Dihydrophenanthrenes from medicinal plants of Orchidaceae: A review

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Abstract

The plants of Orchidaceae are widely distributed in the world, 47 species of which have been used as folk medicines with a long history. The tubers and stems of them exhibit diverse efficacy, including clearing heat and resolving toxin, moistening lung and relieving cough and promoting blood circulation. Since dihydrophenanthrenes were responsible for the medical purposes, the characteristic skeletons, pharmacological effects and clinical applications of dihydrophenanthrenes were summarized in this review, so as to provide a theoretical basis for the comprehensive study, development and application of DPs from medicinal plants of Orchidaceae.

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1. Introduction

Orchidaceae family is the largest group of flowering plants including 24,500 species in 775 genera. Forty-seven species in Orchidaceae family have been used as folk medicines with a long history. For example, the tubers of Bletilla striata (Thunb.) Rchb. f. (Baiji) is recorded in the Chinese Pharmacopoeia (2020) to relieve swelling and traumatic bleeding. In Compendium of Materia Medica (Ben Cao Gang Mu), the tubers of B. striata were reported to be used to stop bleeding by grinding the tubers to powder. Some classical folk prescriptions containing B. striata are used for epistaxis, lung atrophy, furuncle, coughing and low-grade fever, such as “Baiji San”, “Baiji Pipa Wan”, “Bai Zi Gao” and “Jin Xian San”. At present, the tubers of B. striata has been served as the main ingredients of some Chinese patent medicines, and these medicines are recorded in the Chinese Pharmacopoeia (2020) and used to treat peptic ulcer, antral gastritis and digestive tracts, such as “Kuai Wei Tablets”, “Weikangling Capsules” and “Jin Xian San”. As a traditional Chinese medicine and a Mongolian medicine, pseudobulbs of Cremastra appendiculata (D. Don) Makino, one of the botanical origins of Shancigu exhibit the efficacy of clearing heat and resolving toxin, moistening lung and relieving cough. Since the Qing Dynasty, pseudobulbs of C. appendiculata have been used to treat breast cancer and gastric cancer. The New Compendium of Materia Medica records that pseudobulbs of C. appendiculata belongs to “dispelling poison” and can eliminate malignant tumors in human body (Chen, 1996). The pseudobulbs of C. appendiculata can not only inhibit the growth and proliferation of cancer cells, induce apoptosis but also interfere with invasion and migration, which has been widely used in clinical practice. Currently, five Chinese patent medicines containing the pseudobulbs of C. appendiculata have been developed and marked in China, which are used for the treatment of liver cancer and gastric cancer, such as “Ci Dan Capsules”, “Ruanjian Oral Liquid”, “Ai Yu Capsules”, “Jin Pu Capsules” and “Ru Pi Qing Pills” (Dong, 2014; Yang, 2016). Therefore, their bioactive ingredients and pharmacological effects have attracted much attention of the medicinal chemists.

Phytochemical research showed that medicinal plants of Orchidaceae are rich of dihydrophenanthrenes (DPs), flavonoids, triterpenoids, alkaloids and bibenzyls, in which DPs are the major bioactive ingredients. Modern pharmacological studies showed that DPs in medicinal plants of Orchidaceae possess anti-inflammatory, anti-tumor, anti-oxidation and anti-bacterial activities (Ishiuchi, et al, 2015; Ma, Zhang, Ding, Liu & Ling, 2016). DPs might be used in the quality control of TCMs from Orchidaceae plants, mainly spread in Pholidota, Bletilla, Dendrobium and Pleione genus (Fig. 1).

2. DPs isolated from Orchidaceae plants

Up to now, 217 DPs have been isolated from medicinal plants of Orchidaceae. According to the number of DP units, they are usually divided into two major groups: DP monomers and DP polymers (Fig. 2). In addition, the numbers and origins of DPs from medicinal plants of Orchidaceae in each subtype are summarized in Fig. 3.

2.1. DP monomers

Seventy-one percent of the natural DPs from medicinal plants of Orchidaceae are DP monomers (1–155). According to the feature of substituents in the chemical structures, DP monomers are divided into simple DP monomers, dihydrophenanthrenequinones, dihydrophenanthrofurans and dihydrophenanthropyrans.

2.1.1. Simple DP monomers

More than 80% of simple DP monomers are from Pholidota, Bletilla, Dendrobium and Spiranthes. The substituents including hydroxy, methoxy and isoprene groups usually link at C-2, C-6 and C-7. The special type, with a five- or six- membered ring formed at C-4 and C-5, has only been isolated from Pholidota genus. The representative structures are afforded in Fig. 4 and the chemical structures, names and origins displayed in Fig. S1 and Table 1.

2.1.2. Dihydrophenanthrenequinones

Several dihydrophenanthrenequinones have been identified with hydroxy, methyl, methoxy and isoprene groups. The representative structures are afforded in Fig. 5 and the chemical structures, names and origins displayed in Fig. S2 and Table 1.

Fig. 1. Distribution of DPs in medicinal plants of Orchidaceae (Sp. = Species).
2.1.3. Dihydrophenanthrofurans and dihydrophenanthropyrans

In dihydrophenanthrofurans and dihydrophenanthropyrans, the rings are mainly attached to the DP core at C-6 and C-7, C-7 and C-8. Moreover, the absolute configuration of most compounds at C-7 was described to be (R), C-6 and C-8 were described to be (S). The representative structures are afforded in Fig. 6 and the chemical structures, names and origins displayed in Fig. S3 and Table 1.
Table 1

Names, origins of DPs isolated from medicinal plants of Orchidaceae.

| No. | Names                                      | Origins               | References                      |
|-----|--------------------------------------------|-----------------------|---------------------------------|
| 1   | Lusianthridin                              | Pholidota chinensis   | Wang, Wang, & Kitanaka. (2007)  |
| 2   | Cannabidiolhydrophenanthrene               | Pholidota chinensis   | Wang, Wang, & Kitanaka. (2007)  |
| 3   | 4,5-Dihydroxy-2-methoxy-9,10-dihydrophenanthrene | Pholidota chinensis   | Wang, Wang, & Kitanaka. (2007)  |
| 4   | Eulophiol                                  | Pholidota chinensis   | Wang, Wang, & Kitanaka. (2007)  |
| 5   | Orchinol                                   | Pholidota chinensis   | Hu et al. (2018)                |
| 6   | Coelonin                                   | Pholidota chinensis   | Rueda, et al. (2014)            |
| 7   | Hiracinol                                  | Pholidota chinensis   | Wang, Wang, & Kitanaka. (2007)  |
| 8   | 2,4,7-Trihydroxy-9,10-dihydrophenanthrene  | Pholidota chinensis   | Wang, Wang, & Kitanaka. (2007)  |
| 9   | 7-Methoxy-9,10-dihydrophenanthrene-2,4-diol | Pholidota chinensis   | Wu, Qu, & Cheng. (2008)         |
| 10  | Erianthridin                               | Pholidota chinensis   | Wang, Wang, & Kitanaka. (2007)  |
| 11  | 7-Hydroxy-2,3,4-trimethoxy-9,10-dihydrophenanthrene | Phildota chinensis   | Hu et al. (2018)                |
| 12  | 2,5-Dihydroxy-3,4-dimethoxy-9,10-dihydrophenanthrene | Pholidota chinensis   | Hu et al. (2018)                |
| 13  | 2,5-Dihydroxyl-3,4,6-trimethoxy-9,10-dihydrophenanthrene | Pholidota chinensis   | Hu et al. (2018)                |
| 14  | 2,7-Dihydroxy-3,4,6-trimethoxy-9,10-dihydrophenanthrene | Pholidota chinensis   | Hu et al. (2018)                |
| 15  | Pholidotol                                 | Pholidota chinensis   | Hu et al. (2018)                |
| 16  | Phocantol                                  | Pholidota chinensis   | Hu et al. (2018)                |
| 17  | Flavidin                                   | Pholidota chinensis   | Hu et al. (2018)                |
| 18  | Flaccidin                                  | Pholidota chinensis   | Hu et al. (2018)                |
| 19  | Coelolin                                   | Pholidota chinensis   | Hu et al. (2018)                |
| 20  | Imbricatin                                 | Pholidota chinensis   | Hu et al. (2018)                |
| 21  | Isoflavidinin                              | Pholidota chinensis   | Hu et al. (2018)                |
| 22  | 1-(4'-Hydroxybenzyl)-imbricatin            | Pholidota yunnanensis | Dong, et al. (2013)             |
| 23  | iso-Oxoflavidinin                          | Pholidota chinensis   | Hu et al. (2018)                |
| 24  | Oxoflavidin                                | Pholidota chinensis   | Hu et al. (2018)                |
| 25  | 0-methylorchinol                           | Bletilla striata      | Bai, Yamaki, Inoue, & Takagi. (1990) |
| 26  | 2,5,8-Trihydroxy-7-methoxy-9,10-dihydrophenanthrene | Bletilla striata      | Zhou, et al. (2019)             |
| 27  | 2,7-Dihydroxy-1-(4'-hydroxybenzyl)-9,10-dihydrophenanthrene-4'-O-β-D-glucoside | Bletilla striata      | Zhou, et al. (2019)             |
| 28  | Bletillatin C                              | Bletilla striata      | Zhou, et al. (2019)             |
| 29  | 2,7-Dihydroxy-1-(p-hydroxybenzyl)-4-methoxyphenanthrene-9,10-dihydrophenanthrene-4'-O-β-D-glucoside | Bletilla striata      | Zhou, et al. (2019)             |
| 30  | 1-(p-Hydroxybenzyl)-4-methoxy-9,10-dihydrophenanthrene | Bletilla striata      | Bai, Yamaki, Inoue, & Takagi. (1990) |
| 31  | 1-(4'-Hydroxybenzyl)-4,7-dimethoxy-9,10-dihydrophenanthrene-2,8-diol | Bletilla striata      | Zhou, et al. (2019)             |
| 32  | 2,7-Dihydroxy-3-(p-hydroxybenzyl)-9,10-dihydrophenanthrene-4'-O-β-D-glucoside | Bletilla striata      | Zhou, et al. (2019)             |
| 33  | 2,7-Dihydroxy-3-(p-hydroxybenzyl)-4-methoxy-9,10-dihydrophenanthrene | Bletilla striata      | Zhou, et al. (2019)             |
| 34  | 2,7-Dihydroxy-1,6-bis(4-hydroxybenzyl)-4-methoxy-9,10-dihydrophenanthrene | Bletilla striata      | Bai, Inoue, Yamaki, & Takagi. (1991) |
| 35  | 2,7-Dihydroxy-1,3-bis(p-hydroxybenzyl)-4-methoxy-9,10-dihydrophenanthrene | Bletilla striata      | Zhou, et al. (2019)             |
| 36  | Bletillatin B                              | Bletilla ochracea     | Cai, Zhao, & Zhang. (2007)       |
| 37  | 2,7-bis(Allyloxy)-5-methoxy-3-methyl-9,10-dihydrophenanthrene | Dendrobium sinense   | Tan, et al. (2017)              |
| 38  | 4,7-Dihydroxy-2,3,6-trimethoxy-9,10-dihydrophenanthrene | Dendrobium sinense   | Cai, et al. (2020)              |
| 39  | 4,5-Dihydroxy-2,3-dimethoxy-9,10-dihydrophenanthrene | Dendrobium sinense   | Tan, et al. (2017)              |
| 40  | 2,5,7-Trihydroxy-4-methoxy-9,10-dihydrophenanthrene | Dendrobium officinale | Wang, Ma, Yang, & Pan. (1997)   |
| 41  | Ephemeralanthol B                         | Dendrobium officinale | Cui, Lu, Zhao, Liu, & Zhang. (2019) |
| 42  | Ephemeralanthol A                         | Dendrobium officinale | Li. (2011)                      |
| 43  | Cannithrene 2                             | Dendrobium officinale |                                |

(continued on next page)
| No. | Names                                                                 | Origins         | References                                           |
|-----|-----------------------------------------------------------------------|-----------------|------------------------------------------------------|
| 44  | 1,5-Dihydroxy-3,4,7-trimethoxy-9,10-dihydrophenanthrene               | *Dendrobium*    | Zhao, Yang, Zhang, Chen, & Chen. (2016)              |
| 45  | 4,6-Dimethoxy-9,10-dihydrophenanthrene-2,3,7-triol                    | *Dendrobium*    | Majumder, Rahaman, Roychowdhury, & Dhara. (2008)    |
| 46  | 2,4,5-Trihydroxy-9,10-dihydrophenanthrene                            | *Dendrobium*    | Xu, Xu, & Hou. (2014)                               |
| 47  | Emphemathol A                                                         | *Dendrobium*    | Chen, et al. (2020)                                 |
| 48  | 2,4,7-Trimethoxy-9,10-dihydrophenanthrene-3-ol                       | *Dendrobium*    | Zhang, et al. (2015)                                |
| 49  | 3,4,7-Trimethoxy-9,10-dihydrophenanthrene-2,8-diol                    | *Dendrobium*    | Yang, Sung, & Kim. (2007)                           |
| 50  | 4,7-Dimethoxy-9,10-dihydrophenanthrene-2-ol                           | *Dendrobium*    | Yang, Sung, & Kim. (2007)                           |
| 51  | 3,4-Dimethoxy-1-[(methoxymethyl)-9,10-dihydrophenanthrene-2,7-diol   | *Dendrobium*    | Na Ranong, Likhitwitayawud, Mekboonsonglarp & Sritularak. (2019) |
| 52  | Dendroinfundin A                                                      | *Dendrobium*    | Na Ranong, Likhitwitayawud, Mekboonsonglarp & Sritularak. (2019) |
| 53  | Dendroinfundin B                                                      | *Dendrobium*    | Na Ranong, Likhitwitayawud, Mekboonsonglarp & Sritularak. (2019) |
| 54  | Rotundatin                                                            | *Dendrobium*    | Ladan & Ali. (2017)                                 |
| 55  | (9S)-9,10-dihydro-5-methoxy-4,7,9-phenanthrenetriol                  | *Dendrobium*    | Lin, Wang, & Yang. (2013)                           |
| 56  | (9S)-9,10-dihydro-4-methoxy-2,5,7,9-phenanthrenetetrol               | *Dendrobium*    | Lin, Wang, & Yang. (2013)                           |
| 57  | (9S)-9,10-dihydro-5-methoxy-2,4,7,9-phenanthrenetetrol               | *Dendrobium*    | Lin, Wang, & Yang. (2013)                           |
| 58  | (9R)-5,9-dihydroxy-4-methoxy-9,10-dihydrophenanthrene-2-yl-2-hydroxyacetate | *Dendrobium* | Zhou, Zheng, Wu, Chen, & Zhang (2017)               |
| 59  | 2,5,9-Trihydroxy-9,10-dihydrophenanthrene-4-yl-2-hydroxyacetate      | *Dendrobium*    | Ye, Mei, Yang, Cheng, & Kong. (2016)                |
| 60  | 1,2,4,9R-tetrahydroxy-9,10-dihydrophenanthrene-5-O-β-D-glucopyranoside | *Dendrobium*    | Lin, Wang, & Yang. (2013)                           |
| 61  | Spiranthesphenanthrene D                                             | *Spiranthes*    | Liu, et al. (2019a)                                 |
| 62  | 2,4-Dihydroxy-5-methoxy-9,10-dihydrophenanthrene                    | *Spiranthes*    | Liu, et al. (2019a)                                 |
| 63  | Sinensol A                                                            | *Spiranthes*    | Liu, Li, Zhong, Yang, & Li, 2013                    |
| 64  | Sinensol H                                                            | *Spiranthes*    | Liu, Wang, Kuo, & Liu, 2001                         |
| 65  | Spiranthol A                                                          | *Spiranthes*    | Liu, Li, Zhong, Yang, & Li, 2013                    |
| 66  | Spiranthesol B                                                        | *Spiranthes*    | Lin, Huang, Don, & Kuo, 2000                        |
| 67  | Sinensol C                                                            | *Spiranthes*    | Lin, Li, Zhong, Yang, & Li, 2013                    |
| 68  | Sinensol G                                                            | *Spiranthes*    | Lin, Wang, Kuo, & Liu, 2001                         |
| 69  | Spiranthol B                                                          | *Spiranthes*    | Liu, et al. (2019a)                                 |
| 70  | Spirasineol A                                                         | *Spiranthes*    | Lin, Huang, Don, & Kuo, 2000                        |
| 71  | Sinensol B                                                            | *Spiranthes*    | Lin, Huang, Don, & Kuo, 2000                        |
| 72  | Sinensol F                                                            | *Spiranthes*    | Lin, Huang, Don, & Kuo, 2000                        |
| 73  | Shancidin                                                             | *Platynec*      | Zhu (2014)                                           |
| 74  | Pleoanthrenin                                                         | *Cremastra*     | Sun et al. (2018)                                   |
| 75  | 7-Hydroxy-4-methoxy-9,10-dihydrophenanthrene-2-O-β-D-glucopyranoside  | *Cremastra*     | Sun et al. (2018)                                   |
| 76  | 7-Hydroxy-5-methoxy-9,10-dihydrophenanthrene-2-O-β-D-glucopyranoside  | *Cremastra*     | Wang, Guan, & Meng. (2013)                         |
| 77  | 4-Methoxy-9,10-dihydrophenanthrene-2,7-diyl-O-β-D-glucopyranoside     | *Cremastra*     | Liu, et al. (2015)                                  |
| 78  | 2,7-Dihydroxy-1-(4-hydroxybenzyl)-4-methoxy-9,10-dihydrophenanthrene | *Cremastra*     | Zhu (2014)                                           |
| 79  | 1-(3’-Methoxy-4’-hydroxybenzyl)-7-methoxy-9,10-dihydrophenanthrene-2,4-diol | *Cyrtopodium*  | Auberon, et al. (2016)                              |
| 80  | Cephathrene A                                                         | *Cyrtopodium*   | Auberon, et al. (2016)                              |
| 81  | Cephathrene B                                                         | *Cyrtopodium*   | Auberon, et al. (2016)                              |
| No. | Names                                                                 | Origins                                                                 | References                                                                                   |
|-----|-----------------------------------------------------------------------|-------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
| 82  | (95) 3,4-dimethoxy-9,10-dihydrophenanthrene-2,7,9-triol                | *Cyperopium paniculatum*                                                 | Auberon, et al. (2016)                                                                        |
| 83  | 1-[(p-Hydroxybenzoyl)-2-methoxy-4,7-dihydroxy-9,10-dihydrophenanthrene| *Monomeria barbata*                                                     | Yang et al. (2010a)                                                                          |
| 84  | 5,7-Dimethoxy-9,10-dihydrophenanthrene-2,6-diyd diacetate            | *Eria flava*                                                            | Majumder, Pal, & Joardar. (1990)                                                              |
| 85  | Flavanthrin diacetate                                                 | *Eria flava*                                                            | Majumder, Pal, & Joardar. (1990)                                                              |
| 86  | Nudol diacetate                                                       | *Eria flava*                                                            | Majumder, Pal, & Joardar. (1990)                                                              |
| 87  | Lusianthrin diacetate                                                | *Calanthe arisanensis*                                                  | See references                                                                                |
| 88  | 9,10-Dihydro-2,5-dimethoxy-4,6-phenanthreneol                        | *Calanthe arisanensis*                                                  | See references                                                                                |
| 89  | 5,7-Dimethoxy-9,10-dihydrophenanthrene-1,4,6-triol                   | *Calanthe arisanensis*                                                  | See references                                                                                |
| 90  | 9,10-Dihydro-5,6-dimethoxy-1,4,7-phenanthrenetriol                   | *Calanthe arisanensis*                                                  | See references                                                                                |
| 91  | Marylaurencinol A                                                    | *Marie laurencin*                                                       | Yoshikawa et al. (2012)                                                                        |
| 92  | Marylaurencinol B                                                    | *Marie laurencin*                                                       | Yoshikawa et al. (2012)                                                                        |
| 93  | Marylaurencinoside A                                                 | *Plickingeria fimbriata*                                                 | Wu et al. (2017)                                                                              |
| 94  | 2,3,4,7,8-Pentamethoxy-9,10-dihydrophenanthrene                      | *Euphoria graminea macrobulbon*                                          | Temkitthawon, Changwichit, Khorana, Viyo, & Ingkaninan. (2017)                                |
| 95  | 5-Methoxy-9,10-dihydrophenanthrene-2,7,8-triol                       | *Gymnadenia conopsea*                                                   | See references                                                                                |
| 96  | Septeophiol diacetate                                                | *Euphoria graminea fimbriata*                                           | Wu et al. (2017)                                                                              |
| 97  | 9,10-Dihydro-2,5-dimethoxy-1,7-phenanthreneol                       | *Arundina graminifolia*                                                 | See references                                                                                |
| 98  | Gymnocrinon A                                                        | *Agrastophyllum callasum*                                               | Majumder, Banerjee, Lahiri, Mukhoti, & Sen. (1998)                                            |
| 99  | Gymnocrinon B                                                        | *Aerides rosea*                                                         | Nakayama et al. (2015)                                                                       |
| 100 | Arundigram                                                          | *Pholidota chinensis*                                                   | Hu et al. (2018)                                                                              |
| 101 | Callosin                                                             | *Pholidota chinensis*                                                   | Hu et al. (2018)                                                                              |
| 102 | Aerosin                                                              | *Pholidota chinensis*                                                   | Hu et al. (2018)                                                                              |
| 103 | Ochrone A                                                            | *Pholidota chinensis*                                                   | Hu et al. (2018)                                                                              |
| 104 | Phocantone                                                           | *Pholidota chinensis*                                                   | See references                                                                                |
| 105 | Denbinobin B                                                         | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 106 | Dendronone                                                           | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 107 | Epenheranthequinone                                                  | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 108 | 2-Hydroxy-4-methoxy-9,10-dihydrophenanthrene-1,4-dione              | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 109 | Epenheranthequinone B                                                | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 110 | 3-Hydroxy-2,4-dimethoxy-9,10-dihydrophenanthrene-1,4-dione           | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 111 | Dendrodevonin B                                                      | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 112 | Spiranthoquinone                                                     | *Dendrobium sinense*                                                    | Chen, et al. (2013b)                                                                           |
| 113 | Bleochranol C                                                        | *Bletilla ochracea*                                                     | See references                                                                                |
| 114 | Bleochranol D                                                        | *Bletilla ochracea*                                                     | See references                                                                                |
| 115 | ([95,10R]-3-hydroxy-9-(4-hydroxy-3-methoxypheynyl)-1-methoxy-6,8,9,10-tetrahydro-SHcycloponsyl)-9-[b]phenanthren-10-yl]-methyl acetate | *Bletilla striata*                                                      | See references                                                                                |
| 116 | 2-(4-Hydroxy-3-methoxyphenyl)-3-(4-hydroxymethyl)-7-methoxy-2,3,9,10-tetrahydrophenanthren-2,3-bifuran-5-ol | *Pholidota chinensis*                                                   | See references                                                                                |
| 117 | 2-(4-Hydroxy-3,5-dimethoxyphenyl)-3-hydroxymethyl-8-methoxy-2,3,10,11-tetrahydrophenanthren-1,2-bifuran-5,6-diol | *Pholidota chinensis*                                                   | See references                                                                                |
| 118 | 7-(5'S,R-trans)-7-hydroxy-7-(4'-hydroxy-3',5'-dimethoxyphenyl)-8'-hydroxymethyl-5-methoxy-9,10,7,8'-tetrahydrophenanthren-2,3-bifuran | *Pholidota chinensis*                                                   | See references                                                                                |
| 119 | Bletillatilin A                                                      | *Bletilla striata*                                                      | See references                                                                                |
| 120 | Shanciol H                                                           | *Bletilla striata*                                                      | See references                                                                                |
| 121 | Shanciol B                                                           | *Bletilla striata*                                                      | See references                                                                                |
| 122 | [3-Hydroxy-9-(4'-hydroxy-3-methoxypheynyl)-11-methoxy-5,6,9,10-tetrahydrophenanthren-2,3-bifuran-10-yl]-methyl acetate | *Bletilla striata*                                                      | See references                                                                                |
| 123 | 9-(4'-Hydroxy-3'-methoxyphenyl)-10-(4-hydroxymethyl)-11-methoxy-5,6,9,10-tetrahydrophenanthren-2,3,bifuran-10-yl] | *Bletilla striata*                                                      | See references                                                                                |
| 124 | 4,5-Epoxo-2-(4-hydroxy-3,5-dimethoxyphenyl)-3-hydroxymethyl-1-methoxy-2,3,9,10-tetrahydrophenanthren-2,3-bifuran-10-yl] | *Bletilla striata*                                                      | See references                                                                                |

(continued on next page)
| No. | Names                                                        | Origins        | References                                             |
|-----|--------------------------------------------------------------|----------------|--------------------------------------------------------|
| 125 | tetrahydrophenanthro[2,3-b]furan-7-ol                       | chinensis      | Zhou, et al. (2019)                                    |
| 126 | (2R,5S)-7-hydroxy-2-(3-hydroxy-5-methoxyphenyl)-10-methoxy-2,3,4,5-tetrahydrophenanthro[2,1-b]furan-3-ylmethyl acetate | Bletilla striata | Sun et al. (2018)                                      |
| 127 | 127 Pleionesin B                                           | Pleione yunnanensis | Liu, et al. (2019b)                                    |
| 128 | 128 Pleionesin D                                           | Pleione bulbocondioides | Liu, et al. (2019b)                                    |
| 129 | 129 Pleionesin B                                           | Pleione bulbocondioides | Liu, et al. (2019b)                                    |
| 130 | 130 Pleionesin C                                           | Pleione bulbocondioides | Liu, et al. (2019b)                                    |
| 131 | 131 Shanciol G                                             | Pleione bulbocondioides | Liu, et al. (2019b)                                    |
| 132 | (2R,3R)-7-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-N-(4-hydroxyphenethyl)-10-methoxy-2,3,4,5-tetrahydrophenanthro[2,1-b]furan-3-carboxamide | Cyrtopodium paniculatum | Auberon, et al. (2016)                                 |
| 133 | 133 4-Hydroxy-2-methoxy-8-{2,0,20,20-dimethylpyrano[5,0,6,0,7,0,8,0]}-9,10-dihydrophenanthrene | Spiranthes sinensis | Liu, Su, Li, Wen, & Li. (2012)                         |
| 134 | 134 Spiranthesphenanthrene C                               | Spiranthes sinensis | Liu, et al. (2019a)                                    |
| 135 | 135 Spiranthesphenanthrene F                               | Spiranthes sinensis | Liu, et al. (2019a)                                    |
| 136 | 136 Spirantol C                                            | Spiranthes sinensis | Tezuka, Ji, Hirano, Ueda, Nagashima, & Kikuchi. (2010) |
| 137 | 137 Sinensol E                                             | Spiranthes sinensis | Lin, Huang, Don, & Kuo, 2000                          |
| 138 | 138 Shanciol D                                             | Pleione bulbocondioides | Liu, et al. (2019b)                                    |
| 139 | 139 Bletilol C                                             | Pleione bulbocondioides | Zhu (2014)                                              |
| 140 | 140 Chrysotoxol A                                          | Dendrobium chrysotoxum | Hu, Fan, Dong, Miao, & Zhou. (2012)                     |
| 141 | 141 Chrysotoxol B                                          | Dendrobium chrysotoxum | Hu, Fan, Dong, Miao, & Zhou. (2012)                     |
| 142 | 142 Shanciol E                                             | Pleione bulbocondioides | Li. (2016)                                              |
| 143 | 143 Shancil                                                | Pleione bulbocondioides | Li, Chen, & Xin. (2014)                                |
| 144 | 144 Shanciol F                                             | Pleione bulbocondioides | Liu, et al. (2019b)                                    |
| 145 | 145 Shanciol C                                             | Pleione bulbocondioides | Liu, et al. (2019b)                                    |
| 146 | 146 Bletilol A                                             | Pleione bulbocondioides | Zhu (2014)                                              |
| 147 | 147 Bletilol B                                             | Pleione bulbocondioides | Zhu (2014)                                              |
| 148 | 148 Dendrocandin P2                                        | Dendrobium officinale | Zhao, Deng, & Zhang (2018)                             |
| 149 | 149 Erathrin A                                             | Eria bambusifolia | Zhan, Wang, Yin, Liu, & Chen, 2016                      |
| 150 | 150 Spirantesphenanthrene A                               | Spiranthes sinensis | Liu, et al. (2019a)                                    |
| 151 | 151 Spirasineol B                                          | Spiranthes sinensis | Tezuka, Ji, Hirano, Ueda, Nagashima, & Kikuchi. (2010) |
| 152 | 152 4-Hydroxy-2-methoxy-8-(2',2'-dimethylpyrano[5',6',7',8')] 9,10-dihydrophenanthrene | Spiranthes sinensis | Liu, Su, Li, Wen, & Li. (2012)                         |
| 153 | 153 Spirantesphenanthrene B                               | Spiranthes sinensis | Liu, et al. (2019a)                                    |
| 154 | 154 Spirantesphenanthrene E                               | Spiranthes sinensis | Liu, et al. (2019a)                                    |
| 155 | 155 Sinensol D                                            | Spiranthes sinensis | Lin, Huang, Don, & Kuo, 2000                          |
| 156 | 156 Phochinenin A                                          | Pholidota chinensis | Yao, Tang, Li, & Ye. (2009)                            |
| 157 | 157 Phochinenin G                                          | Pholidota chinensis | Hu et al. (2018)                                       |
| 158 | 158 Phochinenin H                                          | Pholidota chinensis | Hu et al. (2018)                                       |
| 159 | 159 Gymconopin C                                          | Pholidota chinensis | Hu et al. (2018)                                       |
| 160 | 160 2',2'-Dihydroxy-5,5',7,7'-tetramethoxy-9,9',10,10'-tetrahydro-3,3'-biphenanthrene | Pholidota chinensis | Li et al. (2013)                                       |
| 161 | 161 Phoyunnanin C                                         | Pholidota chinensis | Hu et al. (2018)                                       |
| 162 | 162 Bletrarianol A                                        | Bletilla striata | Bai, Kato, Inoue, Yamaki, & Takagi. (1991)              |
| No. | Names                        | Origins                 | References                        |
|-----|------------------------------|-------------------------|-----------------------------------|
| 163 | Blestranol B                 | *Bletilla striata*      | Bai, Kato, Inoue, Yamaki, & Takagi. (1991) |
| 164 | Bleformin D                 | *Bletilla formosana*    | Lin, et al. (2016)                |
| 165 | Bleformin H                 | *Bletilla formosana*    | Lin, et al. (2016)                |
| 166 | Amplumthrin                | *Pholidota chinensis*   | Hu et al. (2018)                  |
| 167 | Flavanthrin tetraacetate    | *Pholidota chinensis*   | Hu et al. (2018)                  |
| 168 | Flavanthrin                 | *Pholidota chinensis*   | Majumder, Rahaman, Roychowdhury, & Dhara. (2008) |
| 169 | 9,9',10',10'-Tetrahydro-2,2'-dimethoxy-(1,1'-biphenanthrene)-4,4',7,7'-tetrol | *Cirrhopetalum maculosum* | Majumder, Pal, & Joardar (1990) |
| 170 | 9,9',10',10'-Tetrahydro-2,2'-dimethoxy-(1,1'-biphenanthrene)-4,4',7-triol | *Pholidota chinensis* | Hu et al. (2018) |
| 171 | 2,2'-Dimethoxy-4,4',7,7'-tetrahydroxy-9,9',10',10'-tetrahydro-1,1'-biphenanthrene | *Pholidota chinensis* | Hu et al. (2018) |
| 172 | 4,7,4'-Trimethoxy-9,10'-dihydro(1,1'-biphenanthrene)-2,2',7'-triol | *Bletilla striata* | Lin, Huang, Don, & Kuo. 2000 |
| 173 | 2,2',4,4',7,7'-Hexamethoxy-9,9',10',10'-tetrahydro-1,1'-biphenanthrene | *Bletilla striata* | Lin, Huang, Don, & Kuo. 2000 |
| 174 | Phochinenin C               | *Pholidota chinensis*   | Yao, Tang, Li, & Ye. (2009)       |
| 175 | Phochinenin D               | *Pholidota chinensis*   | Yao, Tang, Li, & Ye. (2009)       |
| 176 | Phochinenin E               | *Pholidota chinensis*   | Yao, Tang, Li, & Ye. (2009)       |
| 177 | Phoyunnanin E               | *Pholidota chinensis*   | Hu et al. (2018)                  |
| 178 | Blestrin A                  | *Pholidota chinensis*   | Hu et al. (2018)                  |
| 179 | Bulbophythin B              | *Bulbophyllum odoratissimum* | Xu, Yu, Qing, Zhang, Liu, & Chen. (2009) |
| 180 | Spiranthesol                | *Sparanthes sinensis*   | Liu, Li, Zong, Yang, & Li. 2013   |
| 181 | Bulbophythin A              | *Bulbophyllum odoratissimum* | Xu, Yu, Qing, Zhang, Liu, & Chen. (2009) |
| 182 | 8,8'-Biflavidin             | *Otochilus porrectus*   | Shi, et al. (2010)                |
| 183 | Blestrin B                  | *Bletilla striata*       | Yamaki, et al. (1992)             |
| 184 | Monobarbatain D             | *Monomeria barbata*     | Yang et al. (2010a)               |
| 185 | 4,4'-Dimethoxy-9,10'-dihydro(6,1'-biphenanthrene)-2,2',7,7'-tetraol | *Cremostra appendiculata* | Sun et al. (2018)                |
| 186 | 4,7,7'-Trimethoxy-9,10'-dihydro(1,1'-biphenanthrene)-2,2',5',5'-triotl | *Bletilla striata* | Lin, Huang, Don, & Kuo. 2000 |
| 187 | 4,4',7,7'-Trimethoxy-9,10'-dihydro(1,1'-biphenanthrene)-2,2',7,7'-trio1 | *Cremostra appendiculata* | Liu, Li, Zeng, Jiang, & Tu. (2016) |
| 188 | 5,6,7'-Trimethoxy-9,10'-dihydro(1,1'-biphenanthrene)-2,2',5,7,7'-tetraol | *Cytopodium paniculatum* | Auberon, et al. (2016) |
| 189 | 3,4,7'-Trimethoxy-9,10'-dihydro(1,1'-biphenanthrene)-2,2',5,7,7'-tetraol | *Cytopodium paniculatum* | Auberon, et al. (2016) |
| 190 | Monobarbatain B             | *Monomeria barbata*     | Yang, Cai, & Tai. (2010b)         |
| 191 | Blestrianol C               | *Bletilla striata*       | Bai, Kato, Inoue, Yamaki, & Takagi. (1991) |
| 192 | Bleformin I                 | *Bletilla formosana*    | Lin, et al. (2016)                |
| 193 | Bulbocodioid G              | *Pieone bicoccidioides* | Wang, Shao, Han, & Li. (2019)     |
| 194 | Phochinenin B               | *Pholidota chinensis*   | Yang, Tang, Li, & Ye. (2009)      |
| 195 | Blestriaren B               | *Bletilla striata*       | Yang, Tang, Zhao, Shu, & Mei. (2012) |
| 196 | 4,7,3',5'-Tetramethoxy-9,10'-dihydro(1,1'-biphenanthrene)-2,2',7,7'-trio1 | *Monomeria barbata* | Lin, Huang, Don, & Kuo. 2000 |
| 197 | Monobarbatain A             | *Bletilla striata*       | Yang, Cai, & Tai. (2010b)         |
| 198 | 4,7,3',5'-Tetramethoxy-9,10'-dihydro(1,2'-biphenanthrene)-2,7'-dil0 | *Bletilla striata* | Zhou et al. (2019)               |
| 199 | Blestrin E                  | *Bletilla striata*       | Apel, Dumontet, Lozach, Meijer, Guéritte & Litaudon. (2012) |
| 200 | Blestrin C                  | *Appendicula reflexa*   | Yamaki, et al. (1992)             |
| 201 | (2,3-truns)-3-[[2,7-Dihydroxy-4-methoxy-phenanthren-1-y]methyl]-2-(4-hydroxy-3-methoxyphenyl]-10-methoxy-2,3,4,5-tetrahydro-phenanthrol[2,1-b]furan-7-ol | *Dendrobium amplum* | Majumder, Rahaman, Roychowdhury, & Dhara. (2008) |
| 202 | Phoyunnanin A               | *Pholidota chinensis*   | Hu et al. (2018)                  |
| 203 | Phochinenin I               | *Pholidota chinensis*   | Hu et al. (2018)                  |
| 204 | Phochinenin J               | *Pholidota chinensis*   | Hu et al. (2018)                  |
2.2. DP polymers

Until now, 61 dimers and a trimer have been reported from medicinal plants of Orchidaceae. DP monomers can connect by their substituents or a single C–C', CH₂, CH₂CH₂ or C-O-C' coupling. According to the different polymeric fragments, DP polymers could be classified into DPs and DPs, DPs and phenanthrenes, DPs and bibenzyls.

2.2.1. DPs and DPs

Twenty-nine constituents belong to this type and connect at different positions, such as C-1,3', C-1,1' (156–160, 169–171, 175, 177), C-1,1' (161–163, 172–174, 176, 181–183), C-2,2' (179), C-3,1' (178, 184) and C-1,2' (164–168, 180). The representative structures are afforded in Fig. 7 and the chemical structures, names and origins displayed in Fig. S4 and Table 1.
2.2.2. DPs and phenanthrenes

The second type is characterized by DPs and phenanthrenes monomers and the connection position at C-1,1’ (185, 188–190, 199–200), C-1,3’ (186–187, 194–198), C-1,2’ (191–193) and C-2,9’ (201). The representative structures are afforded in Fig. 8 and the chemical structures, names and origins displayed in Fig. S5 and Table 1.

2.2.3. DPs and bibenzyls

All DPs are of bibenzyl origin, and a number of DPs and bibenzyls polymers are formed through C-3,1’ (202–204, 206), C-1,1’ (207, 209–211, 213), C-2,1’ (205, 214), C-4,1’ (215), C-11,1’ (212), C-12,1’ (217) linkages between two monomers. The representative compositions are afforded in Fig. 9 and the chemical structures, names and origins displayed in Fig. S6 and Table 1.

3. Pharmacology

The applications of medicinal plants of Orchidaceae have a long history. The tubers of B. striata, stems of Dendrobium nobile Lindl., whole herbs of Pholidota chinensis Lindl. and roots of Spirant hesinensis (Pers.) Ames have been used as traditional Chinese medicines with the efficacy of clearing heat and resolving toxin, moistening lung and relieving cough, promoting blood circulation. However, very few studies have elaborated the relationship between traditional efficacy and modern pharmacology of DPs in medicinal plants of Orchidaceae. At present, some researches have demonstrated that DPs of medicinal plants of Orchidaceae have a wide range of biological activities such as cytotoxic, anti-oxidant, anti-inflammatory activities.

Fig. 8. Representative chemical structures of DPs and phenanthrenes.

Fig. 9. Representative chemical structures of DPs and bibenzyls.

Fig. 10. DPs from medicinal plants of Orchidaceae with significant cytotoxic activities.
3.1. Cytotoxic activity

A large number of natural DPs have been proved to exhibit cytotoxic effects. Xu et al. noticed that the whole herbs of Bulbophyllum odoratissimum (Sm.) Lindl. showed strong cytotoxic activities in human leukemia cell lines K562 and HL-60, human lung adenocarcinoma A549, human hepatoma BEL-7402 and human stomach cancer SGC-7901. Bulbophythrin A (181), reported as a new dimeric DP, could inhibit the growth of HL-60, BEL-7402 and A549 with IC50 values of 1.3, 1.2 and 1.2 nmol/L (Xu, Yu, Qing, Zhang, Liu, & Chen, 2009).

Compounds 88–90, isolated from the roots of Calanthe arisanensis Hayata, exhibited strong cytotoxic activities against A549, MCF-7 and PC-3 cancer cell lines with IC50 values ranged from 2.3 to 7.7 μg/mL by sulforhodamine B assays (Lee, et al., 2009).

Using water-soluble tetrazolium-8 and lactatedehydrogenase assays, ephenmeranthoquinone B (109), being present with high concentration in the roots of Marie laurencin, could inhibit the growth of HL-60, NCI-H460 and M14 cell lines with IC50 values of 2.8, 5.0 and 1.5 μmol/L (Williams et al., 2012).

Monobarbatains B and D (190, 184) from the stems of Monomeria barbata and showed cytotoxic activities against HepG-2 (IC50: 17.1 μmol/L; IC50: 17.6 μmol/L) and HL60 (IC50: 7.3 μmol/L; IC50: 10.2 μmol/L) cell lines by MTT assays (Yang, Tang, Zhao, Shu, & Mei, 2010).

DP monomers have stronger cytotoxic activity compared to polymers. Furthermore, compared with 89 and 90, it appears that the 6-OH and 7-OCH3 groups might increase the cytotoxic activity.

The structures and IC50 values of DPs from medicinal plants of Orchidaceae with significant cytotoxic activities displayed in Fig. 10.

3.2. Anti-inflammatory activity

Inflammation is the defense response of the living tissues to the simulations of injury factors, which plays an important role in the occurrence and development of many diseases (Hou, Sun, Gao & Xiao, 2015).

Lin et al. (2013) reported that compounds 3, 55, 58 and 60 from the ethanol extract of the stems of Dendrobium denneanum Lindl.
showed inhibitory effects on NO production in lipopolysaccharide (LPS)-activated macrophage RAW 264.7 cells (IC₅₀: 7.6 μmol/L; IC₁₀₀: 3.1 μmol/L; IC₂₀₀: 4.2 μmol/L; IC₃₀₀: 0.7 μmol/L).

Lusianthridin (1) and hircinol (7) isolated from 80% ethanol extract of the stems of *Dendrobium loddigesii* Lindl., exerted inhibitory activities on LPS-induced NO production in a murine macrophage-like cell line RAW 264.7 with IC₅₀ values of 4.6 and 29.2 μmol/L. Lusianthridin (1) was more active than that of the positive control aminoguanidine (IC₅₀: 17.5 μmol/L) (Itó et al., 2010).

Phochinenin K (207) was isolated from the dried tubers of *B. striata* and evaluated by LPS-stimulated BV-2 cells with IC₅₀ value of 1.9 μmol/L (Zhou et al., 2019). Compounds 1, 8, 13, 19 and 22, isolated from *Pholidota yunnanensis* were evaluated for their anti-inflammatory activities on LPS-induced NO production in RAW 264.7 cells and showed growth inhibitory effects in the concentration range of 4.2–7.7 μmol/L with MG-132 used as the positive control (IC₅₀: 17.5 μmol/L) (Dong et al., 2013).

Coelonin (6), an active component isolated from the ethanol extract of the tubers of *B. striata*. It significantly inhibited IL-1β, IL-6 and TNF-α expression at 2.5 μg/mL by using the LPS-induced macrophage inflammation model and phospha- tin-ty body arrays (Jiang et al., 2019).

Based on the molecular structures and bioassay activities, we found that most active ingredients were monomers. In addition, we found that 2, 5-O-Glc group might play a role in enhancing anti-inflammatory activity. The structures and IC values of DPs from medicinal plants of Orchidaceae with significant anti-inflammatory activities displayed in Fig. 11.

### 3.3. Anti-oxidant activity

The excessive free radicals can lead to aging, cancer and other diseases, and antioxidants can overcome the damage caused by excess free radicals (Meng et al., 2018). Compounds 1, 4, 8, 20, 171, 202 and 205 were isolated from the whole herbs of *Pholidota yunnanensis*, and proved to be as active (EC₅₀: 22.3 μmol/L; EC₅₀: 27.7 μmol/L; EC₅₀: 10.0 μmol/L; EC₅₀: 8.8 μmol/L; EC₅₀: 47.3 μmol/L; EC₅₀: 55.9 μmol/L; EC₅₀: 26.7 μmol/L) as the positive control resveratrol (EC₅₀: 21.2 μmol/L) using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assays (Chen et al., 2013b).

Among the isolated compounds of the whole herbs of *Monnemia barbata* Lindl, compounds 169, 184, 190 and 197 showed antioxidant activity when using the DPPH radical scavenging assays (Yang et al. 2010; Yang et al. 2014). The antioxidant capacities of coelonin (6), flavidin (17) and imbricatin (20) were measured by DPPH radical-scavenging assays and *OH assays (IC₅₀ values: 8.4, 6.6, and 8.5 μmol/L; DPPH assay; IC₅₀ values: 0.03, 0.08, and 0.08 μmol/L, *OH assay) (Simmler, Antheaume & Lobstein, 2010).

In the above-mentioned compounds, it can be revealed that DPs with 2, 6-O-CH₃, 5, 7-OH groups show higher antioxidant activity. The structures and IC values of DPs from medicinal plants of Orchidaceae with significant anti-oxidant activities displayed in Fig. 12.

### 4. Clinical applications

Over the years, medicinal plants of Orchidaceae showed a wide range of efficacy including clearing heat and resolving toxin, moistening lung and relieving cough and promoting blood circulation. DPs are the major bioactive ingredients of medicinal plants of Orchidaceae, which can prevent and treat diseases in clinic.

Silicosis is a chronic lung disease caused by long-term exposure to silica dust, characterized by progressive pulmonary fibrosis and lung inflammation (Guo, Zhang, & Shao, 2018). The innate immune response mediated by alveolar macrophage plays a key role in silicosis. Coelonin (6), a classical DP monomer was isolated from the tubers of *B. striata* can remarkably elevate the serum SOD level and lower the malondialdehyde, NO level; and it dose dependently decrease all the inflammatory cytokines, and lower hydroxyproline content. Therefore, coelonin (6) can effectively prevent lung fibrosis and through regulating the anti-oxidation system, immune system and cytokine level (Deng et al., 2016).

### 5. Summary

DPs from medicinal plants of Orchidaceae are responsible for the medicinal usage and attract more and more attention. DP structures, especially DP polymers have a lot of chiral centers and are the sources of diverse activities and stereoselectivities. In recent years, most studies on DPs are only focused on simple drug efficacy, more comprehensive pharmacological effects and mechanisms of action have not been fully elucidated. The further studies on the representative components of DPs are helpful to clarify the common material basis of medicinal plants of Orchidaceae and provide scientific basis for new drug development. As a kind of skeleton of active lead compounds, DPs can expand the structural diversity and provide a reference for the development of small molecule drugs by structural modifications, synthesis and other methods.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chmed.2021.10.004.

### References

Apeil, C., Dumontet, V., Lozach, O., Meijer, L., Guérifte, F., & Litaudon, M. (2012). Phenanthrene derivatives from *Appendicula reflexa* as new CDK1/cyclin B inhibitors. Phytochemistry Letters, 5(4), 814–818.

Auberon, F., Olatunji, O., Herbette, G., Raminodon, D., Antheaume, C., Soengas, B., et al. (2016). Chemical constituents from the aerial parts of *Cytropodium paniculatum*. Molecules, 21(10), 1418. https://doi.org/10.3390/molecules21101418.

Auberon, F., Olatunji, O., Krissa, S., Antheaume, C., Herbette, G., Bonté, F., et al. (2016). Two new stilbenoids from the aerial parts of *Arundina graminifolia* (orchidaceae). Molecules, 21(11), 1430. https://doi.org/10.3390/molecules21111430.

Bai, L., Kato, T., Inoue, K., Yamaki, M., & Takagi, S. (1991). Nonpolar constituents from *Bletilla striata*. Part 6. *B. striata*. Phytochemistry, 30(8), 2733–2735.
Jia-xin Qi, D. Zhou, Wan-ru Jiang et al. Chinese Herbal Medicines 13 (2021) 480–493

Bai, L. i., Yamaki, M., Inoue, K., & Takagi, S. (1990). Chemical constituent of Dendrobium sinense (Orchidaceae). Journal of Asian Natural Products Research, 13(7), 709–714.

Bhandari, S. R., & Kapadi, A. H. (1983). A 9,10-dihydrophenanthrene from tubers of Calanthe arisanensis. Phytochemistry, 22(1), 67–70.

Bai, L. J., Yamaki, M., Inoue, K., & Takagi, S. (1990). Blestrin A and B, bis (Orchidaceae) isolated using the combined systems HPLC-EASI-HRMS/MS and HPLC-DAD-MS-SPE-UV-NMR. Phytochemical Analysis, 2(6), 34–39.

Chen, D. N., Wang, Y. Y., Liu, J. Y., Chen, Y. J., Wu, Y. P., Yang, J. K., et al. (2020). Phenanthrenes from aerial parts of Dendrobium plicatum. Natural Product Research, 34(3), 323–328.

Chen, S. (1996). New compilation of Materia Medica. China Press of Traditional Chinese Medicine.

Chen, X. J. (2013a). Chemical components and bioactivities of Dendrobium sinense (Orchidaceae), an endemic species in Hainan Island. Hainan University, Thesis of Master Degree.

Chen, X. J., Mei, W. L., Zuo, W. J., Zeng, Y. B., Song, Y. Q., Song, X. Q., et al. (2013). New dimeric stilbenoids from the orchid Dendrobium signatum (Orchidaceae). Journal of Natural Medicines, 69(3), 422–428.

Dong, W. (2014). Clinical observation on 150 cases of primary liver cancer treated with anti-inflammatory and cytotoxic activity from the rhizomes of Dendrobium chrysotoxum (Orchidaceae). Journal of Natural Products, 63(12), 2421–2426.

Lin, Y., Wang, S. Y., Han, S. W., Li, S. (2019). Atropisomeric bi(9,10-dihydro)phenanthrenes from Dendrobium nobile. Natural Product Research, 33(12), 420–425.

Pei, Z. Y. (1979). Bai Zhi Gao treats tuberculosis. Journal of Traditional Chinese Medicine, 3, 55.

Rueda, D. C., Schöffmann, A., De Mieri, M., Raith, M., Jähne, E. A., Hering, S., et al. (2010). Antioxidant biomarkers of chemopreventive dietary intervention with Eulophia macrobulbon (Pholidota yunnanensis). Journal of Nutritional Biochemistry, 21(11), 645–650.

Meng, X. Y., Wang, Y. F., Li, X. P., Guo, Z. K., Song, X. Q., et al. (2018). A New bibenzyl-phenanthrene derivative from Dendrobium signatum (Orchidaceae) isolated using the combined systems HPLC-EASI-HRMS/MS and HPLC-DAD-MS-SPE-UV-NMR. Phytochemical Analysis, 29(1), 83–84.

Shi, X. L., Li, Z. L., Wang, Y. F., Yang, L. X., Guo, S. M., Wang, Y. S., et al. (2018). Research on chemical constituents and bioactivities of plants of Eulophia macrobulbon (Pholidota yunnanensis). Chinese Journal of Industrial Medicine, 31(10), 120–123.

Lin, Y. L., Huang, R. L., Don, M. J., Kuo, Y. H. (2000). Dihydrophenanthrenes from Spiranea sinensis. Journal of Natural Products, 63(12), 1608–1610.

Lin, Y. L., Wang, W. Y., Kuo, Y. H., & Lin, Y. H. (2001). Homocysteicyclularine and two dihydrophenanthrenes from Spiranea sinensis. Chemical & Pharmaceutical Bulletin, 49(9), 1098–1101.

Lin, L. J., Li, C. Y., Zhong, Y. J., Yang, L., & Li, Y. F. (2013). Chemical constituents from Spiranea sinensis. Biochemical Systematics and Ecology, 46, 724–728.

Lin, L. J., Li, C. Y., Wu, Y. K., Li, J. Y., Tang, Y. Q., & Qin, B. H. (2015). Research on the chemical constituents of Cremastrum appendiculatum. Journal of South-Central University for Nationalities (Nat. Sci. Edition), 34(3), 41–44.

Lin, X. X., Liu, H. D., Pan, L. F., Wu, Y. F., Wu, N., Zhou, X., et al. (2019). Research progress on chemical constituents and bioactivities of plants of Pleione Bulboideae (Fridol) Rolfe. Journal ofjiangxi University of TCM, 31(2), 106–111.

Li, M. B., Lee, C. L., Yen, M. H., Chang, F. R., Wud, C. C., & Wu, Y. C. (2014). Antiplatelet aggregation effects of phenanthrenes from the rhizomes of Vanda coerulea (Orchidaceae). Journal of Asian Natural Products Research, 36(4), 1–9.

Bai, L. J., Yamaki, M., Inoue, K., & Takagi, S. (1990). Blestrin A and B, bis (Orchidaceae). Chemical constituents isolated from the orchid Pholidota yunnanensis. Journal of Natural Medicines, 69(3), 421–426.

Ito, M., Matsushita, M., Dakiyona, A., Wang, N. L., Yao, X. S., et al. (2010). New phenanthrenes and stilbenoids from Dendrobium lodgesii. Chemical & Pharmaceutical Bulletin, 58(5), 628–633.

Jiang, F., Li, M., Wang, H., Ding, B., Zhang, C., Ding, Z., et al. (2019). Coelomisin, an anti-inflammation active component of Blechnum spicant, guided isolation of its potential mechanism. International Journal of Molecular Sciences, 20(18). 4422. https://doi.org/10.3390/ijms20184422.

Jiang, H. W., & He, H. (2013). Treatment of 48 cases of tuberculous hemoptysis by "Bai Zhi Gao". Journal of Traditional Chinese Medicine, 47(7), 49–50.

Ladan, M., & Ali, R. (2017). Three new compounds from the seeds of Trachyspermum cypcticum. International Journal of Food Properties, 20(7), 1597–1602.

Lee, C. L., Chang, F. R., Yen, M. H., Yu, D., Liu, Y. N., Bastow, K. F., et al. (2009). Cytotoxic phenanthrenes and 9,10-dihydrophenanthrenes from Calanthe arisanensis. Journal of Natural Products, 72(2), 210–213.

Lee, C. L., Yen, M. H., Chang, F. R., Wu, C. C., & Wu, Y. C. (2014). Antitplatelet aggregation effects of phenanthrenes from Calanthe arisanensis. Natural Product Communications, 9(11), 83–84.

Li, C. B. (2011). Research on the chemical constituents of Dendrobium croepadatum and flower from Dendrobium chrysotoxum. Jilin Agricultural University, Thesis of Master Degree.

Li, C. Y., Liu, S., Xu, X. H., Yuan, Z. P., Zhong, Y. J., Li, L. Y. F., et al. (2013). New dimeric phenanthrene and flavone from Spiranea sinensis. Asian Natural Products Research, 15(4), 417–421.

Li, Y. J., Kuang, M. T., Yang, L. K., Hou, B. O., Liu, Z. H., et al. (2018). Stilbenes with anti-inflammatory and cytotoxic activity from the rhizomes of Bleilla ochracea Schlr. Flora, 127, 74–80.

Li, Q., Chen, Y. Z., & Xin, H. L. (2014). Research progress on Shanciu on chemical composition and pharmacological effects. Journal of Pharmaceutical Practice, 32(4), 250–253.

Li, L. P. (2016). Chemical constituents from Cremastrum appendiculatum. South-Central University for Nationalities, Thesis of Master Degree.

Lin, L. W., Huang, T. L., Chen, C. A., Fu, H. C., Huang, H. Y., & Wu, T. S. (2016). Chemical constituents of the rhizomes of Bleilla formosana and their potential anti-inflammatory activity. Journal of Natural Products, 79(8), 1911–1921.

Lin, Y., Wang, F., Yang, L. J., Chun, Z. E., Bao, J. K., & Zhang, G. L. (2013). Anti-inflammatory phenanthrene derivatives from stems of Dendrobium denudatum. Phytochemistry, 95, 242–251.
Wang, J., Wang, L., & Kitanaka, S. (2007). Stilbene and dihydrophenanthrene derivatives from Pholidota chinensis and their nitric oxide inhibitory and radical-scavenging activities. Journal of Natural Products, 67(4), 381–386.

Wang, T. S., Ma, G. C., Yang, G. M., & Fan, Y. (1997). Isolation and identification of terpenoids and anthraquinones from Euphorbia fischeriana. Chinese Traditional and Herbal Drugs, 20(7), 353–354.

Wang, Y., Guan, S. H., Meng, Y. H., Zhang, Y. B., Cheng, C. R., Shi, Y. Y., et al. (2013). Phenanthrenes, 9,10-dihydrophenanthrenes, bibenzyls with their derivatives, and malate or tartrate benzyl ester glucosides from tubers of Cremastra appendiculata. Phytochemistry, 94, 268–276.

Wang, Y. G., Wang, Y. L., Zhai, H. F., Liao, Y. J., Zhang, B., & Huang, J. M. (2012). Cytotoxicity of new stilbenoids from Bulbophyllum odoratissimum with cytotoxic activity from Bletilla ochracea. Planta Medica, 78(06), 606–610.

Wang, Y. G., Wang, Y. L., Zhai, H. F., Liao, Y. J., Zhang, B., & Huang, J. M. (2012). Cytotoxicity of new stilbenoids from Bulbophyllum odoratissimum with cytotoxic activity from Bletilla ochracea. Planta Medica, 78(06), 606–610.

Ye, Q., Mei, Y., Yang, P., Cheng, L., & Kong, D. (2016). A new 9,10-dihydrophenanthrene glycoside from Dendrobium primulatum. Chemistry of Natural Compounds, 52(3), 381–383.

Williams, R., Martin, S., Hu, J.-F., Garo, E., Rice, S., Norman, V., et al. (2012). Isolation of apoptosis-inducing stilbenoids from four members of the Orchidaceae family. Planta Medica, 78(02), 160–165.

Wu, B., Qu, H., & Cheng, Y. (2008). Cytotoxicity of new stilbenoids from Pholidota chinensis and their spin-labeled derivatives. Chemistry & Biodiversity, 5(9), 1803–1810.

Wu, L., Lu, Y. E., Ding, Y., Zhao, J., Xu, H., & Chou, G. (2019). Four new compounds from Dendrobium devonianum. Natural Product Research, 33(15), 2160–2168.

Wu, Y. P., Liu, W. J., Zhong, W. J., Chen, Y. J., Chen, D. N., He, F., et al. (2017). Phenolic compounds from the stems of Flickingeria fimbriata. Natural Product Research, 31(13), 1518–1522.

Xu, F. Q., Xu, F. C., Hou, B. O., Fan, W. W., Zi, C. T., Li, Y., et al. (2014). Cytotoxic bibenzyl dimers from the stems of Dendrobium jimbritum Hook. Bioorganic & Medicinal Chemistry Letters, 24(22), 5268–5273.

Xu, J., Yu, H., Qing, C., Zhang, Y., Liu, Y., & Chen, Y. (2009). Two new biphenanthrenes with cytotoxic activity from Bulbophyllum odoratissimum. Fitoterapia, 80(7), 1131–1134.

Yamaki, M., Bai, L. I., Inoue, K., & Takagi, S. (1990). Benzylphenanthrenes from Bletilla striata. Phytochemistry, 29(7), 2285–2287.

Yamaki, M., Bai, L. I., Kato, T., Inoue, K., Takagi, S., Yamagata, Y., et al. (1992). Bisphenanthrene ethers from Bletilla striata. Phytochemistry, 31(11), 3985–3987.

Yang, H., Sung, S. H., & Kim, Y. C. (2007). Antifibrotic phenanthrenes of Dendrobium nobile stems. Journal of Natural Products, 70(12), 1925–1929.

Yang, K. (2015). Clinical study of Aiyu capsule combined with CAF chemotherapy in the treatment of breast cancer. Drug Clinical, 31(12), 1980–1983.

Yang, M., Cai, L. E., Fang, H., Yang, S., Fang, Y., & Ding, Z. (2014). Phenolic Compounds from Monomeria barbata. Chemistry of Natural Compounds, 50(1), 88–92.

Yang, M. H., Cai, L. E., Li, M. H., Zeng, X. H., Yang, Y. B., & Ding, Z. T. (2010). Three new phenanthrenes from Monomeria barbata. Chinese Chemical Letters, 21(3), 325–328.

Yang, M., Cai, L. E., Tai, Z., Zeng, X., & Ding, Z. (2010). Four new phenanthrenes from Mononora barbata Lindl. Fitoterapia, 81(8), 992–997.

Yang, X., Tang, C., Zhao, P., Shu, G., & Mei, Z. (2012). Antimicrobial constituents from the tubers of Bletilla ochracea. Planta Medica, 78(06), 606–610.

Yao, S., Tang, C. P., Li, X. Q., & Ye, Y. (2009). Phochinenins A-F, dimeric 9,10-dihydrophenanthrene derivatives, from Pholidota chinensis. Helvetica Chimica Acta, 91, 2122–2129.

Yao, S., Tang, C. P., Ye, Y., Kurtân, T., Kiss-Szikszai, A., Antus, S., et al. (2008). Stereochemistry of atropisomeric 9,10-dihydrophenanthrene dimers from Pholidota chinensis. Tetrahedron: Asymmetry, 19(17), 2007–2014.

Ye, Q., Mei, Y., Yang, P., Cheng, L., & Kong, D. (2016). A new 9,10-dihydrophenanthrene glycoside from Dendrobium primulatum. Chemistry of Natural Compounds, 52(3), 381–383.

Yoshikawa, K., Ito, T., Iseki, K., Baba, C., Imagawa, H., Yagi, Y., et al. (2012). Phenanthrene derivatives from Cymbidium Great Flower Marie Laurencin and their biological activities. Journal of Natural Products, 75(4), 605–609.

Zhan, R., Wang, Z. C., Yin, B. L., Liu, Y., & Chen, Y. G. (2016). Novel 9,10-dihydrophenanthrene derivatives from Eria bambusifolia with cytotoxicity against human cancer cells in vitro. Chinese Journal of Natural Medicine., 14(8), 621–625.

Zhang, Y. Y., Song, X. Q., Mei, W. L., Zuo, W. J., Cai, C. H., Cheng, J., et al. (2015). Chemical constituents from Dendrobium hainanense (Orchidaceae) in Hainan. Journal of Tropical and Subtropical Botany, 23(3), 317–322.

Zhang, Y. Y., Wang, P., Song, X. Q., Zuo, W. J., Wang, H., Chen, L. L., et al. (2019). Chemical constituents from Dendrobium hainanense. Journal of Asian Natural Products Research, 21(9), 873–886.

Zhou, D. I., Chen, G., Ma, Y. P., Wang, C. G., Lin, B., Yang, Y. Q., et al. (2019). Isolation, structural elucidation, optical resolution, and antineuroinflammatory activity of phenanthrene and 9,10-dihydrophenanthrene derivatives from Bletilla striata. Journal of Natural Products, 82(8), 2238–2245.

Zhou, X. M., Zheng, C. J., Wu, J. T., Chen, G. Y., Zhang, B., & Sun, C. G. (2017). A new phenolic glycoside from the stem of Dendrobium nobile. Natural Product Research, 31(9), 1042–1046.

Zhu, Y. (2014). Studies of chemical constituents from Cremastra appendiculata. Hubei University of Chinese Medicine, Thesis of Master Degree.