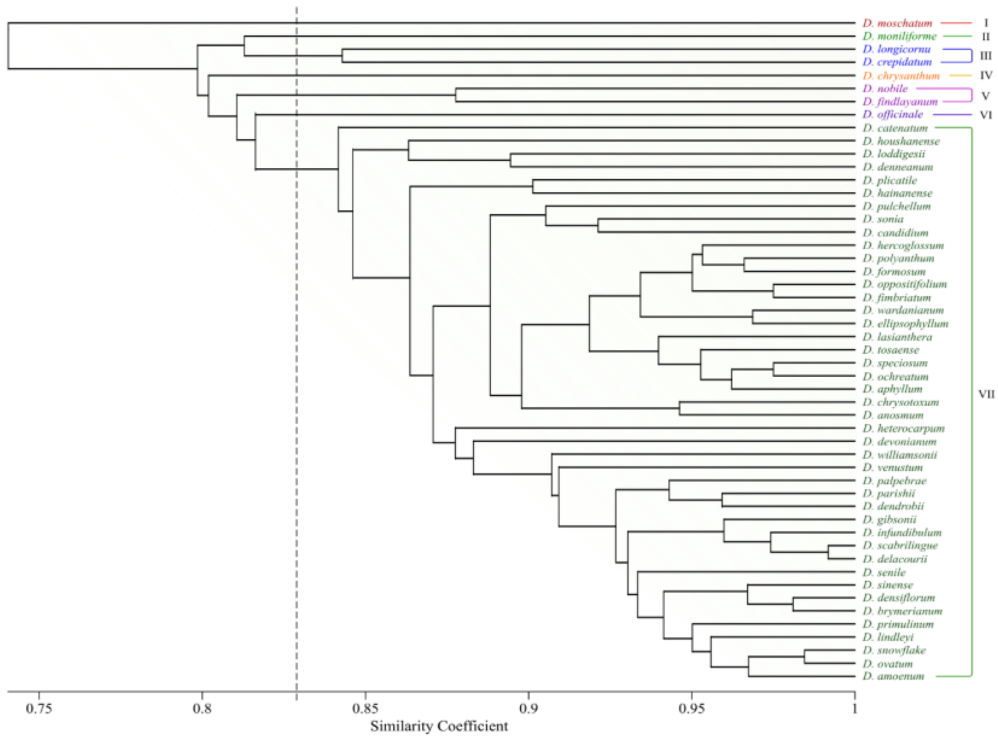

Figure 4. Dendrogram showing the genetic relationship of *Dendrobium* based on bioactive compounds and its bioactivities

Based on a morphological marker, namely internode number (flowering shoot), *D. moschatum* had a close relationship with *D. secundum, D. chrysanthum*, and *D. aphyllum* (De et al., 2015). *D. aphyllum* alone had a close relationship with *D. loddigesii* following the ISSR marker (Wang et al., 2009). Using four chloroplast markers, i.e., *rbc*L, *mat*K, *trn*H-*psb*A, and *trn*L intron, including the internal transcribed spacer (ITS) of the nuclear ribosomal DNA, (Xiang et al., 2013) also reported the closed relationship between *D. aphyllum* and *D. loddigesii*. However, by the ITS and the SSR (simple sequence repeat), *D. moschatum* had to be closed with *D. denneanum* and *D. fimbriatum* (Yuan et al., 2009), including *D. heterocarpum* (Zhao et al., 2019). Finally, *D. moschatum* had a close relationship with *D. crumenatum*, *D. anosmum*, *D. macrophyllum*, and *D. spectabile* by chromosome number (2n = 38) (Zheng et al., 2018).

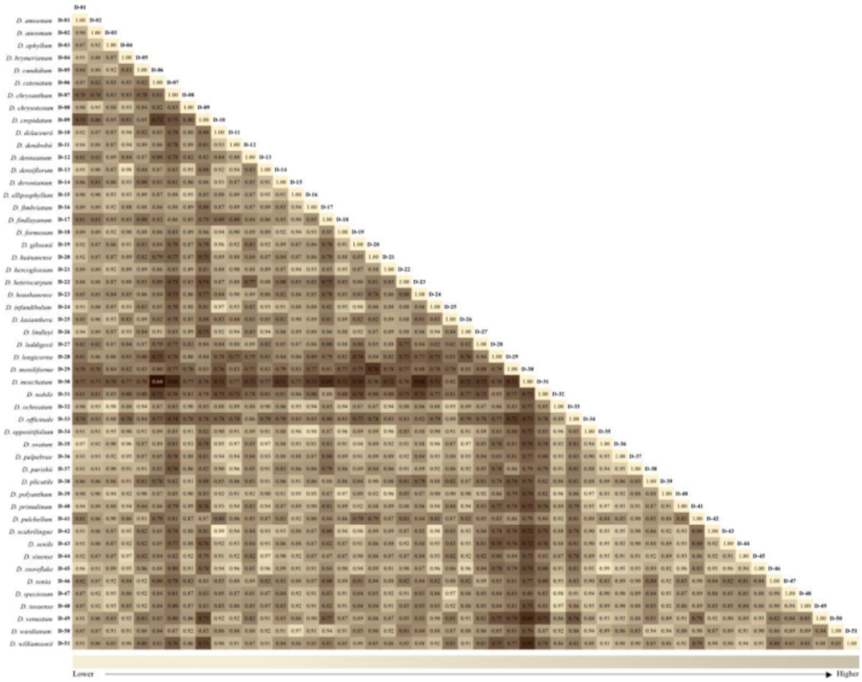

Figure 5. Genetic distance between *Dendrobium* species based on bioactive compounds and its bioactivities, revealed by maximum likelihood (ML)

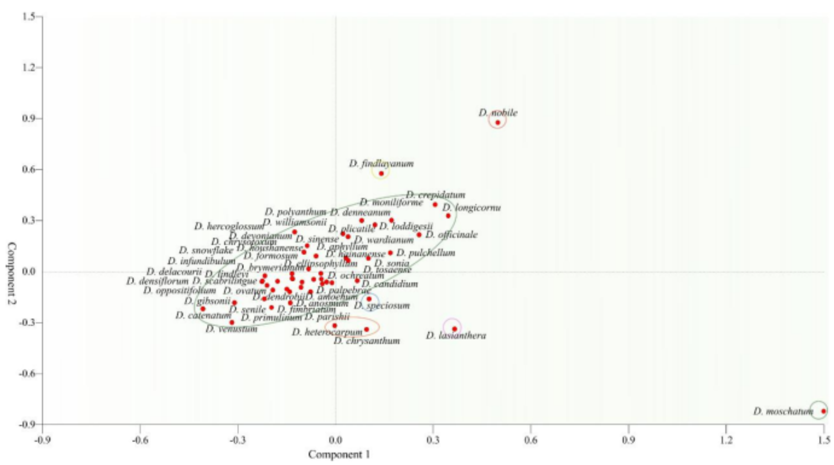

Figure 6. Grouping of *Dendrobium* based on bioactive compounds and its bioactivities, revealed by principle component analysis (PCA)

4. Conclusion

Based on bioactive compounds, their biological activities, and plant organs, *Dendrobium* shows unique genetic diversity and relationships. In this case, the highest genetic diversity was shown by polyphenols (H' index = 0.90) as substances, neuroprotective (H' = 0.80) for activity, and the leaf organ with an H' index of 0.89. The UPGMA analysis showed that *Dendrobium* grouped into seven clusters, where the furthest relationship had presented by *D. moschatum* and *D. catenatum*. Meanwhile, the closest relation was by *D. scabrilingue* with *D. delacourii*, including *D. snowflake* and *D. ovatum*. This information is valuable for future *Dendrobium* conservation and breeding programs.

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Supplementary

Table S1. List of *Dendrobium* species, including their class compound, source, and biological activities

No	Dendrobium Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
1	*D. amoenum*	1	1	Terpenoid	Unspecified	Whole	Antibacteria	Shrestha et al. (2015)
2	*D. anosmum*	1	1	Terpenoid	Unspecified	Culture cell	Antioxidant	Prasetyo et al. (2020)
3	*D. aphyllum*	14	14	Phenanthrene	(1) Aphyllone A, (2) Aphyllone B, (3) Aphyllals C, (4) Aphyllals D, (5) Aphyllas E, (6) Moscatin, (7) Hircinol, (8) Moscatiline, (9) Gigantol, (10) Batatasin III, (11) Tristin, (12) Dihydroresveratrol, (13) Trigonopol B, (14) Tricetine	Stem	Antioxidant	Yang et al. (2015)
4	*D. brymerianum*	8	8	Flavonoid	(1) Mostaciline, (2) Gigantol, (3) Lusianthridine, (4) Dendroflorin, (5) Flavanthrinin, (6) Nobilone, (7) Denchrysan, (8) Tristan	Whole	Anticancer	Klongkumnuankarn et al. (2015)
5	*D. candidium*	1	1	Polysaccharide	2,4-Dinitrofluorobenzene	Stem	Antihypertensive Antiinflammatory, antioxidant	Xiao et al. (2018) Liang et al. (2022)
			1	Peptide	unspecified	Whole	Antiproliferative	Zheng et al. (2015)
6	*D. catenatum*	2	1	Polysaccharide	O-acetylated glucomannan	Stem	Immunomodulator	Liu et al. (2022); Qi et al. (2022)
						Stem	Antihyperlipidemic	Han et al. (2021)
7	*D. chrysanthum*	13	7	Phenylpropanoids	(1) p-hydroxyphenylpropionic acidic, (2) p-coumaric acid lactone, (3) Caffeic acid, (4) Methoxybenzoic acid, (5) Coumarin, (6) Phenilalanin, (7) Tri-p-coumaric acidic ester	Stem	Antipyretic, immunomodulator	Cai et al. (2018)

Table S1. Continued..

No	Dendrobium Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
7	*D. chrysanthum*		2	Flourenone	(1) Denchrysans A, (2) Denchrysans B	Stem	Immunomodulator	Ye et al. (2003)
			1	Phenanthrene	Phenanthrenediglycodiglycoside denchryside A			
			3	Saponin	(1) Glucopyranosyl, (2) (25R)-26-O-(α-d-glucopyranosyl)-(1→2)-α-lrhamnopyranosyl-furost-5-ene-3β, (3) 22α, 26-triol-3-O-α-d glucopyranoside	Stem	Anticancer	Yang et al. (2019)
8	*D. chrysotoxum*	1	1	Bibenzyl	Erianin	Culture cell	Anticancer	Chen et al., (2020); Wang (2021)
9	*D. crepidatum*	15	5	Polyphenol	(1) Stigmasterol, (2) 2-methoxy-4-vinylphenol, (3) 2-methoxy-5-1-propenyl-phenol, (4) p-mesyloxyphenol, (5) 2,6-dimethoxy-4-(2-propenyl)-phenol)	Stem	Antioxidant	Paudel et al. (2019)
			4	Flavonoid	(1) Tetracosane, (2) Triacontane, (3) Tetradecanoic acid, (4) Hexadecanoic acid	Stem	Anticancer	Paudel et al. (2019)
			4	Alkaloid	Dendrocrepidamine A, Dendrocrepidamine B, Crepidamine, Isocrepidamine,	Stem	Antiinflamatory	Hu et al. (2020)
			2	Indolizidine	(1) Crepidatumin C, (2) Crepidatumin D	Stem	Antidiabetic	Xu et al. (2020)
10	*D. delacourii*	11	11	Flavonoid	(1) Hircinol, (2) Ephemerantho-quinone, (3) Densifloral B, (4) Moscatin, (5) 4,9-dimethoxy-2,5-phenanthrenediol, (6) Gigantol, (7) Batatasin III, (8) Lusianthridin, (9) 4,4′,7,7′-tetrahydroxy-2,2′dimethoxy-9,9′,10,10′-tetrahydro-1,1′-biphenanthrene, (10) Phoyunnanin E, (11) Phoyunnanin C	Whole	Antidiabetic	Thant et al. (2022)

Table S1. Continued..

No	Dendrobium Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
11	*D. dendrobii*	4	4	Flavonoid	(1) 4-hydroxybenzoic acid, (2) Vanillic acid, (3) Syringic acid, (4) Ferulic acid	Whole	Antiinflammatory	Yoo et al. (2017)
12	*D. denneanum*	26	6	Alkaloid	Denneanoside A - F	Stem	Antitumor	Li et al. (2013)
			8	Phenanthrene	three new phenanthrene glycosides, three new 9,10-dihydrophenanthrenes, and two new 9,10-dihydro- phenanthrenes glycosides	Stem	Antiinflammatory	Lin et al. (2013)
			8	Flavonoids	(1) Apigenin-6,8-di-C-glucoside, (2) Isoschaftoside, (3) Schaftoside, (4) Quercetin-3-O-rutinoside-7-O-glucoside, (5) Rutin, (6) Kaempferol-3-O-rutinoside, (7) Apigenin-7-O-rutinoside, (8) Apigenin-6-C-glucosyl-2-O-xyloside.	Stem	Antitumor	Zhou et al. (2018)
13	*D. densiflorum*	1	1	Alkaloid	Cypripedin	Whole	Anticancer	Wattanathamsan et al. (2018)
14	*D. devonianum*	18	14	Flavonoid	(1) 5- hydroxy-3-methoxy-flavone-7-O-[b-D-apiosyl-(1 6)]-b-D-glucoside, (2) Gigantol, (3) Syringaresinol, (4) N-trans-feruloyl tyramine, (5) Paprazine, (6) Vanillic acid, (7) p-hydroxybenzoic acid, (8) p-hydroxybenzaldehyde, (9) Oleanolic acid, (10) Vomifoliol, (11) 7-oxo-b-sitosterol, (12) 3b-hydroxy-5a,8a-epidioxyergosta-6,9,22 triene, (13) b-sitosterol, (14) Daucosterol	Whole	Antidiabetic	Sun et al. (2014)
			4	Alkaloid	(1) Dendrodevonin A, (2) Dendrodevonin B, (3) Dendrodevonic acid A, (4) Dendrodevonic acid B	Stem	Anticancer	Wu et al. (2019)

Table S1. Continued..

No	Dendrobium Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
15	*D. ellipsophyllum*	1	1	Bibenzyl	4,5,4′-trihydroxy-3,3′-dimethoxy bibenzyl	Stem	Anticancer	Hlosrichok et al. (2018)
16	*D. fimbriatum*	4	4	Glycosides	(1) Gigantol-5-O-β-d-glucopyrano side, (2) 9,10-dihydro-aphyllone A-5-O-β-d-gluco pyranoside, (3) Ficusal-4-Oβ-d-glucopyranoside, (4) Botry diol-15-O-β-d-glucopyranoside	Stem	Antipyretic	Xu et al. (2017)
			9	Alkaloid	(1) Dendrofinline A; (2) Dendrofin line B; (3) Findlayinine A; (4) Find layines E; (5) Findlayines F; (6) 6-hydroxy-dendroxine; (7) Nobiline; (8) Dihydronobilonine; (9) Mubironine	Stem	Anticancer	Yang et al. (2020)
17	*D. findlayanum*	27	9	Bibenzyl	(1) 3, 4, 4′-trihydroxy-5-metho xybibenzyl, (2) (R)-3, α-di hydroxy-4, 5, 4′-trimethoxy bibenzyl, (3) 3, 4-dihydroxy-5, 3′, 4′-trimethoxy bibenzyl, (4) 4, 4′- dihydroxy-3, 3′, (5) 5-trimethoxy bibenzyl, (6) 3′, 4-dihydroxy-3, 5-dimethoxy bibenzyl, (7) 3, 3′- di hydroxy-5-me thoxy bibenzyl, (8) 3, 3′- dihy droxy-4, 5′-dimethoxy bibenzyl, 3, 4′-di hydroxy-5-methoxy bibenzyl, (9) 4, 4′-dihydroxy-3, 5-dimethoxy bibenzy	Stem	Anticancer	Liu et al. (2020)
			9	Terpenoids	(1) 3, α-dihydroxy-4, 4′, 5 -tri, 3, 4 dihydroxy- 3′, 4′, 5-, (2) 14-trihydroxyalloaromadendrane, (3) Trimethoxybibenzyl, (4) Methoxybibenzy, (5) 0β, 12, 14-tridroxyaromadendrane, (6) 10β, 13, 14-tridroxyaromadendrane, (7) Dendroside A, (8) dendronobilin I, (9) Dendronobilin N	Stem	Immunomodulator	Yang et al. (2019)

Table S1. Continued..

No	*Dendrobium Species*	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
18	*D. formosum*	6	6	Flavonoid	(1) Coelonin, (2) Erianthridin, (3) Moscatilin, (4) Lusianthridin, (5) Gigantol, (6) Batatasin III	Stem	Antidiabetic	Pengdee et al. (2020)
19	*D. gibsonii*	9	9	Flourene	(1) Dihydrodengibsinin; (2) Dendrogibsol; (3) Ephemeranthol A; (4) Dengibsinin; (5) Nobilone; (6) Aloifol I; (7) Lusianthridin; (8) Denchrysan A; (9) 4-methoxy-9H-fluorene-2,5,9-triol	Whole	Antidiabetic	Thant et al. (2020)
20	*D. hainanense*	14	14	Flavonoid	(1) 2-hydroxy-3-(4-hydroxy-3-methoxyphenyl)-3-methoxypropyl 3-(4-hydroxyphenyl)propanoate, (2) 3,4-dimethoxy-1-(methoxymethyl)-9,10-dihydrophenanthrene-2,7-diol, (3) Dihydroconiferyl dihydro-p-coumarate, (4) 7-hydroxy-2,3,4-trimethoxy-9,10-dihydro-phenanthrene, (5) Alatusol A, (6) Threo-8S-7-methoxysyringylglycerol, (7) (E)-coniferyl aldehyde, (8) Sinapical dehyde, (9) E-p-hydroxy cinnamic acid, (10) 4-hydroxymethyl-2-Methoxyphenol, (11) Vanillin, (12) Syringaldehyde, (13) p-hydroxyphenylpropionic methyl ester, (14) 2,6-dimthoxy-4-allyphenol	Aerial parts	Antibacterial	Zhang et al. (2019)
21	*D. hercoglossum*	5	1	Bibenzyl	4,5-dihydroxy-3,3′-dimethoxybibenzyl	Stem	Supplement	Hu et al. (2020)
			4	Flavonoid	(1) 3-hydroxy-3-methylglutaryl, (2) p-coumaroyl, (3) Feruloyl, (4) Sinapoyl			

Table S1. Continued..

No	*Dendrobium Species*	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
22	*D. heterocarpum*	7	6	Bibenzyl, Phenylpropanoid	(1) Amoenylin, (2) Methyl 3-(4-hydroxyphenyl) propionate, (3) 3,4-dihydroxy-5,4'-dimethoxybibenzyl, (4) Dendrocandin B, (5) Dendrofalconerol A, (6) Syringaresinol	Whole	Anti-obesity	Warinhomhoun et al. (2022)
			1	Flavonoid	unspecified	Leaf	Antioxidant	Longchar & Deb (2022)
			4	Bibenzyl	(1) 3-hydroxy-5-methoxybibenzyl, (2) 3-hydroxy-5,40-dimethoxybibenzyl, (3) Dendrocandin U, (4) Dendrocandin B	Stem	Anti-inflammatory	Li et al. (2020)
23	*D. houshanense*	6	1	Polysaccharides	Tyramin	Whole	Anti-inflammatory	Xie et al. (2018, 2019)
			1	Polysaccharides	Heteropolysaccharide	Culture cell	Antitumor	Si et al. (2018)
24	*D. infundibulum*	9	9	Alkaloid, Bibenzyl	(1) Dendoinfundin A, (2) Dendoinfundin B, (3) Batatasin III, (4) Dendrosinen B, (5) Ephemeranthol A, (6) Moscatilin, (7) Aloifol I, (8) 3,3′-dihydroxy-4,5 dimethoxybibenzyl, (9) 5,4′-dihydroxy-3,4,3′-trimethoxybibenzyl	Whole	Antidiabetic	Na Ranong et al. (2019)
25	*D. lasianthera*	2	2	Alkaloid, Tannin	unspecified	Leaf and stem	Antioxidant	Pratiwi et al. (2021)
26	*D. lindleyi*	5	5	Bibenzyl, Alkaloid	Chrysotoxine, Cypripedin, Gigantol, Moscatilin, Novel 4,5-dihydroxy-3,3´,4´-trimethoxybibenzyl	Whole	Immunomodulator	Pratiwi et al. (2021)
27	*D. loddigesii*	18	4	Polyphenol	Moscatilin, Gigantol, Tristin, 2,4,7-trihydroxyl-9,10-dihydro-phenanthrene	Stem	Anti-inflammatory	Li et al. (2018)

Table S1. Continued..

No	*Dendrobium Species*	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
			1	Bibenzyl	Moscatilin		Unspecified	Cardile et al. (2020)
27	*D. loddigesii*	18	14	Flavonoid	(1) Threo-7-Oethyl-9-O-(4-hydro xyphenyl)propionyl-guaiacylglycerol, (2) (R)-4,5,4′-trihydroxy-3,3′,α-tri methoxybibenzyl, (3) (S)5,5′,7-trihydroxy-3′,4′-dimethoxyflavanone, (4) Crepidatin, (5) Moscatilin, (6) 4,5,4′-trihydroxy3,3′-dimetho xybibenzyl, (7) 4′,5-dihydroxy-3,3′dimethoxybibenzyl, (8) Tristin, (9) Batatasin III 9, (10) 3,5,3′-hydroxybibenzyl, (11) Aphyllals C, (12) Densiflorol A, (13) Dihydro coniferyl dihydro-p-coumarate, (14) p-hydroxyphenethyl trans-ferulate 14	Stem	Antiaging	Ma et al. (2019)
			5	Polyphenol	(1) Tetracosanoicacid, (2) 9-Hexa decyn-1-ol, (3) 3-Heptadecanol, (4) Pentafluoropropionate trans-2-dode cen-1-ol, 6,10-Dimethyl-4-unde canol, (5) α-Cadinol	Stem	Antioxidant, anticancer	Paudel et al. (2020)
28	*D. longicornu*	22	17	Flavonoid	(1) Hydroxyacetic acid, (2) 4-Pyri dinecarboxylic acid, (3) Docosanoic acid, (4) Cedrene, (5) 14-methyl-pentadecanoic acid, (6) 7-Hexa decenoic acid, (7) 15-methyl-hexa decanoic acid, (8) 5-Isopentyl-4-methyl-2-(methylsulfanyl)-6-((trimethylsilyl)oxy) pyrimidine, (9) Hexahydro-2,5-Methano-2H-furo [3,2-b]-pyran-8-ol, (10) 8-Methyl-6-nonenoic acid, (11) E,E,Z,-1,3,12-Nonadecatriene-5 14-diol, (12) (Z,Z,Z)-9,12,15-Octadecatrienoic	Culture cell	Antibacteria	Paudel et al. (2020)

Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
28	*D. longicornu*			Flavonoid	acid, (13) 9-Methoxy-11-Oxa tetracyclo [4.2.1.1(2,5).1(7,10)] undec-3-ene, (14) 8-Methyl-8-oxide-8-Azabicyclo [3.2.1] octan-3-ol, (15) Pentafluoropropionate-trans-2-dodecen-1-ol, (16) Cyclobutane carboxylic acid, (17) Methyl-6-methyl-3-pyridyl ketone-4-cyclo hexyl-thiosemicarbazone	Culture cell	Antibacteria	Paudel et al. (2020)
29	*D. moniliforme*		25	Phenanthrene	(1) 9,10-dihydrophenanthrene,1,5-dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene, (2) Hircinol, (3) (2R*,3S*)-3-hydroxymethyl-9-methoxy-2-(40-hydroxy-30,50-dimethoxyphenyl)-2,3,6,7-tetrahydro phenanthro[4,3-b]furan-5,11-diol, (4) diospyrosin, (5) Aloifol I, (6) Moscatilin, (7) 3,40-dihydroxy-30,4,5-trimethoxybibenzyl, (8) Gigantol, (9) 3,30-dihydroxy-4,5-dimethox ybibenzyl, (10) Long icornuol A, (11) N-trans-cinna moyltyramine, (12) Paprazine, (13) N-trans-feruloyl 30-O-methyl dopamine, (14) Moupinamide, (15) Dihydroconiferyldihydro-p-couma rate, (16) Dihydrosinapyl dihydro-p-coumarate, (17) 3-isopropyl-5-aceto xycyclohexene-2-one-1, (18) p-hydro xybenzaldehyde, (19) Vanillin, (20) p hydroxyphenylpropionic acid, (21) Vanillic acid, (22) Protocatechuic acid, (23) (þ)-syringaresinol, (24) b-sitosterol, (25) Daucosterol	Whole	Anti-inflammatory, immunomodulator	Zhao et al. (2015)

Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
29	*D. moniliforme*		20	Bibenzyl, Polyphenol	(1) Dimethylsulfoxonium formylmethylide, (2) 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl, (3) 3-Cyclohexene-1-methanol,.alpha.,alpha.,4-trimethyl-,(S), (4) 3(2H)-Furanone, 4-methoxy-2,5-dimethyl- (5) Thiophene-3-ol, tetrahydro-, 1,1-dioxide, (6) 2-Furancarboxaldehyde, 5-(hydroxymethyl) (7) 5-Acetoxymethyl-2-furaldehyde, (9) 2-Methoxy-4-vinylphenol (10) Phenol, 2,6-dimethoxy-, (11) 4-Methyl-2,5-dimethoxybenzaldehyde, (12) Cinnamic acid, 4-hydroxy-3-methoxy-, (13) Phenol, 2,6-dimethoxy-4-(2-propenyl), (14) 4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol, (15) Pentadecanoic acid, (16) Methyl (3,4-dimethoxyphenyl)(hydroxy) acetate, (17) Benzenemethanol, 2,5-dimethoxy-, acetate, (18) Bis[(4-methoxyphenyl)methyl]disulfide, (19) Tetradecanal, (20) .gamma.-Sitosterol	Stem	Antioxidant, anticancer	Paudel et al. (2018)
30	*D. moschatum*	10	10	Flavonoids, tannins, saponins, alkaloids, glycosides, steroids and phenols	(1) Coumarin, (2) oxalic acid, (3) palmitin, (4) dihydrocoumarin, (5) 2,4-dimethyl-2-pentanol, (6) sulfurous, (7) 2-benzedicarboxylic acid, (8) bis (2-methylpropyl) ester, (9) 1-iodo-2-methylnonane, (10) palmitic acid	Leaf	Antioxidant, antimicrobial, anti-inflammatory, anticancer, anti hiv	Rajput & Saikia (2020)

Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
			4	Bibenzyl	benzedicarboxylic acid, bis (2-methyl propyl) ester, 1-iodo-2-methyl nonane, palmitic acid	Stem	Antibacteria	Cheng et al. (2020)
			4	Alkaloid	(1) Noresinol, (2) Syringaresinol, (3) dihydroconiferyl dihydro-p-coumara, (4) dihydrosinapyl dihydro-p-coumarate			
31	*D. nobile*	33	8	Terpenoid	(1) 12-trihydroxypicrotoxane-2(15)-lactone, (2) 3,11,13-trihydro xypicrotoxane-2(15)-lactone, (3) 8,12-dihydroxy-copacamphan-3-en-2-one, (4) Quinate, (5) Uinic acid butyl ester, (6) n-butyl-1-O-α-L-rhamnopyranoside, (7) benzyl-O-β-D-glucopyranoside, (8) d p-hydroxy phenylethanol	Stem	Neuroprotective	Ma et al. (2019)
			10	Bibenzyl	(1) Nobilin D, (2) Nobilin E, (3) Nobilon, (4) Crepidatin, (5) chryso tobibenzyl, (6) Dendrobin A, (7) Chrysotoxine, (8) Moscatilin, (9) Gigantol, (10) Dendroflorin	Stem	Antioxidant	Zhang et al. (2007)
			5	Terpenoids	(1) Dendronobilin A, (2) Dendro nobilin B, (3) Dendrodensiflorol, (4) Dendrobine, (5) Findlayanin	Stem	Anticancer	Meng et al. (2017)
			2	Bibenzyl	(1) Dendrocoumarin, (2) Itolide A, (3) Dendrodise	Stem	Anticancer	Zhou et al. (2018)
32	*D. ochreatum*	1	1	Flavonoid	Unspecified	Stem	Antioxidant	Banerje et al. (2015)
33	*D. officinale*	19	2	Polysaccharides	(1) DOP1-DES, (2) DOP2-DES	Stem	Antioxidant	Liang et al. (2018); Xing et al. (2018); Zhao et al. (2017)

Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
33	*D. officinale*		2	Polysaccharides	(1) DWDOP, (2) FWDOP	Stem	Antitumor	Yu et al. (2018)
			1	Flavonoid	Gigantol	Leaf		Zheng et al. (2018)
			1	polysaccharides	Unspecified		Antioxidant	Zhao et al. (2019)
			7	Alkaloid	Glicoperine, Xanthoplanine, Senkirkenine, Pelletierine, Hordenine, Piperidine, Quinine		Unspecified	Jiao et al. (2018)
			6	Alkaloid	Betaine isohemiphloin, Hordenine, Piperidine, Quinine, Theobromine, Trigonelline	Leaf, stem	Unspecified	Cao et al. (2019)
34	*D. oppositifolium*	4	4	Glycoside	(1) Caffeoylcholine 6-glucoside, (2) Cocamidopropyl, (3) Dopamine hydrocloride, (4) Putrescine	Stem	Unspecified	Takamiya et al. (2018)
35	*D. ovatum*	1	1	Bibenzyl	Moscatilin	Whole	Unspecified	Pujari et al. (2021)
36	*D. palpebrae*	10	1	Alkaloid	dendropalpebrone	Whole	Antioxidant	Kyokong et al. (2019)
			9	Flavonoid	(1) Gigantol, (2) Lusianthridin, (3) Nobilone, (4) 1,5,7-trimethoxyphenanthrene-2,6-diol, (5) 2,5-dihydroxy-4,9-dimethoxyphenanthrene, (6) Moscatilin, (7) Scoparone, (8) 4,5,4′-trihydroxy-3,3′-dimethoxybibenzyl, (9) dendroflorin			
37	*D. parishii*	7	7	Bibenzyl	(1) 4,3′,4′-trihydroxy-3,5-dimethoxybibenzyl, (2) -Dendroparishiol, (3) s flavanthrinin, (4) Moscatilin, (5) 4,5,4′-trihy droxy-3,3′-dimethoxybibenzyl, (6) Dendrocandin E, (7) Asiatic acid	Whole	Antioxidant, antiinflammatory	Kongkatitham et al. (2018)

362 Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
38	*D. plicatile*	16	5	Bibenzyl	(1) 2-chloro-3, 4'-dihydroxy-3',5-dimethoxybibenzyl, (2) 3-methyl gigantol, (3) 3'-hydroxy-3,4,4',5-tetramethoxybibenzyl, (4) Batatasin III, (5) Moscatilin	Aerial parts	Anticancer	Chen et al. (2020)
			11	Alkaloids	(1) Erianthridin, (2) Coelonin, (3) 2,5-dihydroxy-4-methoxy-9,10-di hydrophenanthrene, (4) Lusian thridin, (5) 1,4,7-trihydroxy-2-me thoxy9,10 dihydrophenanthrene, (6) Emphernathol A, (7) 3,7-dihydroxy-2,4-dimethoxy-9,10-dihydrophe nanthrene, (8) Calanhydroquinone, (9) 3,7-dihydroxy-2,4-dimethoxy-phe nanthrene, (10) Nudol, (11) Denthy rsinin			
39	*D. polyanthum*	10	10	Flavonoid	(1) Moscatilin, (2) Gigantol, (3) Bata tasin, (4) Moscatin, (5) 9,10-dihydro moscatin, (6) 10-dihydrophenan threne-2,4,7-triol, (7) Corchoionoside C, (8) β-sitosterol, (9) Daucosterol, (10) 3,6,9-trihydroxy-3,4-dihydro anthracen-1(2H)-one	Stem	Unspecified	Hu et al. (2009)
40	*D. primulinum*	12	12	Glycoside	(1) 2,4,5,9S-tetrahydroxy-9,10-di hydrophenanthrene 4-O- -D-gluco pyranoside, (2) 2,4,7-trihydroxy-9,10 -dihydrophenanthrene, (3) Denthyr sinol, (4) Moscatin , (5) moscatilin, (6) Gigantol, (7) Batatasin III, (8) Tristin, (9) 3,4 ,5-trihydroxybibenzyl, (10) 3,6,9-trihydroxy-3,4-dihydro anthracen-1(2H)-one, (11) -sitosterol, (12) -daucosterol	Whole	Unspecified	Ye et al. (2016)

Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
41	*D. pulchellum*	5	4	Bibenzyl	(1) Chrysotobibenzyl, (2) Chrysotoxine, (3) Crepidatin, (4) Moscatilin	Stem	anticancer, antiinflammatory, antioxidant, anti platelet aggregation	Chanvorachote et al. (2013)
			1	Bibenzyl	Chrysotoxine	Stem	Anticancer	Bhummaphan et al. (2018)
42	*D. scabrilingue*	10	1	Bibenzyl	Dendroscabrol	Whole	Antidiabetic	Sarakulwattana et al. (2020)
			1	Alkaloids	Dinaphthalenone			
			8	Flavonoid	(1) (Z)-ferulic acid tetracosyl ester, (2) (E)-ferulic acid tetra cosyl ester, (3) Gigantol, (4) Batatasin III, (5) Coelonin, (6) Aloifol I, (7) Lusianthridin, (8) RF-3192C			
43	*D. senile*	8	8	Alkaloids	(1) 2,5,7-trihydroxy-4-methoxyphe nanthrene, (2) Moscatin, (3) 2,5-di hydroxy-4,9-dimethoxyphenanthrene, (4) Moscatilin, (5) Aloi fol I, (6) 4, 40,8,80-tetramethoxy[1,10-biphenan threne]-2,20,7,70-tetrol, (7) 2,20,7, 70-tetrahydroxy-4,40-dimetho xy-1,1-biphenanthrene, (8) Bleformin G	Whole	Antiobesity	Pann Phyu et al. (2022)
44	*D. sinense*	16	16	Bibenzyl	(1) Dendrosinens A, (2) Dendrosinens B, (3) Dendrosinens C, (4) Dendrosinens D, (5) 3,4,30-trimethoxy-5,40-dihydroxybibenzyl (DTB), (6) AloifolI, (7) 5,30-dihydroxy-3,4-dimethoxybibenzyl, (8) Longicornuol A, (9) Trigonopol A, (10) Coniferyl p-coumarate, (11) Sinapyl p-coumarate, (12) Coniferyl aldehyde, (13) Syringaldehyde, (14) 3-hydroxy-1-(4-hydroxy-3,5-dimethoxyphenyl)-1-propanone, (15) Tectochrysin, (16) Syringaresinol	Whole	Anticancer	Chen et al. (2014)

Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
45	*D. snowflake*	5	2	Terpenoids	(1) Flakinins A, (2) Flakinins B	Whole		Morita et al. (2000)
			3	Alkaloid	(1) Mubironines A, (2) Mubironine B, (3) Mubironine C			
			1	Flavonoid	Anthocyanin	Flowers	Antioxidant	Obsuwan et al. (2019)
46	*D. sonia*	11	10	Flavonoid	(1) Dencoumarin, (2) 6-feruloyloxyhexanoic ester, (3) Psoralen, (4) 6,7-dimethoxycoumarin, (5) Sinapaldehyde, (6) 2-hydroxy-5-methoxypropiophenone, (7) Zhebeiresinol, (8) Pinoresinol, (9) Syringaresinol, (10) Sesqui-illisimonan A	Stem	Antiinflamatory	Xiang Cai et al. (2020)
47	*D. speciosum*	1	1	Flavonoid	unspecified	Stem, leaf	Antioxidant	Moretti et al. (2013)
48	*D. tosaense*	1	1	Polyphenol	Gigantol	Stem	Antioxidant, melanogenesis inhibitor	Chan et al. (2018)
49	*D. venustum*	7	7	Flavonoid	(1) Flavanthrinin, (2) Gigantol, (3) Densiflorol B, (4) Lusianthridin, (5) Batatasin III, (6) Phoyunnanin C, (7) Phoyunnanin C,	Whole	Antimalaria, antiherpetic	Sukphan et al. (2014)
			1	Terpenoids	Wardianumine A			
			1	Bibenzyl	Dendocandin			
50	*D. wardianum*	13	11	Alkaloid, Bibenzyl	(1) Denbinobin, (2) 9,10-dihydro-denbinobin, (3) Mostatin, (4) loddigesiinols A, (5) Moscatilin, (6) 5-hydroxy-3,4′-dimethoxybibenzyl, (7) 3,4-dihydroxy-5,4′-dimethoxy bibenzyl, (8) Dendrocandin A, (9) Gigantol, (10) Dendrocandin U, (11) Dihydroshihunine,	Stem	Anticancer	Zhang et al. (2017)

Table S1. Continued..

No	*Dendrobium* Species	Total compound	Number of compounds	Class compounds	Specific compounds	Plant organ/ source	Bioactivity	References
51	*D. williamsonii*	23	23	Bibenzyl	(1) Dendrowillol, (2) Moniliformine, (3) Amoenylin, (4) 4,4′-dihydroxy-3,5-dimethoxybibenzyl, (5) Aloifol I, (6) Moscatilin, (7) 3-(2-(7-methoxybenzo[d][1,3] dioxol-5 yl)ethyl)phenol, (8) Rel-(3R,3′S,4R,4′S)-3,3′,4,4′-tetrahydro-6,6′-dimethoxy[3,3′-bi-2H-benzopyran]-4,4′-diol, (9) (+)-syringaresinol, (10) Coniferyl p-coumarate, (11) Balanophonin, (12) Scoparone, (13) 3-hydroxy-1-(4-hydroxy-3,5 dimethoxyphenyl)-1-pro panone, (14) p-hydroxybenzoic acid, (15) Salicylic acid, (16) Methyl 4-hydroxybenzoate, (17) Vanillin, (18) Ergosta-8(9),22-diene-3,5,6,7 tetraol, (19) Stigmast-4-en-3α,6β-diol, (20) 3β-hydroxy-5α,8α-epidioxyergosta-6,9,22-triene, (21) Betulin, (22) β-sitosterol, (23) Daucosterol	Whole	Antitumor	Yang et al. (2018)

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