


Review

# Chemical Constituents and Biological Activity Profiles on *Pleione* (Orchidaceae)

Xiao-Qian Wu <sup>1,2</sup>, Wei Li <sup>1,2</sup>, Jing-Xin Chen <sup>3</sup>, Jun-Wen Zhai <sup>1,2</sup>, Hui-You Xu <sup>3</sup>, Lin Ni <sup>3,\*</sup>  and Sha-Sha Wu <sup>1,2,\*</sup>

<sup>1</sup> College of Landscape Architecture, Fujian Agriculture and Forestry University, Fuzhou 350002, China

<sup>2</sup> Key Laboratory of National Forestry and Grassland Administration for Orchid Conservation and Utilization at College of Landscape Architecture, Fujian Agriculture and Forestry University, Fuzhou 350002, China

<sup>3</sup> College of Plant Protection, Fujian Agriculture and Forest University, Fuzhou 350002, China

\* Correspondence: nilin\_fjau@126.com (L.N.); shashawu1984@126.com (S.-S.W.)

Academic Editor: Bruno Botta

Received: 19 July 2019; Accepted: 1 September 2019; Published: 3 September 2019



**Abstract:** *Pleione* (Orchidaceae) is not only famous for the ornamental value in Europe because of its special color, but also endemic in Southern Asia for its use in traditional medicine. A great deal of research about its secondary metabolites and biological activities has been done on only three of 30 species of *Pleione*. Up to now, 183 chemical compounds, such as phenanthrenes, bibenzyls, glucosyloxybenzyl succinate derivatives, flavonoids, lignans, terpenoids, etc., have been obtained from *Pleione*. These compounds have been demonstrated to play a significant role in anti-tumor, anti-neurodegenerative and anti-inflammatory biological activities and improve immunity. In order to further develop the drugs and utilize the plants, the chemical structural analysis and biological activities of *Pleione* are summarized in this review.

**Keywords:** *Pleione*; chemical structures; phenanthrenebibenzyl; bibenzyls; glucosyloxybenzyl succinate derivatives; anti-tumor activity; anti-neurodegenerative

## 1. Introduction

Orchidaceae is one of the largest family of flowering plants. There are about 42 genus that are used for traditional medicine in China, but thus far, no phytochemical investigation has been conducted on 70% of them [1]. As one of unexplored medicinal orchid [2], *Pleione* contains about 30 species in the habitats of terrestrial, epiphytic or lithophytic, among which 12 are endangered [3]. It mainly distributes in China, Vietnam, Burma, Bangladesh and the Northeast Indian at elevation of 600–4200 m [4]. China is the central region, with 23 species distributed here and 12 of them are endemic [5–8].

The *Pleione* is attracting increasing attention nowadays in terms of the ornamental and medicinal values [9–11]. As a special colorful flower, *Pleione* was introduced to Europe from China in 1904 [4]. Currently, there are more than 400 cultivars [12]. In China, the dry pseudobulbs of *P. bulbocodioides* and *P. yunnanensis*, as well as *Cremastra appendiculata*, were the sources of the traditional Chinese medicine (TCM) ‘shan-ci-gu’. They are used for removing heat, counteracting toxicity, dissipating phlegm and resolving masses. They can also be applied on symptoms such as furuncles, carbuncles, scrofulous sputum, snake and insect bites, abdominal masses and lumps [13]. However, only three species of *Pleione*, including *P. humulis*, *P. praecox* and *P. maculate*, were used as traditional medicine in Northeastern India, applied on laceration wounds, colds, upper respiratory infection, liver complaints and stomach ailments [2]. In summary, five species have been commonly used in traditional medicines, but scientific studies have only been performed on three of them. More detailed research is needed to on *Pleione*.

The phytochemical research could be traced back to 1996. Li et al. [14–20] extracted 30 chemical compounds from the pseudobulbs of *P. bulbocodioides*, such as dihydrophenanthropyrans, bibenzyls, bichroman, polyphenol and flavan-3-ol. Among them, the dihydrophenanthropyran **35** was the first one isolated from *Pleione* and the chemical structure of dihydrophenanthropyran with a 4H [2, 1-b] pyran system was reported [15]. Although China is the *Pleione* distribution center, there was no phytochemical investigation there until 2007. Liu [1] initiated the chemical investigation of *P. bulbocodioides* leading to six novel compounds and 24 known compounds, among which 18 compounds were obtained from the *Pleione* for the first time. In addition, the ethyl acetate (EtOAc) extracted fraction from *P. bulbocodioides* was found to have a certain inhibitory effect on mice cancer cells LA795, exerting significant activity of anti-tumor. Since then, the EtOAc fraction has been the key research part. Due to few researches focused on *P. yunnanensis*, Dong et al. [21–23] carried out the phytochemical on *P. yunnanensis* in 2009, discovering 12 novel compounds and 12 known compounds. In addition, since the pseudobulbs of *P. formosana* have been used as the substitute of Shan-ci-gu in Taiwan Island, Shiao [24] performed chemical investigation on them in 2009 and isolated three novel compounds.

The structural diversity of *Pleione* prompted Wang's group [25,26] to continue the phytochemical investigation and isolated sixty compounds from *P. bulbocodioides* and *P. yunnanensis*, occupied more than 30% of the total compounds. It is noteworthy that all compounds were tested for several assays of biological activities in vitro, generally known as free radical scavenging activity, cytotoxic activity, inhibition of NO production activity and neurotoxicity activity. In addition, the experiment turned to the study on the high-polarity fraction, which led to the isolation of 10 glucosyloxybenzyl succinate derivatives [27]. Encouraged by previous phytochemical researches on *Pleione*, Li et al. [28,29] isolated pyrrolidone substituted bibenzyls and prenylated flavones from *P. bulbocodioides*, which enriched the contents of the chemical constituents.

Moreover, there were 152 patents published referring to the *Pleione* in China; 88.8% of them were related to the pharmacological activity against breast cancer, lung cancer, liver cancer, stomach cancer, colon cancer, etc. In order to benefit future research on the phytochemistry and biological of the *Pleione*, this review will discuss about the chemical compound isolation from the *Pleione*, structural analysis of the metabolites and the corresponding biological activities evaluation.

## 2. Chemical Constituents

### 2.1. Phenanthrenes

Phenanthrenes is one of the typical compounds extracted from the *Pleione* [30]. Fifty-seven phenanthrenes have been isolated (Table 1 & Figure 1), including three simple dihydrophenanthrenes (1–3), 10 benzyl substituted dihydrophenanthrenes (4–10, 21–23), three dihydrophenanthrene dimers (11–13), five dimers of phenanthrene (15–17, 24, 25), three phenanthrene and dihydrophenanthrene polymers (14, 18–19), three dihydrophenanthrene and bibenzyl polymers (20, 26, 27), one dihydrophenanthrene and glycoside polymer (28), 18 dihydrophenanthrene and phenylpropanoid polymers (29–46), one phenanthrene and phenylpropanoid polymers (47) and 10 phenanthrene polymers (48–57). The spectroscopic data of Compound 1–57 are shown in Tables 2 and 3. Of these compounds, the dihydrophenanthrene **1**, **3** and the bibenzyls **58** and **61** may be the main bioactive compounds for anti-tumor, anti-inflammatory and anti-oxidant activities, which might also be the result of their synergy [31]. The **27** was the first dihydrophenanthrene component connected with the bibenzyl isolated from the *Pleione* [15]. Three novel 9, 10-dihydrophenanthrofurans **29–31** were isolated by Dong in 2009 [21]. The properties of 9, 10-dihydrophenanthrofurans with a phenyl from the *Pleione* species were may be deemed to be a chemtaxonomic marker of this species. One dihydrophenanthrene connecting with a  $\beta$ -D-glucopyranosyl **28** as the first reported structure of glucosyloxybenzyl 2-isobutylmalates in *Pleione* was also obtained in 2013 [22]. The compounds synthesized by aldol reaction of condensation of acetone with 9, 10-phenanthrene were firstly obtained from *Pleione* **48**, **49** by Wang [25] in 2014. Wang [26] demonstrated that there was a structure-biological

activity relationship of phenanthrenes isolated from *P. yunnanensis*. The structure of **39** is very similar with **40**, but the former showed stronger neurotoxic activity than the latter. This is because that the carbon-9' (C9') of **39** is acetylation, resulting in the carbonyl oxygen atom hydrogen to the receptor. Based on Wang's research [25], Shao [32] determined eight phenanthrenequinone enantiomers configuration of **50–57** by means of the spectroscopy techniques, such as Nuclear Magnetic Resonance (NMR), High Resolution Electrospray Ionization Mass Spectroscopy (HRESIMS) and Executive Creative Director (ECD). The possible biosynthetic pathways can be inferred based on structural analysis.

Table 1. Phenanthrenes from *Pleione* genus.

No.	Compound	Plant	Reference	No.	Compound	Plant	Reference
1	Coelonin	B*, Y*	[22,29]	30	Pleionesin B	Y	[33,34]
2	Lusianthridin	B, Y	[22,29]	31	Pleionesin C	Y	[33,34]
3	Hircinol	B	[33]	32	Shanciol H	B, Y	[21,35]
4	4, 7-dihydroxy-1-( <i>p</i> -hydroxybenzyl)-2-methoxy-9, 10-dihydrophenanthrene	Y	[22,34]	33	(4'-hydroxy-3'-methoxyphenyl)-10-hydroxymethyl-11-methoxy-5, 6, 9, 10-tetrahydrophenanthrene[2, 3- <i>b</i> ]furan-3-ol	B	[36]
5	2, 7-dihydroxy-4-methoxy-1-( <i>p</i> -hydroxybenzyl)-9, 10-dihydrophenanthrene	Y	[22]	34	hydroxy-9-(4'-hydroxy-3'-methoxyphenyl)-11-methoxy-5, 6, 9, 10-tetrahydrophenanthrene-azaspiro[2, 3- <i>b</i> ]furan-10-yl)methylethyl	B	[37]
6	1-( <i>p</i> -hydroxybenzyl)-4, 7-dihydroxy-2-methoxy-9, 10-dihydrophenanthrene	B	[6]	35	Shanciol	B, Y	[15]
7	Pleioanthrenin	F*	[24]	36	Shanciol E	B	[20]
8	2, 7-dihydroxy-1-( <i>p</i> -Hydroxybenzyl)-4-methoxy-9, 10-diphenanthrene	B, Y	[22,33]	37	(7' <i>S</i> , 8' <i>R</i> )-7-hydroxy-7-(4'-hydroxy-3', 5'-dimethoxy-phenyl)-8'-hydroxymethyl-5-methoxy-9, 10, 7', 8-tetrahydro-phenanthrene-[2, 3- <i>b</i> ]furan	B	[25]
9	(4-Hydroxybenzyl)-4-methoxy-9, 10-dihydrophenanthrene-2, 7-diol	B	[28]	38–39	Pleionesin D–E	Y	[25]
10	(4-hydroxybenzyl)-4, 7-dimethoxy-9, 10-dihydrophenanthrene-2-ol	B, F	[24,28]	40	(7', 8'-trans)-7-hydroxy-10-methoxy-7'-(4'-hydroxy-3'-methoxyphenyl)-8'-hydroxymethyl-9, 10, 7', 8'-tetrahydro-[2, 1- <i>b</i> ]furan	Y	[26]
11	Blestrianol A	B	[25]	41–43	Bletilol A–C	B	[11,15]
12	4, 4', 7, 7'-tetrahydroxy-2,2'-dimethoxy-9, 9', 10, 10'-tetrahydro-1, 1'-biphenanthrene	B	[28]	44	Shanciol F	B, Y	[20,21]
13	Blestriarene A	B	[33,34]	45	Shanciol C	B	[19]
14	Blestriarene B	B	[21]	46	Shanciol G	B	[35]
15	Blestriarene C	Y	[22]	47	Shanciol D	B	[19]
16–20	Bulbocodioidin G–K	B	[25]	48	Bulbocodioidin A	B	[25]
21	1-( <i>p</i> -hydroxybenzyl)-2, 7-dihydroxy-4-methoxy-phenanthrene	B	[22]	49	Bulbocodioidin B	B	[25]
22	Shancidin	Y	[22]	50	(9 <i>R</i> ) bulbocodioidins A	B	[32]
23	7-hydroxy-2,4-dimethoxy-1-( <i>p</i> -hydroxybenzyl)-phenanthrene	Y	[33]	51	(9 <i>S</i> ) Bulbocodioidins A	B	[32]
24	Monbarbatain A	B	[33]	52	(9 <i>R</i> ) Bulbocodioidins B	B	[32]
25	2, 7, 2'-didroxy-4, 4', 7'-trimethoxy-1, 1'-biphenanthrene	B	[28]	53	(9 <i>S</i> ) Bulbocodioidins B	B	[32]
26	Phoyunnanin A	B	[28]	54	(9 <i>R</i> ) Bulbocodioidins C	B	[32]
27	Shancilin	B	[14]	55	(9 <i>S</i> ) Bulbocodioidins C	B	[32]
28	Shancigusins G	B, Y	[22]	56	(10 <i>S</i> ) Bulbocodioidins D	B	[32]
29	Pleionesin A	Y	[21]	57	(10 <i>R</i> ) Bulbocodioidins D	B	[32]

Note: \* B: bulbocodioides; \* Y: yunnanensis; \* F: formosana. The same as below.

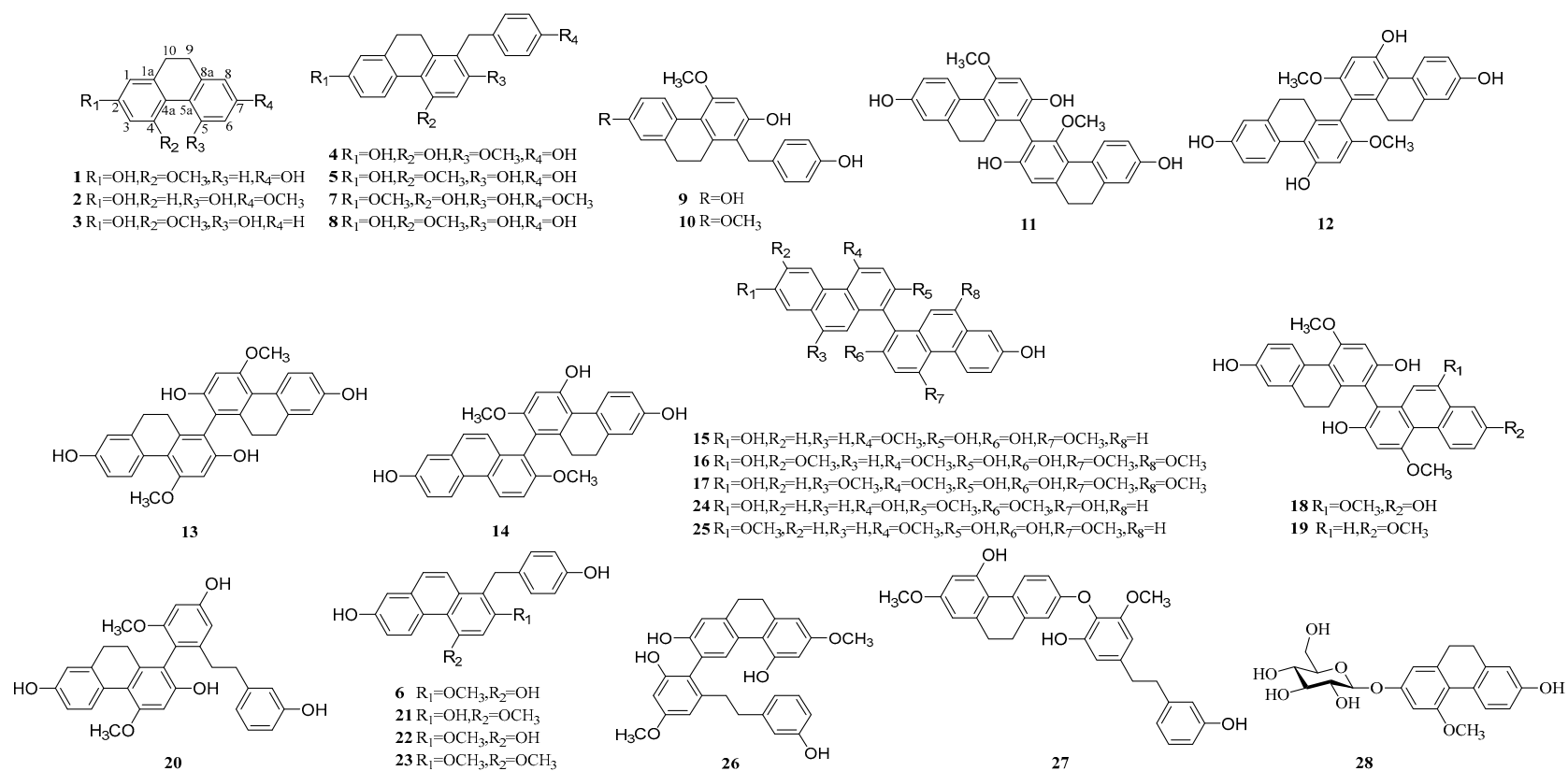


Figure 1. Cont.

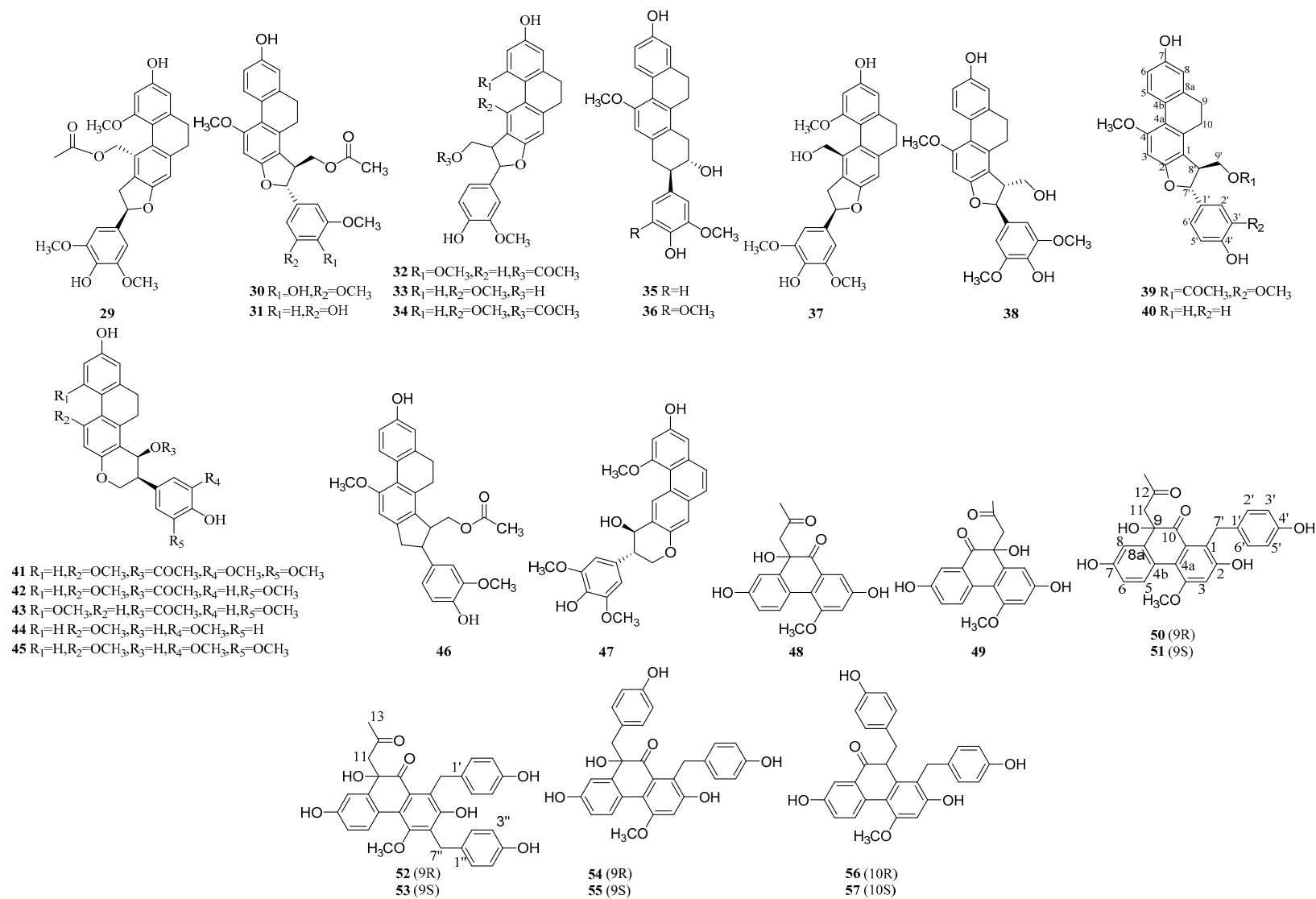


Figure 1. The structures of Phenanthrenes.

Table 2. <sup>13</sup>C NMR data of compounds 1–57.

No.	Solvent	Position													
		1	2	3	4	4a	4b	5	6	7	8	8a	9	10	10a
1	MeOH- <i>d</i> <sub>4</sub>	106.9	154.6	97.9	157.7	115.4	124.8	128.6	112.2	156.0	113.6	139.1	30.4	29.8	140.4
2	MeOH- <i>d</i> <sub>4</sub>	108.3	159.1	99.3	156.1	116.8	126.2	130.0	115.0	157.5	113.6	140.5	31.8	31.2	141.8
3	Acetone- <i>d</i> <sub>6</sub>	109.7	156.3	99.8	158.5	114.6	128.1	154.7	118.2	120.1	128.1	144.1	31.6	31.8	141.3
4	Acetone- <i>d</i> <sub>6</sub>	118.0	156.8	98.9	155.1	117.1	125.9	130.1	114.5	156.1	113.4	139.8	30.5	27.1	140.4
5	DMSO- <i>d</i> <sub>6</sub>	116.9	154.2	98.0	155.1	115.0	124.1	128.8	112.6	155.0	113.8	138.5	19.4	26.0	138.9
6	MeOH- <i>d</i> <sub>4</sub>	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7	MeOH- <i>d</i> <sub>4</sub>	118.3	156.0	96.1	156.3	120.1	126.1	130.5	130.5	157.4	114.6	140.6	30.9	27.5	140.7
8	DMSO- <i>d</i> <sub>6</sub>	116.9	154.2	98.0	155.1	115.0	124.1	128.8	112.6	155.0	113.8	138.5	19.4	26.0	138.9
9	MeOH- <i>d</i> <sub>4</sub>	118.6	157.2	99.3	155.6	117.5	126.5	130.3	114.6	156.0	113.5	140.4	30.9	27.4	140.9
10	MeOH- <i>d</i> <sub>4</sub>	141.6	155.4	99.1	158.5	117.5	126.5	130.3	113.5	156.1	114.7	140.8	31.0	28.2	140.3
11	Acetone- <i>d</i> <sub>6</sub>	120.3	157.8	115.2	155.4	116.8	125.6	129.1	112.0	156.0	114.1	140.8	30.7	28.3	140.1
12	Acetone- <i>d</i> <sub>6</sub>	118.4	157.6	99.4	155.1	115.8	126.3	130.2	113.4	156.1	114.7	140.2	30.6	28.4	141.1
13	MeOH- <i>d</i> <sub>4</sub>	115.7	158.4	98.9	155.4	117.5	126.5	130.3	113.5	156.1	114.7	141.6	31.0	28.2	140.8
14	MeOH- <i>d</i> <sub>4</sub>	115.0	160.3	100.3	155.4	117.8	126.6	130.5	113.6	155.4	114.8	142.4	30.9	28.3	140.8
15	MeOH- <i>d</i> <sub>4</sub>	111.0	157.8	99.6	153.2	114.2	123.5	128.7	110.7	154.0	116.6	133.4	126.7	124.7	132.4
16	Acetone- <i>d</i> <sub>6</sub>	109.2	155.3	98.3	160.0	112.3	126.4	130.2	117.6	155.3	106.0	128.1	154.3	101.4	135.8
17	Acetone- <i>d</i> <sub>6</sub>	109.3	155.3	98.2	160.0	112.4	126.5	130.2	117.6	155.3	106.0	127.9	154.3	101.3	135.6
18	Acetone- <i>d</i> <sub>6</sub>	109.9	154.8	98.2	159.7	112.2	126.4	130.2	117.6	155.3	106.1	127.9	154.4	100.9	135.2
19	Acetone- <i>d</i> <sub>6</sub>	111.0	154.6	100.3	160.0	116.2	126.1	130.1	117.2	157.6	109.1	133.9	128.6	125.4	134.7
20	MeOH- <i>d</i> <sub>4</sub>	116.2	154.7	99.0	157.9	116.8	126.3	130.1	113.4	156.0	114.7	140.2	30.7	28.2	140.8
21	Acetone- <i>d</i> <sub>6</sub>	114.4	153.5	100.2	158.4	116.4	125.4	130.3	117.3	155.2	111.9	133.8	128.2	124.4	133.7
22	MeOH- <i>d</i> <sub>4</sub>	-	-	-	-	-	-	-	-	-	-	-	-	-	-
23	Acetone- <i>d</i> <sub>6</sub>	117.0	156.2	97.1	159.1	117.0	125.4	130.7	117.5	155.9	112.3	134.1	128.7	124.6	133.5
24	Acetone- <i>d</i> <sub>6</sub>	110.0	160.2	100.4	155.1	116.5	125.4	130.2	112.0	155.3	117.4	135.1	128.3	125.6	134.1
25	Chloroform- <i>d</i>	105.7	153.2	98.5	160.4	116.6	125.0	129.4	117.0	156.0	108.4	133.1	129.1	123.9	133.8
26	Acetone- <i>d</i> <sub>6</sub>	106.1	159.4	101.6	156.0	115.8	126.2	132.9	120.9	154.0	115.6	139.4	30.5	31.6	141.5
27	MeOH- <i>d</i> <sub>3</sub>	100.9	158.8	98.9	157.1	114.8	140.0	126.9	112.7	153.6	110.6	135.2	30.0	30.5	136.9
28	MeOH- <i>d</i> <sub>4</sub>	101.2	156.4	108.4	159.9	118.6	125.6	131.0	113.9	156.5	115.0	140.8	31.2	31.9	141.9
29	MeOH- <i>d</i> <sub>4</sub>	109.2	158.8	125.0	125.2	127.6	116.8	159.1	99.3	157.7	108.3	142.0	31.8	31.5	140.7
30	MeOH- <i>d</i> <sub>4</sub>	116.0	160.8	94.1	160.0	118.5	126.3	130.5	114.0	156.6	115.3	140.5	31.1	28.2	138.1
31	MeOH- <i>d</i> <sub>4</sub>	115.7	160.5	93.9	159.7	118.2	126.0	130.2	113.7	156.2	115.0	140.2	30.8	27.9	137.8
32	MeOH- <i>d</i> <sub>4</sub>	109.5	159.1	125.3	125.5	127.9	117.1	159.4	99.6	158.0	108.6	142.3	32.1	31.8	141.0
33	MeOH- <i>d</i> <sub>4</sub>	104.9	159.6	117.3	155.2	120.3	124.6	128.0	113.1	155.6	114.0	139.5	29.9	30.8	141.8
34	MeOH- <i>d</i> <sub>4</sub>	106.2	160.5	117.7	156.4	121.7	125.6	129.2	114.4	156.9	115.2	140.7	31.0	32.0	143.5
35	MeOH- <i>d</i> <sub>3</sub>	132.0	112.1	99.8	157.6	118.8	126.1	130.4	114.8	156.4	113.7	140.4	26.5	30.7	139.9

Table 2. Cont.

No.	Solvent	Position													
		1	2	3	4	4a	4b	5	6	7	8	8a	9	10	10a
36	MeOH- <i>d</i> <sub>3</sub>	131.1	154.7	99.8	157.7	118.9	126.1	130.4	113.7	156.4	114.8	140.4	26.5	30.7	139.9
37	MeOH- <i>d</i> <sub>4</sub>	108.7	158.7	125.9	125.2	126.7	116.5	158.7	99.1	157.4	108.1	141.4	31.4	31.1	139.4
38	Acetone- <i>d</i> <sub>6</sub>	117.2	158.8	93.5	160.2	116.7	137.0	129.9	113.5	156.0	114.9	139.7	30.4	27.4	136.4
39	MeOH- <i>d</i> <sub>4</sub>	116.0	160.8	94.2	160.0	118.5	126.3	130.5	114.0	156.6	115.3	140.5	31.1	28.2	138.1
40	MeOH- <i>d</i> <sub>4</sub>	116.7	160.5	93.9	159.4	118.0	126.2	130.2	113.7	156.2	115.0	140.2	30.9	27.9	137.5
41	MeOH- <i>d</i> <sub>4</sub>	133.0	153.6	93.0	159.3	114.4	116.9	129.3	113.0	158.5	114.3	136.7	26.9	29.7	134.9
42	MeOH- <i>d</i> <sub>4</sub>	125.8	153.6	92.9	159.2	114.3	116.8	129.2	114.3	158.4	114.5	136.6	26.8	29.8	133.8
43	MeOH- <i>d</i> <sub>4</sub>	107.4	146.8	98.3	157.7	116.8	123.8	124.1	125.9	154.7	114.4	133.1	30.4	30.6	133.1
44	MeOH- <i>d</i> <sub>3</sub>	118.1	159.5	94.0	160.6	116.9	137.6	130.2	113.8	156.2	115.0	140.3	28.0	30.9	135.8
45	MeOH- <i>d</i> <sub>3</sub>	118.2	159.5	93.9	160.6	116.8	137.7	130.2	113.8	156.3	115.1	140.3	28.0	30.9	136.3
46	MeOH- <i>d</i> <sub>4</sub>	118.2	160.1	94.3	159.4	118.3	126.1	130.8	113.7	156.3	115.0	140.3	30.9	28.0	137.8
47	MeOH- <i>d</i> <sub>3</sub>	108.4	159.0	99.5	159.4	125.9	136.5	125.5	134.7	157.7	109.0	142.0	31.6	31.9	117.0
48	MeOH- <i>d</i> <sub>4</sub>	106.5	158.7	106.6	159.0	118.7	122.3	130.9	115.4	157.7	112.9	141.8	79.8	205.0	133.2
49	MeOH- <i>d</i> <sub>4</sub>	105.9	159.2	100.5	160.0	112.1	128.9	130.9	121.9	157.1	113.5	132.3	204.7	80.0	143.4
50	MeOH- <i>d</i> <sub>4</sub>	121.8	157.3	105.1	156.3	118.2	122.8	131.2	115.3	157.3	112.3	141.2	80.0	206.5	132.4
51	MeOH- <i>d</i> <sub>4</sub>	121.8	157.3	105.1	156.3	118.2	122.8	131.2	115.3	157.3	112.3	141.2	80.0	206.5	132.4
52	MeOH- <i>d</i> <sub>4</sub>	126.5	155.2	130.0	155.7	123.4	122.6	130.4	116.1	158.1	112.4	141.5	80.0	205.6	130.2
53	MeOH- <i>d</i> <sub>4</sub>	126.5	155.2	130.0	155.7	123.4	122.6	130.4	116.1	158.1	112.4	141.5	80.0	205.6	130.2
54	MeOH- <i>d</i> <sub>4</sub>	122.1	157.0	105.7	156.5	119.7	122.9	131.0	114.9	157.0	113.0	141.6	82.5	207.6	131.9
55	MeOH- <i>d</i> <sub>4</sub>	122.1	157.0	105.7	156.5	119.7	122.9	131.0	114.9	157.0	113.0	141.6	82.5	207.6	131.9
56	MeOH- <i>d</i> <sub>4</sub>	119.3	157.2	99.8	158.4	113.6	130.9	131.5	121.9	156.9	112.4	132.6	205.7	55.7	139.2
57	MeOH- <i>d</i> <sub>4</sub>	119.3	157.2	99.8	158.4	113.6	130.9	131.5	121.9	156.9	112.4	132.6	205.7	55.7	139.2



Table 3. <sup>1</sup>H NMR data of compounds 1–57.

No.	Solvent	Position								
		1	3	4	5	6	7	8	9	10
1	MeOH- <i>d</i> <sub>4</sub>	6.29 d (2.5)	6.38 d (2.5)	-	7.99 d (9.0)	6.61 m	-	6.61 m	2.61 m	2.61 m
2	Acetone- <i>d</i> <sub>6</sub>	6.36 d (2.0)	6.44 d (2.0)	-	8.03 d (8.5)	-	-	-	2.62 s	2.62 s
3	chloroform- <i>d</i>	6.51 s	-	-	-	6.86 d (7.5)	7.15 dd (8.0, 7.5)	6.95 d (8.0)	2.69–2.70 m	2.65–2.67 m
4	Acetone- <i>d</i> <sub>6</sub>	-	6.61 s	-	8.01 d (9.0)	6.65 br d (9.0)	-	6.67 br s	2.60 m	2.52 m
5	Acetone- <i>d</i> <sub>6</sub>	-	6.60 s	-	8.00 d (9.0)	6.65 br d (9.0)	-	6.64 d (2.0)	2.57–2.60 m	2.50–2.53 m
6	chloroform- <i>d</i>	-	6.47, s	-	8.14 d, (8.6)	6.62 m	-	6.60, d, 3.0	2.13–2.61 m	2.13–2.61 m
7	MeOH- <i>d</i> <sub>4</sub>	-	6.64 s	-	8.00 d (8.0)	6.60 dd (8.0, 2.0)	-	6.62 d (2.0)	2.58 m	2.50 m
8	Acetone- <i>d</i> <sub>6</sub>	-	6.60 s	-	8.00 d (9.0)	6.65 br d (9.0)	-	6.64 d (2.0)	2.57–2.60 m	2.50–2.53 m
9	MeOH- <i>d</i> <sub>4</sub>	-	6.51 s	-	7.96 d (8.5)	6.60 dd (8.5, 2.5)	-	6.58 d (2.5)	2.45–2.57 m	2.45–2.57 m
10	MeOH- <i>d</i> <sub>4</sub>	-	6.57 s	-	8.04 d (8.0)	6.64 dd (8.0, 2.0)	-	6.60 d (2.0)	2.51–2.57 m	2.28–2.36 m
11	MeOH- <i>d</i> <sub>4</sub>	-	6.57 s	-	8.03 d (8.4)	6.62 dd (8.4, 2.4)	-	6.59 d (2.4)	2.44–2.46 m	2.53–2.55 m
12	Acetone- <i>d</i> <sub>6</sub>	-	6.58 s	-	8.24 d (8.5)	6.70 dd (8.5, 2.7)	-	6.67 d (2.7)	2.56 m	2.52 m
13	Acetone- <i>d</i> <sub>6</sub>	-	6.60 s	-	8.09 d (8.5)	6.69 dd (8.5, 3.0)	-	6.66 d (3.0)	2.53 m	2.33 m
14	MeOH- <i>d</i> <sub>4</sub>	-	-	-	8.09 d (8.8)	6.64 dd (2.8, 8.8)	-	6.56 d (2.8)	2.45 m	2.21 m
15	MeOH- <i>d</i> <sub>4</sub>	-	6.93 s	-	9.40 d (9.2)	7.03 dd (9.2, 2.8)	-	7.00 d (2.8)	7.23 d (9.2)	6.92 d (9.2)
16	Acetone- <i>d</i> <sub>6</sub>	-	6.87 s	-	9.50 d (9.6)	7.19 dd (9.6, 2.4)	-	7.61 d (2.4)	-	6.44 s
17	Acetone- <i>d</i> <sub>6</sub>	-	6.88 s	-	9.51 d (9.0)	7.20 dd (9.0, 3.0)	-	7.62 d (3.0)	-	6.51 s
18	Acetone- <i>d</i> <sub>6</sub>	-	6.81 s	-	9.47 d (9.6)	7.18 dd (9.6, 3.0)	-	7.65 d (3.0)	-	6.60 s
19	Acetone- <i>d</i> <sub>6</sub>	-	6.98 s	-	9.52 d (9.6)	7.20 dd (9.6, 3.0)	-	7.31 d (3.0)	-	7.25 d (9.0)
20	Acetone- <i>d</i> <sub>6</sub>	-	6.59 s	-	8.08 d (9.0)	6.67 dd (9.0, 2.4)	-	6.64 d (2.4)	2.51 m	2.30 m
21	Acetone- <i>d</i> <sub>6</sub>	-	6.99 s	-	9.43 d (9.5)	7.12 dd (9.5)	-	7.19 d (2.5)	7.53 d (9.5)	7.80 d (9.5)
22	chloroform- <i>d</i>	-	6.47, s	-	8.14 d (8.6)	6.62 m	-	6.60, d, 3.0	2.13–2.61 m	2.13–2.61 m
23	Acetone- <i>d</i> <sub>6</sub>	-	7.24 s	-	9.55 d (9.0)	7.24 dd (9.0, 2.0)	-	7.30 d (2.0)	7.64 d (9.5)	7.92 d (9.5)
24	Acetone- <i>d</i> <sub>6</sub>	-	7.02 s	-	9.51 d (8.4)	7.19 dd (8.4, 3.0)	-	7.18 d (3.0)	7.37 d (9.0)	7.03 d (9.0)
25	chloroform- <i>d</i>	-	7.05 s	-	9.57 d (10.0)	7.29 dd (10.0, 3.0)	-	7.18 d (3.0)	7.49 d (8.5)	7.11 d (8.5)
26	Acetone- <i>d</i> <sub>6</sub>	6.39 d (2.5)	6.41 d (2.5)	-	8.21 s	-	-	6.85 s	2.76 m	2.76 m
27	MeOH- <i>d</i> <sub>3</sub>	-	6.42 d, 2.3	-	7.92 d (8.6)	6.71, dd, 8.6, 2.6	-	6.74, d, 2.6	2.68–2.70, m	2.68–2.70 m
28	MeOH- <i>d</i> <sub>4</sub>	6.69 d (2.7)	6.45 d (2.7)	-	8.18 d (8.7)	6.60 dd (8.7, 2.7)	-	6.57 d (2.7)	2.58 m	2.63 m
29	MeOH- <i>d</i> <sub>4</sub>	6.61 s	-	8.00 s	-	6.35 d (2.0)	-	6.26 d (2.0)	2.57–2.62 m	2.57–2.62 m
30	Acetone- <i>d</i> <sub>6</sub>	-	6.59 s	-	8.04 d (8.4)	6.68 dd (8.4,3.0)	-	6.69 d (3.0)	2.59–2.77 m	2.59–2.77 m
31	MeOH- <i>d</i> <sub>4</sub>	-	-	-	-	-	-	-	-	-
32	chloroform- <i>d</i>	6.74 s	-	8.07 s	-	6.42 d (2.0)	-	6.36 d (2.0)	2.70–2.71 m	2.70–2.71 m
33	MeOH- <i>d</i> <sub>4</sub>	6.54 s	-	-	8.00 d (9.0)	6.65 m	-	6.67 d (2.5)	2.68 m	2.68 m
34	MeOH- <i>d</i> <sub>4</sub>	6.57 s	-	-	8.03 d (9.6)	6.70 dd (9.6, 2.4)	-	6.68 d (2.4)	2.70 m	2.70 m
35	MeOH- <i>d</i> <sub>3</sub>	-	6.5, s	-	7.99 d (8.5)	6.62 dd (8.5, 2.5)	-	6.64, d, 2.5	2.62, m	2.62, m

Table 3. Cont.

No.	Solvent	Position								
		1	3	4	5	6	7	8	9	10
36	MeOH- <i>d</i> <sub>3</sub>	-	6.51 s	-	8.00 d (8.5)	6.62 dd(8.5, 2.6)	-	6.65 d (2.6)	2.60–2.67 m	2.60–2.67 m
37	Acetone- <i>d</i> <sub>6</sub>	6.68 s	-	-	8.09 s	6.45 d (2.4)	-	6.38 d (2.4)	2.65 m	2.66 m
38	Acetone- <i>d</i> <sub>6</sub>	-	6.55 s	-	8.03 d (9.0)	6.67 dd (9.0, 2.5)	-	6.67 d (2.5)	2.55–2.73 m	2.55–2.73 m
39	Acetone- <i>d</i> <sub>6</sub>	-	6.53 s	-	8.09 d (8.5)	6.72 dd (8.5, 2.5)	-	6.69 d (2.5)	-	-
40	Acetone- <i>d</i> <sub>6</sub>	-	6.54 s	-	8.03 d (9.5)	6.67 dd (9.5, 2.5)	-	6.68 br s	2.63 m	2.63 m
41	MeOH- <i>d</i> <sub>4</sub>	-	6.53 s	-	8.09 d (8.6)	6.72 dd (8.6, 3.0)	-	6.69 d (3.0)	2.7 m	2.7 m
42	MeOH- <i>d</i> <sub>4</sub>	-	6.51 s	-	8.09 d (8.4)	6.71 dd (8.4, 2.6)	-	6.69 d (2.6)	2.67–2.69 m	2.67–2.69 m
43	MeOH- <i>d</i> <sub>4</sub>	6.34 d (2.1)	6.42 d (2.1)	-	8.08 s	-	-	6.74 s	2.67–2.76 m	2.67–2.76 m
44	MeOH- <i>d</i> <sub>3</sub>	-	6.54 s	-	7.99 d (9.4)	6.62 m	-	6.61 d (2.6)	2.56–2.70 m	2.56–2.70 m
45	MeOH- <i>d</i> <sub>3</sub>	-	6.56 s	-	8.00 d (9.2)	6.62 dd (9.6, 2.8)	-	6.61 d (2.8)	2.59–2.71 m	2.59–2.71 m
46	MeOH- <i>d</i> <sub>4</sub>	-	6.58 s	-	8.09 d (8.5)	6.63 m	-	6.65 d (2.5)	2.67 m	2.67 m
47	MeOH- <i>d</i> <sub>3</sub>	6.31 d (2.1)	6.41 d (2.1)	-	8.06 s	-	-	6.69 s	2.62–2.69 m	2.62–2.69 m
48	MeOH- <i>d</i> <sub>4</sub>	6.80 d (2.4)	6.76 d (2.4)	-	8.23 d (9.0)	6.69 dd (9.0, 2.4)	-	7.13 d (2.4)	-	-
49	MeOH- <i>d</i> <sub>4</sub>	6.83 d (2.4)	6.47 d (2.4)	-	8.30 d (8.4)	7.00 dd (8.4, 3.0)	-	7.13 d (3.0)	-	-
50	MeOH- <i>d</i> <sub>4</sub>	-	6.76 s	-	8.07 d (9.0)	6.67 dd (9.0, 2.4)	-	7.05 d (2.4)	-	-
51	MeOH- <i>d</i> <sub>4</sub>	-	6.76 s	-	8.07 d (9.0)	6.67 dd (9.0, 2.4)	-	7.05 d (2.4)	-	-
52	MeOH- <i>d</i> <sub>4</sub>	-	-	-	8.11 d (8.4)	6.72 dd (8.4, 2.4)	-	7.06 d (2.0)	-	-
53	MeOH- <i>d</i> <sub>4</sub>	-	-	-	8.11 d (8.4)	6.72 dd (8.4, 2.4)	-	7.06 d (2.0)	-	-
54	MeOH- <i>d</i> <sub>4</sub>	-	6.83 s	-	8.10 d (8.4)	6.81 d (2.4)	-	-	-	-
55	MeOH- <i>d</i> <sub>4</sub>	-	6.83 s	-	8.10 d (8.4)	6.81 d (2.4)	-	-	-	-
56	MeOH- <i>d</i> <sub>4</sub>	-	6.60 s	-	8.37 d (9.0)	7.02 dd (9.0, 2.4)	-	7.01 d (2.4)	-	3.86 d (9.6)
57	MeOH- <i>d</i> <sub>4</sub>	-	6.60 s	-	8.37 d (9.0)	7.02 dd (9.0, 2.4)	-	7.01 d (2.4)	-	3.86 d (9.6)

## 2.2. Bibenzyls

Bibenzyls are also abundant in *Pleione* with a number of 44 (Table 4 & Figure 2) [30], including nine simple bibenzyls (58–66), 23 benzyl substituted bibenzyls (67–89), one bibenzyl and fluorene polymer (85), five bibenzyl and glycoside polymers (91–95), two bibenzyl and phenylpropanoid polymers (96, 97) and four bibenzylamide polymers (98–101). The spectroscopic data of Compound 1–57 are shown in Tables 5 and 6. The character of bibenzyls is that the carbon-3 (C3), carbon-5 (C5) and carbon-4' (C4') positions are often hydroxyl or methoxy on the core structure, and the carbon-2 (C2) or/and carbon-4 (C4) often have a *p*-hydroxyl or phenyl substitution. Two typical structures were isolated from *Pleione* in 1997 [30]. One was a single structure that mediates an ether combined dihydrophenanthrene with dibenzyl 27, the other was the bibenzyl with two *p*-hydroxybenzyl groups 76, 77. Another four bibenzyls 67, 68, 78, 79 have only hydroxyl and *p*-hydroxybenzyl substituents, which is not common in bibenzyl derivatives [23]. It was meaningful to understand such particular structures. Li [28] isolated four pyrrolidone substituted bibenzyl 98–101 from *P. bulbocodiodes*, which further enriched the chemical compounds of the *Pleione* species.

Table 4. Bibenzyls from *Pleione* genus.

No.	Compound	Plant	Reference	No.	Compound	Plant	Reference
58	Batatasin III	B, Y	[17,28]	78	Shancigusin A	Y	[23]
59	3'-O-methylbatatasin III	B, Y	[17,22]	79	Shancigusin B	Y	[23]
60	3, 5-Dimethoxy-3'-hydroxybibenzyl <a href="https://scifinder.cas.org/scifinder/view/text/javascript;">https://scifinder.cas.org/scifinder/view/text/javascript;</a>	B	[22]	80	Arundin	F	[24]
61	Gigantol	B	[33]	81	5-O-Methylshanciguol	B, Y, F	[23,24,28]
62	Bauhinol C	B	[28]	82	Blestritin B	B	[28]
63	2, 5, 2', 5'-Tetrahydroxy-3-methoxybibenzyl	B	[28,38]	83	2, 6-bis-(4-hydroxybenzyl)-3', 5-dimethoxy-3-hydroxybibenzyl	F	[24]
64	2, 5, 2', 3'-tetrahydroxy-3-methoxybibenzyl	B	[28]	84	Bulbocodin	B	[18]
65	hydroxy-3',5-dimethoxybibenzyl	Y	[22]	85	Bulbocodin C	B, F	[20]
66	3, 3'-dihydroxy-5-methoxybibenzyl	Y	[22]	86	Bulbocodin D	B	[20,31]
67	Shancigusin C	Y	[23]	87	Pleiobibenzynin A	F	[24]
68	Shancigusin D	Y	[23]	88	Pleiobibenzynin B	F	[24]
69	3, 3'-dihydroxy-2-( <i>p</i> -hydroxybenzyl)-5-methoxybibenzyl	B, Y, F	[18,23,38]	89	6'-(3''-hydroxyphenethyl)-4'-methoxydiphenyl-2, 2', 5'-triol	B	[39]
70	3', 5-dihydroxy-2-( <i>p</i> -hydroxybenzyl)-3-methoxybibenzyl	B, Y, F	[18,23,24]	90	2-(4''-hydroxybenzyl)-3-(3'-hydroxy-phenethyl)-5-methoxy-cyclohexa-2, 5-diene-1, 4-dione	B	[39]
71	Gymconopin D	B	[36,37,40]	91	Batatsin III-3-O-glucoside	B, Y	[17,22]
72	Bulbocol	B, F	[18,24]	92	3', 5-dimethoxybibenzyl-3-O-β-D-glucopyranoside	B, Y	[17,22]
73	Arundinin	Y, F	[28]	93–94	Shancigusins E-F	Y	[22]
74	Isoarundinin I	B	[28]	95	5-methoxyl bibenzyl-3, 3'-di-O-β-D-glucopyranoside	B	[27]
75	Isoarundinin II	B	[28]	96–97	Shanciols A–B	B	[19]
76	3, 3'-dihydroxy-4-( <i>p</i> -hydroxybenzyl)-5-methoxybibenzyl	B, Y	[18]	98–101	Dusuanlansins A–D	B	[28]
77	Shanciguol	B, Y	[14,23]				

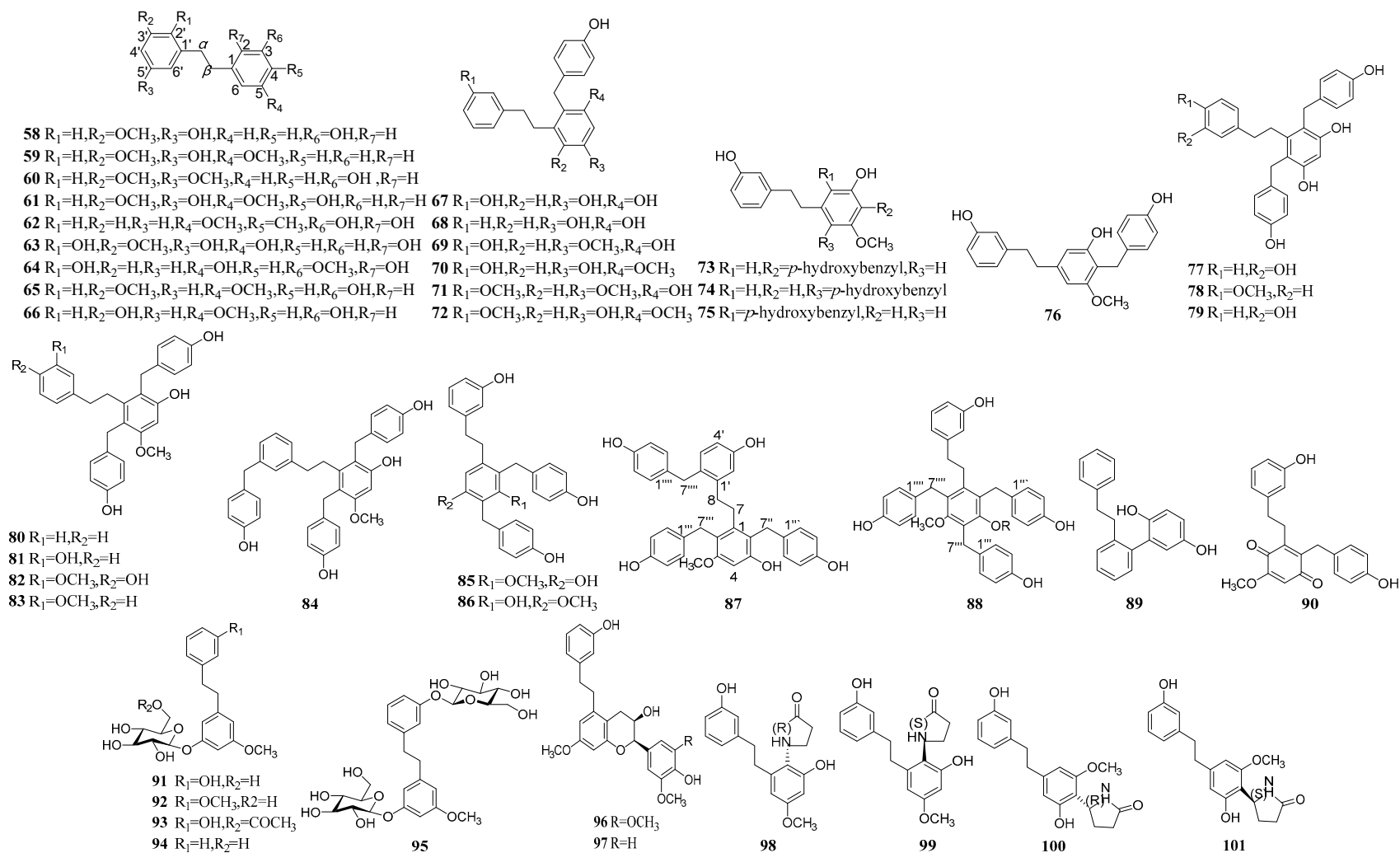


Figure 2. The structures of Bibenzyls.

Table 5. <sup>13</sup>C NMR data of compounds 58–101.

No.	Solvent	Position													
		1	2	3	4	5	6	1'	2'	3'	4'	5'	6'	C-α	C-β
58	Acetone- <i>d</i> <sub>6</sub>	145.1	108.8	159.3	99.7	161.8	106.2	144.3	116.2	158.2	113.6	130.0	120.4	38.6	38.2
59	Chloroform- <i>d</i>	146.5	107.7	156.4	98.8	161.3	106.4	145.1	113.7	159.9	111.5	129.5	120.4	35.8	36.0
60	Chloroform- <i>d</i>	144.1	106.6	160.7	97.9	160.7	106.6	143.7	115.4	155.6	129.5	120.9	112.9	38.0	37.5
61	Acetone- <i>d</i> <sub>6</sub>	145.1	108.9	159.2	99.7	161.8	106.3	134.1	115.5	148.0	145.2	112.9	121.6	38.0	39.1
62	Chloroform- <i>d</i>	141.8	128.5	128.3	125.9	128.3	128.5	140.7	103.6	154.0	110.0	158.7	108.1	37.8	37.9
63	MeOH- <i>d</i> <sub>4</sub>	116.9	142.0	159.2	99.4	157.6	108.5	126.1	140.6	113.7	130.2	156.2	115.1	31.9	31.4
65	Chloroform- <i>d</i>	144.0	107.8	158.0	98.8	159.8	105.4	143.2	113.9	160.9	128.8	120.6	111.1	37.6	37.4
67	MeOH- <i>d</i> <sub>3</sub>	144.0	118.6	157.5	101.4	157.0	108.0	145.0	116.2	158.3	113.7	130.2	120.7	36.5	38.6
68	MeOH- <i>d</i> <sub>3</sub>	143.9	118.6	157.5	101.3	157.1	108.8	143.4	129.4	129.2	126.7	129.2	129.4	36.6	38.6
69	Acetone- <i>d</i> <sub>6</sub>	143.6	119.1	157.0	100.1	159.6	107.0	144.5	113.6	158.2	116.1	130.0	120.3	36.2	38.1
70	Acetone- <i>d</i> <sub>6</sub>	143.2	119.3	159.7	97.8	157.5	109.1	144.5	113.6	158.3	116.1	130.1	120.3	36.0	38.2
71	Chloroform- <i>d</i>	142.4	119.9	155.5	96.5	158.8	105.8	143.8	115.3	158.9	112.8	129.5	120.8	35.2	37.2
72	MeOH- <i>d</i> <sub>3</sub>	143.7	121.8	161.2	98.1	157.6	109.5	144.9	114.9	160.3	112.6	130.2	120.0	36.4	38.6
73	MeOH- <i>d</i> <sub>4</sub>	-	-	-	-	-	-	-	-	-	-	-	-	-	-
74	Chloroform- <i>d</i>	142.6	122.2	158.6	106.4	150.8	113.2	142.9	121.3	150.4	119.1	129.1	125.7	36.8	34.8
75	Chloroform- <i>d</i>	142.1	124.3	150.8	102.7	158.4	114.2	143.0	121.3	150.0	119.0	129.1	125.6	36.7	34.5
76	Acetone- <i>d</i> <sub>6</sub>	141.9	109.9	156.3	114.9	159.3	103.5	144.4	115.4	158.3	113.6	129.9	120.3	38.6	38.4
77	MeOH- <i>d</i> <sub>3</sub>	145.4	119.1	155.7	101.8	155.7	119.1	142.8	116.1	168.3	113.8	130.2	120.6	33.4	37.7
78	MeOH- <i>d</i> <sub>3</sub>	142.9	118.9	155.6	101.5	155.6	118.9	134.7	130.1	116.0	156.3	116.0	130.1	33.8	36.9
79	MeOH- <i>d</i> <sub>3</sub>	142.7	118.9	155.6	101.6	155.6	118.9	143.8	129.3	129.2	126.7	129.2	129.3	33.5	37.7
80	MeOH- <i>d</i> <sub>4</sub>	142.6	119.5	158.4	98.0	155.9	120.2	143.6	129.1	129.2	126.7	129.2	129.1	33.4	37.7
81	Acetone- <i>d</i> <sub>6</sub>	142.2	119.9	157.8	98.0	158.3	119.0	144.7	113.6	156.0	115.7	130.1	120.1	33.2	37.2
82	MeOH- <i>d</i> <sub>4</sub>	143.2	121.8	158.7	98.4	156.2	120.7	135.6	113.3	149.0	145.8	116.3	121.8	34.0	38.2
83	MeOH- <i>d</i> <sub>4</sub>	142.7	120.3	156.0	98.1	161.0	119.5	145.2	112.6	158.4	114.5	130.2	121.5	37.6	33.3
84	MeOH- <i>d</i> <sub>3</sub>	142.9	120.4	156.7	98.4	158.5	119.5	131.5	155.9	113.9	116.6	142.8	132.1	34.7	37.9
85	MeOH- <i>d</i> <sub>3</sub>	144.9	124.4	159.5	120.5	158.3	113.6	141.9	116.4	156.2	113.8	130.2	120.8	29.8	31.6
86	MeOH- <i>d</i> <sub>4</sub>	145.0	130.6	157.9	120.7	158.3	106.0	140.9	116.5	154.8	113.8	130.2	120.9	29.0	31.4
87	MeOH- <i>d</i> <sub>4</sub>	140.8	119.4	156.3	98.2	158.4	120.2	142.7	116.5	156.6	113.8	132.0	131.4	31.7	34.6
88	MeOH- <i>d</i> <sub>4</sub>	140.8	124.9	154.1	121.1	157.7	125.7	145.1	116.0	158.3	113.7	130.1	120.6	33.4	37.7
89	MeOH- <i>d</i> <sub>4</sub>	143.1	117.6	155.6	99.1	160.0	106.3	144.0	115.0	157.0	112.4	128.9	119.6	36.6	37.1
90	MeOH- <i>d</i> <sub>4</sub>	143.4	145.3	189.1	108.0	160.1	184.0	144.0	116.3	158.5	114.1	130.4	120.7	30.2	35.6

Table 5. Cont.

No.	Solvent	Position													
		1	2	3	4	5	6	1'	2'	3'	4'	5'	6'	C- $\alpha$	C- $\beta$
91	MeOH- $d_4$	144.6	110.6	158.4	102.7	162.2	109.7	145.6	116.6	160.2	114.0	130.3	121.0	38.6	38.6
92	MeOH- $d_4$	144.6	110.5	160.2	102.6	162.1	109.7	145.4	115.4	161.2	112.5	130.3	122.1	38.8	38.8
93	MeOH- $d_4$	144.5	110.4	158.4	102.0	162.2	109.2	145.4	116.5	160.0	113.9	130.3	120.9	38.7	39.1
94	MeOH- $d_4$	145.4	110.3	160.1	101.6	162.0	109.5	143.0	129.6	129.3	126.9	129.3	129.6	39.2	38.7
95	DMSO- $d_6$	143.8	108.9	158.6	99.9	160.2	107.8	143.1	116.5	157.5	113.6	129.2	122.0	37.0	36.7
96	Chloroform- $d$	143.3	109.5	160.4	100.5	156.6	112.5	144.6	116.5	158.5	113.9	130.4	120.9	35.9	37.8
97	Chloroform- $d$	143.3	109.4	160.4	100.5	156.6	112.5	144.6	116.1	158.5	114.0	130.4	121.4	35.9	37.8
98	MeOH- $d_4$	143.4	119.5	159.0	101.4	161.1	107.4	144.4	120.9	158.5	114.0	130.3	116.5	36.8	39.7
99	MeOH- $d_4$	143.4	119.5	159.0	101.4	161.1	107.4	144.4	120.9	158.5	114.0	130.3	116.5	36.8	39.7
100	MeOH- $d_4$	144.4	109.8	157.4	114.8	160.2	104.3	144.5	116.4	158.4	113.8	130.2	120.8	39.0	38.7
101	MeOH- $d_4$	144.4	109.8	157.4	114.8	160.2	104.3	144.5	116.4	158.4	113.8	130.2	120.8	39.0	38.7

Table 6. <sup>1</sup>H NMR data of compounds 58–101.

No.	Solvent	Position											
		2	3	4	5	6	2'	3'	4'	5'	6'	H- $\alpha$	H- $\beta$
58	Acetone- <i>d</i> <sub>6</sub>	6.30 dd (1.8, 1.8)	-	-	-	6.32 dd (1.8, 1.8)	6.71 d (1.8)	-	6.65 dd (7.8, 1.8)	7.07 dd (7.8, 7.8)	6.70 d (7.8)	2.75–2.80 m	2.75–2.80 m
59	Chloroform- <i>d</i>	6.40 t (2.0)	-	6.46 t (2.0)	-	6.23 t (2.0)	-	-	6.72 m	7.08 t (9.0)	6.72 m	-	-
60	Chloroform- <i>d</i>	6.33 m	-	6.31 t (2.5)	-	6.33 m	6.66 m	-	6.66 m	7.15 t (7.5)	6.76 m	2.85 m	2.85 m
61	Acetone- <i>d</i> <sub>6</sub>	-	-	-	-	6.29 dd (1.8, 1.8)	6.80 d (1.8)	-	-	6.71 d (7.8)	6.65 dd (7.8, 1.8)	2.27–2.59 m	2.27–2.59 m
62	Chloroform- <i>d</i>	7.24 m	7.33 m	7.33 m	7.33 m	7.24 m	6.32 br s	-	-	-	6.36 br s	-	-
63	MeOH- <i>d</i> <sub>4</sub>	-	-	6.39 d (2.1)	-	6.30 d (2.1)	-	6.62 br s	7.99 d (8.8)	-	6.60 d (2.6)	2.63 br s	2.63 br s
65	Chloroform- <i>d</i>	-	-	6.17 t (1.5)	-	6.23 m	6.71 m	-	6.72 m	7.15 t (8.0)	6.75 m	2.79 m	2.79 m
67	MeOH- <i>d</i> <sub>3</sub>	-	-	6.23 d (2.0)	-	6.19 d (2.0)	6.55 br s	-	6.57 br d (8.0)	7.03 t (8.0)	6.54 br d (8.0)	2.65–2.69 m	2.52–2.55 m
68	MeOH- <i>d</i> <sub>3</sub>	-	-	6.17 d (2.4)	-	6.13 d (2.4)	6.98 d (7.2)	7.14 t (7.2)	7.07 t (7.2)	7.14 t (7.2)	6.98 d (7.2)	2.61–2.64 m	2.51–2.55 m
69	Acetone- <i>d</i> <sub>6</sub>	-	-	6.39 d (1.5)	-	6.36 d (1.5)	6.67 br s	-	6.62 br d (8.0)	7.05 t (8.0)	6.62 br d (8.0)	2.77 m	2.61 m
70	Acetone- <i>d</i> <sub>6</sub>	-	-	6.39 d (2.0)	-	6.37 d (2.0)	6.65 br s	-	6.61 br d (8.0)	7.05 t (8.0)	6.63 br d (8.0)	2.73 m	2.59 m
71	Chloroform- <i>d</i>	-	-	6.34 d (2.0)	-	6.29 d (2.0)	6.49 br s	-	6.69 m	7.11 t (8.5)	6.64 m	2.79 m	2.65 m
72	MeOH- <i>d</i> <sub>3</sub>	-	-	6.34 d (2.6)	-	6.27 d (2.6)	6.55 t (2.1)	-	6.69 dd (7.9, 1.7)	7.11 t (7.9)	6.64 m	2.56–2.64 m	2.56–2.64 m
73	MeOH- <i>d</i> <sub>4</sub>	6.19 d (2.0)	-	-	-	6.25 d (2.0)	6.55 s	-	6.52 m	6.99 t (8.0)	6.59 dd (8.0, 2.0)	2.71–2.74 m	2.71–2.74 m
74	Chloroform- <i>d</i>	-	-	6.67 d (2.1)	-	6.79 d (2.1)	6.90 d (3.0)	-	6.93 d (8.4)	7.25 t (8.4)	7.16 d (8.4)	2.70 m	2.82 m
75	Chloroform- <i>d</i>	-	-	6.61 d (2.1)	-	6.58 d (2.1)	6.82 br	-	6.97 d (8.2)	7.26 apt t (8.7, 8.1)	6.97 dd	2.73 m	2.85 m
76	Acetone- <i>d</i> <sub>6</sub>	6.37 s	-	-	-	6.40 s	-	-	6.67 br d (7.2)	7.05 t (7.8)	6.70 br s (8.0)	2.86 m	2.75 m
77	MeOH- <i>d</i> <sub>3</sub>	-	-	6.39 s	-	-	6.51 t (2.1)	-	6.56 ddd (7.7, 2.6, 1.9)	7.01 t (7.7)	6.47 d (7.7)	2.24–2.30, m	2.24–2.30, m
78	MeOH- <i>d</i> <sub>3</sub>	-	-	6.32 s	-	-	6.74 d (8.4)	6.57 d (8.4)	-	6.57 d (8.4)	6.74 d (8.4)	2.54–2.57 m	2.16–2.20 m
79	MeOH- <i>d</i> <sub>3</sub>	-	-	6.34 s	-	-	6.92 d (7.2)	7.13 t (7.2)	7.04 t (7.2)	7.13 t (7.2)	6.92 d (7.2)	2.58–2.62 m	2.24–2.28 m
80	MeOH- <i>d</i> <sub>4</sub>	-	-	-	-	-	6.97 d (7.0)	7.18 t (7.5)	7.10 t (7.5)	7.18 t (7.5)	6.97 d (7.0)	2.66–2.72 m	2.66–2.72 m
81	Acetone- <i>d</i> <sub>6</sub>	-	-	6.58 s	-	-	6.64 br s	-	6.61 m	7.04 t (8.0)	6.58 m	2.74 m	2.37 m
82	MeOH- <i>d</i> <sub>4</sub>	-	-	6.48 s	-	-	6.38 d (1.8)	-	-	6.60–6.65 m	6.44 dd (8.0, 1.8)	2.61–2.71 m	2.30–2.40 m
83	MeOH- <i>d</i> <sub>4</sub>	-	-	6.49–7.15 m	-	-	6.49–7.15 m	-	-	6.49–7.15	-	2.23–2.37 m	2.64–2.73 m
84	MeOH- <i>d</i> <sub>3</sub>	-	-	6.45 s	-	-	-	6.57 d (8.2)	6.53 dd (8.2, 3.3)	-	6.58 d (3.3)	2.43–2.46 m	2.43–2.46 m
85	MeOH- <i>d</i> <sub>3</sub>	-	-	-	-	6.56 s	6.50 s	-	6.57 dd (8.4, 2.2)	7.01 t (8.4)	6.50 m	2.59–2.66 m	2.59–2.66 m



Table 6. Cont.

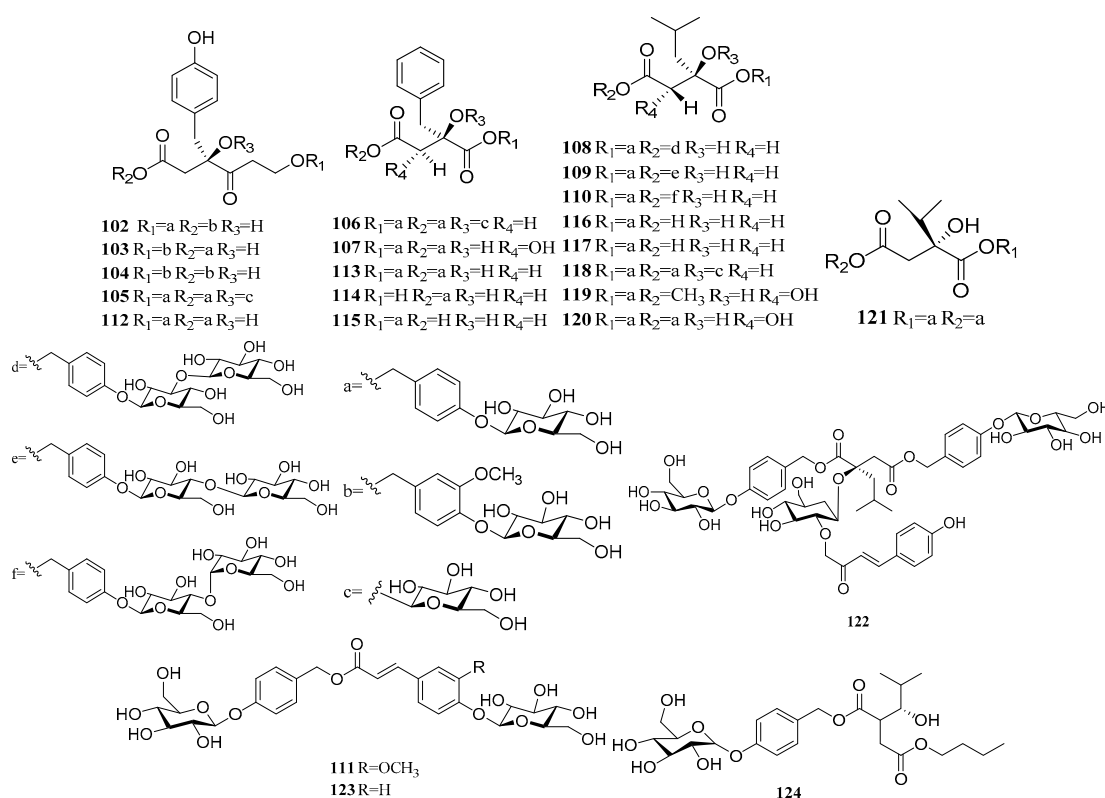
No.	Solvent	Position											
		2	3	4	5	6	2'	3'	4'	5'	6'	H- $\alpha$	H- $\beta$
86	MeOH- $d_4$	-	-	-	-	6.33 s	6.53 m	-	6.57 dd (8.2, 2.3)	7.02 t (8.2)	6.53 m	2.59–2.77 m	2.59–2.77 m
87	MeOH- $d_4$	-	-	6.46 s	-	-	6.57 d (2.0)	-	6.51 dd (8.5, 2.0)	6.77 d (8.5)	-	2.66 m	2.42 m
88	MeOH- $d_4$	-	-	-	-	-	6.47 dd (2.1, 2.0)	-	6.55 ddd (8.0, 2.1, 2.0)	7.00 t (8.0)	6.46 ddd (8.0, 2.1, 2.0)	2.67 m	2.35 m
89	MeOH- $d_4$	-	-	6.33 m	-	6.34 m	6.41 m	-	6.52 m	6.96 t (8.0)	6.39 m	2.56 m	2.56 m
90	MeOH- $d_4$	-	-	6.02 s	-	-	6.59 m	-	6.62 m	7.06 t (8.0)	6.58 m	2.75 m	2.46 m
91	MeOH- $d_4$	6.52 t (2.0)	-	6.51 t (2.0)	-	6.40 t (2.0)	6.59 t (2.0)	-	6.61 dd (7.5, 2.8)	7.05 t (7.7)	6.63 br d (7.7)	2.83 m	2.83 m
92	MeOH- $d_4$	6.52 t (2.0)	-	6.50 t (2.0)	-	6.40 t (2.0)	6.70 br d (1.7)	-	6.73 dd (8.6, 7.7)	7.14 t (8.6)	6.74 br d (7.7)	2.84 m	2.84 m
93	MeOH- $d_4$	6.41 m	-	6.40 m	-	6.35 br s	6.54 m	-	6.54 m	7.00 br t (7.8)	6.57 d (7.8)	2.71–2.81	2.71–2.81
94	MeOH- $d_4$	6.51 m	-	6.51 m	-	6.39 s	7.15 m	7.24 t (7.5)	7.15 m	7.24 t (7.5)	7.15 m	2.83–2.91	2.83–2.91
95	DMSO- $d_6$	6.51 br s	-	6.45 br s	-	6.44 br s	6.92 br s	-	6.86 br d (7.8)	7.18 t (7.8)	6.87 br d (7.8)	2.81 m	2.81 m
96	Chloroform- $d$	6.37 d (2.6)	-	6.31 d (2.6)	-	-	6.61 m	-	6.61 m	7.05 t (7.7)	6.63 d (7.7)	2.80 m	2.80 m
97	Chloroform- $d$	6.36 d (2.6)	-	6.29 d (2.6)	-	-	6.61 m	-	6.61 m	7.05 t (7.7)	6.64 d (7.7)	2.79 m	2.79 m
98	MeOH- $d_4$	-	-	6.25 d (2.5)	-	6.22 d (2.5)	6.60 br s	-	6.61 m	7.07 t (7.5)	6.62 d (7.5)	2.94 m	2.76 m
99	MeOH- $d_4$	-	-	6.25 d (2.5)	-	6.22 d (2.5)	6.60 br s	-	6.61 m	7.07 t (7.5)	6.62 d (7.5)	2.94 m	2.76 m
100	MeOH- $d_4$	6.28 br s	-	-	-	6.27 br s	6.59 d (2.5)	-	6.57 m	7.07 t (7.5)	6.64 d (7.5)	2.76–2.81 m	2.76–2.81 m
101	MeOH- $d_4$	6.28 br s	-	-	-	6.27 br s	6.59 d (2.5)	-	6.57 m	7.07 t (7.5)	6.64 d (7.5)	2.76–2.81 m	2.76–2.81 m

### 2.3. Glucosyloxybenzyl Succinate Derivatives

The *Pleione* is also rich in glucosyloxybenzyl succinate derivatives [41]. The succinic acid is the basic structure and it often combines with saccharides to form glycosides (102–124) (Table 7 and Figure 3). The biological studies indicated that the glucosyloxybenzyl succinate derivatives compounds were documented to exert significant activities against delaying aging and improving learning and memory ability of aging mice [42]. Cui [43] used the succinic acid derivatives as an indicator compound for High Performance Liquid Chromatography (HPLC) content determination. The result indicated that the 117 and 118 can be used to distinguish three sources of TCM shan-ci-gu. Lv [44] established the HPLC fingerprint analysis of the *P. bulbocodioides* via measuring the content of the indicator compound 117. The similar values in the ten producing areas were all more than 0.980 of Chinese medicine. The relative retention time (in the fingerprints was similar, but the Relative Standard Deviation (RSD) values of the relative peak areas were quite different. This was assumed to be the effects of the wild environment and growth years. On account of the difficulty to obtain high-polarity compounds 117, 118, 123 and 145, Wang [45] developed a rapid and efficient method Elution-extrusion Counter-current Chromatography Separation (EECCC): the solvent system composed of *n*-butanol, ethanol and water with a volume ratio of 20:1:20. The upper phase was stationary phase, the lower phase was mobile phase at a flow rate of 1.5 mL·min<sup>-1</sup>, with a rotation speed of 850 rpm at temperature of 35 °C. Five high-polarity compounds were extracted in 371 min simultaneously by this method. The other four kinds of acids, the glucosyloxybenzyl succinate derivatives Pleionosides A–J (102–111) connected, are (2*R*)-2-*p*-hydroxybenzylmalic acid (102–105), (2*R*)-2-benzylmalic acid (106), (2*R*, 3*S*)-2-benzyl tartaric acid (107) and (2*R*)-2-isobutylmalic (108–110). Their properties confirmed that they could support further chemotaxonomic researches in Orchidaceae as the specialized metabolites [27].

**Table 7.** Glucosyloxybenzyl succinate derivatives from *Pleione* genus.

No.	Compound	Plant	Reference	No.	Compound	Plant	Reference
102–111	Pleionosides A–J	B	[27]	118	Dactylorhin A	B, Y	[22,27]
112	Vandateroside II	B	[27]	119	(-)-(2 <i>R</i> ,3 <i>R</i> )-1-(4- <i>O</i> -β- <i>D</i> -glucopyranosyloxybenzyl)-4-methyl-2-isobutyltartrate	B	[27]
113	Grammatophylloside B	B	[27]	120	Loroglossin	B	[27]
114	Grammatophylloside A	B	[27]	121	(-)-(2 <i>S</i> )-1-[(4- <i>O</i> -β- <i>D</i> -glucopyranosyloxy)benzyl]-2-isopropyl-4-[(4- <i>O</i> -β- <i>D</i> -glucopyranosyloxy)benzyl]malate	B	[27]
115	Cronupapine	B	[27]	122–123	Shancigusins H-I	Y	[22]
116	Gymnoside I	B, Y	[22,27]	124	Bletillin A	B	[28]
117	Militarine	B	[27,28]				



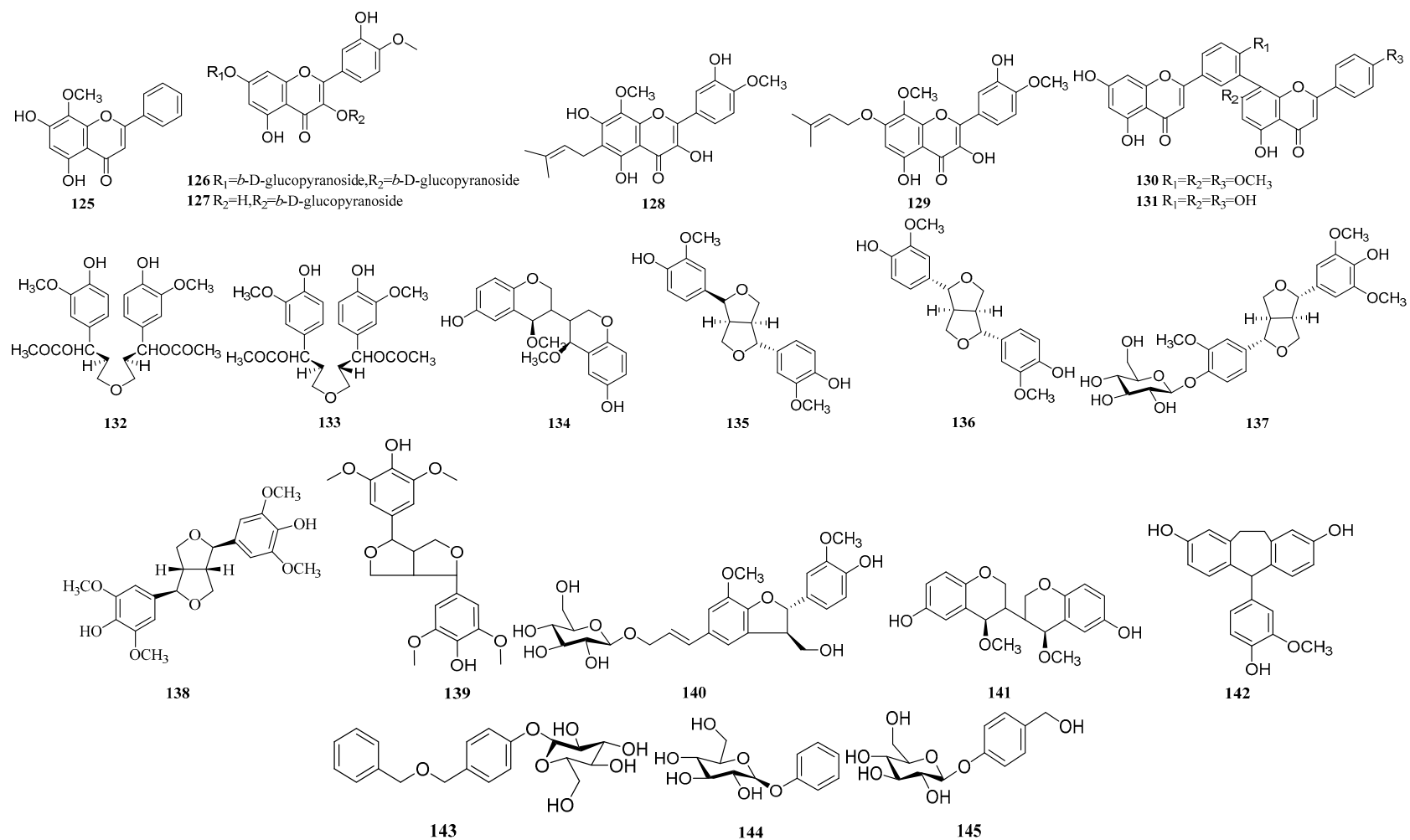
**Figure 3.** The structures of Glucosyloxybenzyl succinate derivatives.

#### 2.4. Other Compounds

Other compounds consist of seven flavones (**125–131**), eight lignans (**132–139**) and 44 others (**140–183**) (Table 8 & Figure 4). The flavones contained three simple flavones (**125–127**), two prenylated flavones (**128, 129**) and two biflavonoids (**130, 131**). The lignans consist of three simple lignans (**132–134**) and five tetrahydrofuran lignans (**135–139**). Yuan [40] isolated biflavonoids **131** from *Pleione* for the first time in 2012. Li [16] isolated two isomerized lignan compounds **132** and **133** from *P. bulbocodioides* in 1997. The pseudobulbs of *P. formosana* have been used as one of the substitute of *Shan-ci-gu* [46,47]. However no phytochemical investigation was performed on it. Thus, Shiao [24] began the chemical research in 2009 and it was the first time to isolate the cycloartane triterpenoid compound **167** from the natural product. Yang [48] analyzed the chemical compounds of the *P. bulbocodioides*, *P. yunnanensis* and *P. limprichtii* from fifteen producing areas by High Performance Liquid Chromatography Diode Array Detection (HPLC-DAD). The Cluster Analysis and Principal Component Analysis were used for quality evaluation, but the compounds corresponding to the chromatographic peak were not determined.

Table 8. Other compounds from *Pleione* genus.

No.	Compound	Plant	Reference	No.	Compound	Plant	Reference
125	5, 7-dihydroxy-8-methoxyflavone	B	[38]	155	3-hydroxybenzoic acid	B	[49]
126	Isorhamnetin-3, 7-di- <i>O</i> - $\beta$ - <i>D</i> -glucopyranoside	B	[29]	156	Methyl 3-(3-hydroxyphenyl)Propionate	B	[31]
127	3'- <i>O</i> -methylquercetin-3- <i>O</i> - $\beta$ - <i>D</i> -glucopyranoside	B	[29]	157	4-(4''-hydroxybenzyl)-3-(3'-hydroxy-phenethyl) furan	B, Y	[49]
128	3, 5, 7, 3'-tetrahydroxy-8, 4'-dimethoxy-6-(3-methylbut-2-enyl)flavone	B	[29]	158	Methyl 3-(4-hydroxyphenyl)propionate	B	[1]
129	3, 5, 3'-trihydroxy-8, 4'-dimethoxy-7-(3-methylbut-2-enyloxy) Flavone	B	[29]	159	3-(3'-hydroxyphenethyl)furan-2(5 <i>H</i> )-one	B	[49]
130	Kayaflavone	B	[40]	160	Ergosta-4, 6, 8(14), 22-tetraen-3-one	B	[33]
131	5, 5', 7, 4', 4''', 7''-hexadroxy-[3'-8'']Biflavone	B	[40]	161	Tetracosanol	Y	[26]
132–133	Sanjidin A-B	B	[16,40]	162	( <i>E</i> )-ferulic acid hexacosyl ester	Y	[34]
134	Phillygenin	B	[38]	163	( <i>Z</i> )-ferulic acid hexacosyl ester	Y	[34]
135	Epipinoresinol	B	[22]	164	Gallicacid	Y	[26]
136	Syringaresinol	B, Y	[22,33]	165	5-hydroxymethylfurfural	B	[31]
137	Syringaresinol Mono- <i>O</i> - $\beta$ - <i>D</i> -glucoside	B	[27]	166	Methyl 3-(3'-hydroxyphenethyl)furan-2(5 <i>H</i> )-one	B	[49]
138	Lirioresinol	B	[29]	167	(24 <i>R</i> )-cyclomargenyl <i>p</i> -coumarate	F	[24]
139	( <i>E</i> )- <i>p</i> -hydroxycinnamic acid	Y	[45]	168	(24 <i>R</i> )-cyclomargeno	F	[24]
140	(7 <i>S</i> , 8 <i>R</i> )-dehydrodiconiferyl alcohol-9'- <i>O</i> - $\beta$ - <i>D</i> -glucopyranoside	B	[27]	169	Tetacosanoic acid-2, 3-dihydroxypropyl ester	Y	[26]
141	Pleionin	B	[16]	170	Hydroquinone	B	[40]
142	Pleionol	B	[18]	171	$\beta$ -sitosterol	B, Y	[22,31]
143	Gastrodioside	B	[29]	172	$\beta$ -daucosterol	Y	[34]
144	Phenl- $\beta$ - <i>D</i> -glucopyranoside	B	[29]	173	Methyl 4-hydroxyphenylacetate	Y	[40]
145	Gastrodin	B	[27,45]	174	Daucostero	B, Y	[22]
146	( <i>E</i> )-ferulic acid	Y	[34]	175	Physcion	B	[40]
147	Cinnamic acid	B	[1]	176	Chrysophanol	B	[26]
148	<i>p</i> -hydroxybenzoic acid	B, Y	[39,40]	177	4, 4'-dihydroxydiphenylmethane	B	[38]
149	<i>p</i> -hydroxybenzaldehyde	B	[39,40]	178	4-oxopentanoic	B	[1]
150	Methy (4-OH) phenylacetate	B	[25]	179	Monopalmttin	Y	[26]
151	4-(ethoxymethyl)phenol	B	[1]	180	Amber Acid	Y	[22]
152	4-(methoxymethyl)phenol	B	[1]	181	Adenosine	Y	[22]
153	<i>p</i> -dihydroxy benzene	B	[35,37]	182	Pholidotin	Y	[34]
154	3-hydroxybenzenepropanoic acid	B	[45]	183	Triphyllol	Y	[34]



**Figure 4.** The structures of other compounds.

### 3. Biological Activities

Previous studies showed that the compounds extracted from *P. bulbocodiodes*, *P. yunnanensis* and *P. formosana* exerted anti-tumor, anti-neurodegenerative, anti-inflammatory anti-oxidation activities. That is why *Pleione* has been gaining increasing attention. The *Pleione*'s biological activities are tightly related to the traditional efficacy of "curing fever, detoxifying the body, mitigating the swelling and cleaning the blood stasis" in Chinese Pharmacopoeia [13]. Research on biological activities will establish a foundation for the further pharmacological researches and enlighten the drug discovery for anti-tumor usage.

#### 3.1. Anti-Tumor Activity

The biological activities of *Pleione* can be attributed primarily to the phenanthrenes and bibenzyls. Among those activities, that against tumors was the most significant. Liu [37] proved that the ethyl acetate extract of *P. bulbocodiodes* had a certain inhibitory effect on mice cancer cells LA795, while the petroleum ether extract only had an inhibition rate of 75.58% at 800  $\mu\text{g}\cdot\text{mL}^{-1}$ , but no remarkable inhibition at 400  $\mu\text{g}\cdot\text{mL}^{-1}$  and below. However, the *n*-butanol extract did not exert inhibitory at all. This result laid the foundation for the later chemical compounds study, and regarded the ethyl acetate as key fraction for research. The compounds such as **26**, **34**, **44**, **58**, **60** and **153** were demonstrated certain inhibitory effects against LA795 at 100  $\mu\text{g}\cdot\text{mL}^{-1}$ . Liu [37] confirmed that **34** and **153** showed the cytotoxic activity against LA795 cells with  $\text{IC}_{50}$  value of 66 and 12  $\mu\text{g}\cdot\text{mL}^{-1}$ . Compound **58** exhibited cytotoxic activity and anti-allergic activity. Wang [33] found that the bibenzyls **58** and **61** isolated from *P. bulbocodiodes* significantly inhibited the growth of leukemia cells K562, HL-60, liver cancer cells BEL-7402, gastric cancer cells SGC-7901, lung cancer cells A569 [50], H460 and melanoma cells M14. Wang's group [32,34] indicated that **58** isolated from *P. yunnanensis*, performed strong activity against the growth of LA795 cells with  $\text{IC}_{50}$  value of 76.21  $\mu\text{M}$ , but only moderate inhibition against A569 cells and BEL-7402 cells. Compound **40** was shown to exert moderate cytotoxic activity against A569 cells. Compound **48** was proved significant cytotoxic activity against cancer cells at  $10^{-6}$  M. Compound **49** exerted cytotoxic activities against colon cancer cells HepG2, liver cancer cells BGC-823 and breast cancer cells MCF-7 with  $\text{IC}_{50}$  values of 8.3, 2.3 and 2.5  $\mu\text{M}$ , respectively [32]. Compound **56** exerted moderate activities in colon cancer cells HCT-116, HepG2 cells and MCF-7 cells with  $\text{IC}_{50}$  values of 8.1, 8.4 and 3.9  $\mu\text{M}$ , respectively. It suggested that the stereochemistry of 9(10)*H*-phenanthren-10(9)-one is of great significance to the cytotoxic activity. Tumor cell invasion and metastasis determined the prognosis of cancer patients [51]. In a word, a number of studies confirmed that the compounds isolated from the *Pleione* have an optimistic effect on anti-tumor treatment.

#### 3.2. Anti-Neurodegenerative Activity

Glycosides were found to inhibit the proliferation of tumor cells, which is meaningful for anti-tumor therapy [52]. The glucosyloxybenzyls were subjected to evaluation for learning and memory deficits of mice caused via scopolamine and D-Gal +  $\text{NaNO}_2$  [53]. Zhang [54] discussed that the Dactylorhin B, **117**, **118** and **120** isolated from *Coeloglossum viride* var. *bractestum* were demonstrated to exert activities of anti-apoptosis, promoting intelligence and delaying aging. The *P. bulbocodiodes* consists of the three components mentioned above, except Dactylorhin B [27]. **145** was documented to exhibit activities of neuroprotective, neurasthenia and epilepsy [55]. **29** and **58** performed certain neurotoxic activities of mice hippocampal neurons (SY-SH-5Y) at  $10^{-5}$  M [25]. In addition, **2**, **32** and **39** indicated significant neurotoxic activity at  $10^{-5}$  M [45]. Han [27] reported the hepatoprotective activity of glucocopyloxybenzyl succinate derivatives for the first time in 2019. These neuroprotective effects may be related to the management of antioxidants, malondialdehyde (MDA), glutathione (GSH) levels as well as the improvement of adenosine triphosphatase (ATPase) [56]. The active metabolite of APAP was reported to deplete the glutathione and initiate mitochondrial oxidative stress. Moreover, the reactive oxygen species (ROS) produced during the latter process would destroy the normal function of the

mitochondria, ultimately leading to the death of necrotic cell [57–59]. These studies fully clarified the pharmacodynamic basis of the *Pleione* and laid a material foundation for anti-dementia activity.

### 3.3. Anti-Inflammatory and Anti-Oxidation Activity

Some compounds of *Pleione* exert activities of anti-bacterial and anti-inflammatory (Table 9). Wang [25,33] illustrated that **1** significantly inhibited NO production in mice peritoneal macrophages at  $10^{-5}$  M. Compounds **1** and **3** had strong inhibition activity on NO production. Compounds **3** and **61** showed good performance in calmodulin inhibition and antifungal action. Li [28,29] suggested that the compounds of **4**, **63** and **64** significantly inhibited NO production induced via LPS in BV-2 cells with IC<sub>50</sub> values of 5.44, 2.46 and 3.14  $\mu$ M, respectively. They may be the promising compounds for the development of anti-inflammatory drugs. However **9**, **25**, **26**, **58**, **62**, **73**, **74**, **75**, **81**, **82**, **86** and **117** only exhibited moderate inhibition on NO production. Liu [49] suggested that **170** was documented to have strong activities of anti-cytotoxicity and anti-bacterial.

**Table 9.** The LPS-stimulated NO production of BV-2 microglial cells.

No.	IC <sub>50</sub> ( $\mu$ M)	No.	IC <sub>50</sub> ( $\mu$ M)
<b>1</b>	2.35	<b>82</b>	21.0
<b>2</b>	1.74	<b>86</b>	21.8
<b>63</b>	2.46	<b>81</b>	26.1
<b>64</b>	3.14	<b>14</b>	14.4
<b>58</b>	50.2	<b>12</b>	24.5
<b>62</b>	38.0	<b>26</b>	13.1
<b>75</b>	23.2	<b>10</b>	17.7
<b>74</b>	17.5	<b>25</b>	23.4
<b>73</b>	56.7	<b>117</b>	59.2

### 3.4. Others

In addition to the anti-tumor, anti-neurodegenerative, anti-inflammatory and anti-oxidation activities, the *Pleione* also exhibited activities of inhibiting antigen-induced degranulation, free radical scavenging as well as anti-oxidant. Wang [26,34] proved that **58**, **69**, **70**, **76** and **81** were shown the activity of antigen-induced degranulation in RBL-2H3 cells [60]. The inhibition efficiency of **58**, **69** and **70** was between 65.5% and 99.4%.

## 4. Conclusions

The chemical investigation of the *Pleione* has attracted much attention around the world and some breakthrough progress has been made. Up to now, the family of the compounds had become more and more abundant, especially 9(10)*H*-phenanthren-10(9). This can not only provide significant evolutionary and chemotaxonomic knowledge of the genus *Pleione*, but also enlighten the further development and utilization of new drugs.

The future important focal points on the *Pleione* researches are summarized as follows. Firstly, the research range of species of the genus *Pleione* need to be widened except for the *P. bulbocodioides*, *P. yunnanensis* and *P. formosana* in order to seek for novel substitutes. The mechanism of the biological activity should be figured out to shine more clear therapy pattern. Secondly, water-soluble and fat-soluble extracts are necessary to be explored. Thirdly, research needs further progress for clinical application to serve for the patients. Lastly, there needs to be immediate scientific protection for *Pleione* plants because of their endangered status.

**Author Contributions:** X.-Q.W. conceptualized the review and drafted the initial version of the manuscript. J.-X.C., and W.L. undertook the database search for the literature. J.-W.Z., H.-Y.X., L.N., and S.-S.W. significantly contributed in gathering of information and discussions of the manuscript. All authors read and approved the final manuscript.

**Funding:** This work was financially supported by the Natural Science Foundation of Fujian (No. 2019J01410); 2018 Agricultural “Five New” Project of Fujian Development and Reform Commission (Min Financial (2018) No. 0438); CITES Orchids Product Trade Status Survey and Evaluation Project from National Forestry and Grassland Administration.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Liu, X.Q. Studies on the Chemical Constituents and their Anti-tumor Activity of *Pleione bulbocodioides*. Master’s Thesis, Tianjin University, Tianjin, China, May 2007.
2. Sympli, H.D.; Choudhury, M.G.; Borah, V.V. A review of the unexplored medicinal orchids of the genus *Pleione*. *MIOS J.* **2018**, *19*, 3–12.
3. IUCN. The IUCN Red List of Threatened Species. Version. 2018-2. 2018. Available online: [www.iucnredlist.org](http://www.iucnredlist.org) (accessed on 20 July 2019).
4. Cribb, P.; Butterfield, I. *The Genus Pleione*, 2nd ed.; Natural History Publications: Borneo, Malaysia, 1999; ISBN 983-812-040-5.
5. Chen, X.; Cribb, P.J.; Gale, S.W. “*Pleione*” in *Flora of China 25 (Orchidaceae)*; Wu, Z.Y., Raven, P.H., Hong, D.Y., Eds.; Science Press: Beijing, China; Missouri Botanical Garden Press: St. Louis, MO, USA, 2009.
6. Hareesh, V.S.; Kumar, P.; Sabu, M. *Pleione arunachalensis* (Orchidaceae: Epidendroideae: Arethuseae: Coelogyninae), a new species from North-East India. *Phytotaxa* **2017**, *291*, 294–298. [[CrossRef](#)]
7. Jiang, M.T.; Wu, S.S.; Liu, Z.J.; Lan, S.R. *Pleione jinhuaense*, a new species of *Pleione* (Epidendroideae: Orchidaceae) from China based on morphological and DNA evidence. *Phytotaxa* **2018**, *345*, 43–50. [[CrossRef](#)]
8. Zhang, W.; Qin, J.; Yang, R.; Yang, Y.; Zhang, S.B. Two new natural hybrids in the genus *Pleione* (Orchidaceae) from China. *Phytotaxa* **2018**, *350*, 247–258. [[CrossRef](#)]
9. Zhang, Y.; Li, S.F.; Li, B. The research status of *Pleione bulbocodioides*. *North. Hortic.* **2010**, *19*, 232–234. [[CrossRef](#)]
10. Wu, S.S.; Zhou, Y.Z.; Li, S.X.; Ma, X.Y.; Peng, D.H. Population dynamics and reproductive modes of *Pleione formosana* Hayata. *J. Fujian Coll. For.* **2014**, *34*, 297–303. [[CrossRef](#)]
11. Li, Y.X.; Zhang, Y.Y.; Guo, Y.S.; Peng, D.H.; Zhai, J.W.; Wu, S.S. Photosynthetic Characteristics of Four *Pleione* Species. *J. Yunnan Agric. Univ. (Nat. Sci.)* **2018**, *33*, 891–897. [[CrossRef](#)]
12. RHS. Orchid Hybrid Lists. 2018. Available online: <https://www.rhs.org.uk/about-the-rhs/publications> (accessed on 20 July 2019).
13. Chinese Pharmacopoeia Commission. *Chinese Pharmacopoeia, Part I*; People’s Medical Publishing House: Beijing, China, 2015; p. 32.
14. Li, B.; Masea, Y.; Shuzo, T. Stilbenoids from *Pleione bulbocodioides*. *Phytochemistry* **1996**, *42*, 853–856. [[CrossRef](#)]
15. Li, B.; Masea, Y.; Yuriko, Y.; Shuzo, T. Shanciol, a dihydrophenanthropyran from *Pleione bulbocodioides*. *Cheminform* **1996**, *27*, 625–628. [[CrossRef](#)]
16. Li, B.; Masea, Y.; Shuzo, T. Lignans and a bichroman from *Pleione bulbocodioides*. *Phytochemistry* **1997**, *44*, 341–343. [[CrossRef](#)]
17. Li, B.; Noriko, M.; Masea, Y.; Shuzo, T. Two bibenzyl glucosides from *Pleione bulbocodioides*. *Phytochemistry* **1997**, *44*, 1565–1567. [[CrossRef](#)]
18. Li, B.; Noriko, M.; Masea, Y.; Shuzo, T. A polyphenol and two bibenzyls from *Pleione bulbocodioides*. *Cheminform* **1998**, *47*, 1637–1640. [[CrossRef](#)]
19. Li, B.; Noriko, M.; Masea, Y.; Shuzo, T. Flavan-3-ols and dihydrophenanthropyran from *Pleione bulbocodioides*. *Phytochemistry* **1998**, *47*, 1125–1129. [[CrossRef](#)]
20. Li, B.; Noriko, M.; Masea, Y.; Shuzo, T. Four stilbenoids from *Pleione bulbocodioides*. *Phytochemistry* **1998**, *48*, 327–331. [[CrossRef](#)]
21. Dong, H.L.; Wang, C.L.; Li, Y.; Guo, S.X.; Yang, J.S. Complete assignments of  $^1\text{H}$  and  $^{13}\text{C}$  NMR data of three new dihydrophenanthrofurans from *Pleione yunnanensis*. *Magn. Reson. Chem.* **2010**, *48*, 256–260. [[CrossRef](#)] [[PubMed](#)]
22. Dong, H.L.; Liang, H.Q.; Wang, C.L.; Guo, S.X.; Yang, J.S. Shancigusins E-I, five new glucosides from the tubers of *Pleione yunnanensis*. *Magn. Reson. Chem.* **2013**, *51*, 371–377. [[CrossRef](#)]



23. Dong, H.L.; Wang, C.L.; Guo, S.X.; Yang, J.S. New bibenzyl derivatives from the tubers of *Pleione yunnanensis*. *Chem. Pharm. Bull. (Tokyo)* **2009**, *57*, 513–515. [[CrossRef](#)]
24. Shiao, Y.J.; Chen, W.P.; Lin, Y.L. New polyphenols and triterpene from the pseudobulbs of *Pleione formosana*. *J. Chin. Chem. Soc.* **2009**, *56*, 828–833. [[CrossRef](#)]
25. Wang, C. Study on the Chemical Constituents from the EtOAc Fraction of *Pleione bulbocodioides* (Franch.) Rolfe. Master's Thesis, Peking Union Medical College, Beijing, China, May 2014.
26. Wang, X.J. Study on the Chemical Constituents from the EtOAc Fraction of *Pleione yunnanensis* (Franch.) Rolfe. Master's Thesis, Peking Union Medical College, Beijing, China, May 2014.
27. Han, S.W.; Wang, C.; Cui, B.S.; Sun, H.; Zhang, J.J.; Li, S. Hepatoprotective activity of glucosyloxybenzyl succinate derivatives from the pseudobulbs of *Pleione bulbocodioides*. *Phytochemistry* **2019**, *157*, 71–81. [[CrossRef](#)]
28. Li, Y.; Zhang, F.; Wu, Z.H.; Zeng, K.W.; Zhang, C.; Jin, H.W.; Zhao, M.B.; Jiang, Y.; Li, J.; Tu, P.F. Nitrogen-containing bibenzyls from *Pleione bulbocodioides*: Absolute configurations and biological activities. *Fitoterapia* **2015**, *102*, 120–126. [[CrossRef](#)]
29. Li, Y.; Wu, Z.H.; Zeng, K.W.; Zhao, M.B.; Jiang, Y.; Li, J.; Tu, P.F. A new prenylated flavone from *Pleione bulbocodioides*. *J. Asian Nat. Prod. Res.* **2017**, *19*, 738–743. [[CrossRef](#)] [[PubMed](#)]
30. Dong, H.L.; Guo, S.X.; Wang, C.L.; Yang, J.S.; Xiao, P.G. Advances in studies on chemical constituents in plants of *Pseudobulbus Cremastrae* seu *Pleiones* and their pharmacological activities. *Chin. Tradit. Herb. Drugs* **2007**, *38*, 1734–1738. [[CrossRef](#)]
31. Liu, X.Q.; Yuan, Q.Y.; Shao, J.M. Chemical Constituents of *Pleione bulbocodioides*. *J. S.-Cent. Univ. Natl. (Nat. Sci. Ed.)* **2011**, *30*, 54–56. [[CrossRef](#)]
32. Shao, S.Y.; Wang, C.; Han, S.W.; Sun, M.H.; Li, S. Phenanthrenequinone enantiomers with cytotoxic activities from the tubers of *Pleione bulbocodioides*. *Org. Biomol. Chem.* **2019**, *17*, 567–572. [[CrossRef](#)] [[PubMed](#)]
33. Wang, C.; Han, S.W.; Cui, B.S.; Wang, X.J.; Li, S. Chemical constituents from *Pleione bulbocodioides*. *Chin. J. Chin. Mater. Med.* **2014**, *39*, 442–447.
34. Wang, X.J.; Cui, B.S.; Wang, C.; Li, S. Chemical constituents from *Pleione yunnanensis*. *Chin. J. Chin. Mater. Med.* **2014**, *39*, 851–856. [[CrossRef](#)]
35. Liu, X.Q.; Guo, Y.Q.; Gao, W.Y.; Zhang, T.J.; Yan, L.L. Two new phenanthrofurans from *Pleione bulbocodioides*. *J. Asian Nat. Prod. Res.* **2008**, *10*, 453–457. [[CrossRef](#)]
36. Liu, X.Q.; Yuan, Q.Y.; Guo, Y.Q. A new bibenzyl derivative from *Pleione bulbocodioides*. *Chin. Chem. Lett.* **2008**, *19*, 559–561. [[CrossRef](#)]
37. Liu, X.Q.; Gao, W.Y.; Guo, Y.Q.; Zhang, T.J.; Yan, L.L. A new phenanthro [2, 3-b] furan from *Pleione bulbocodioides*. *Chin. Chem. Lett.* **2007**, *18*, 1089–1091. [[CrossRef](#)]
38. Zhang, F.; Zhao, M.B.; Li, J.; Tu, P.F. Chemical constituents from *Pleione bulbocodioides*. *Chin. Tradit. Herb. Drugs* **2013**, *44*, 1529–1533. [[CrossRef](#)]
39. Liu, X.Q.; Yuan, Q.Y.; Guo, Y.Q. Two new stilbenoids from *Pleione bulbocodioides*. *J. Asian Nat. Prod. Res.* **2009**, *11*, 116–121. [[CrossRef](#)] [[PubMed](#)]
40. Yuan, Q.Y.; Liu, X.Q. Chemical constituents from *Pleione bulbocodioides*. *J. Chin. Med. Mater.* **2012**, *35*, 1602–1604.
41. Han, S.W.; Wang, C.; Cui, B.S.; Li, S. Studies on glucosyloxybenzyl 2-isobutylmalates of *Pleione bulbocodioides*. *Chin. J. Chin. Mater. Med.* **2015**, *40*, 908–914. [[CrossRef](#)]
42. Li, M.; Guo, S.X.; Wang, C.L.; Yang, J.S.; Xiao, P.G. Studies on chemical constituents of the tubers of *Gymnadenia conopsea*. *Chin. Pharm. J.* **2008**, *43*, 409–412. [[CrossRef](#)]
43. Cui, B.S.; Song, J.; Li, S.; Ma, L.; Shi, J.G. Determination of dactylorhin A and militarine in three varieties of *Cremastrae Pseudobulbus/Pleiones Pseudobulbus* by HPLC. *Chin. J. Chin. Mater. Med.* **2013**, *38*, 4347–4350. [[CrossRef](#)]
44. Lv, L.F.; Jiang, Y.H.; Zhu, X.; Zhong, N.Y. Study on HPLC fingerprints of *Cremastrae Pseudobulbus Pleiones pseudobulbus*. *Chin. J. Mod. Appl. Pharm.* **2016**, *33*, 1276–1280. [[CrossRef](#)]
45. Wang, Y.; Guan, S.H.; Feng, R.H.; Zhang, J.X.; Li, Q.; Chen, X.H.; Bi, K.S.; Guo, D.A. Elution-extrusion counter-current chromatography separation of two new benzyl ester glucosides and three other high-polarity compounds from the tubers of *Pleione bulbocodioides*. *Phytochem. Anal.* **2013**, *24*, 671–676. [[CrossRef](#)]
46. Chiu, N.Y.; Chang, K.H. *The Illustrated Medicinal Plants of Taiwan*; SMC Publishing Inc.: Taipei, Taiwan, 1992; Volume 3, p. 278.

47. Yang, Y.P.; Liu, H.Y.; Lin, T.P. *Manual of Taiwan Vascular Plant*; The Council of Agriculture, the Executive Yuan: Taipei, Taiwan, 2001; Volume 5, p. 281.
48. Yang, Z.N.; Gui, Y.; Yu, Z.W.; Liu, Z.Y.; Luo, S.Q.; Zhu, G.S. Quality evaluation of *Cremastra appendiculata* based on Hierarchical clustering analysis (HCA) and Principal components analysis (PCA). *Guangdong Agric. Sci.* **2012**, *39*, 90–92. [[CrossRef](#)]
49. Liu, X.Q.; Gao, W.Y.; Guo, Y.Q.; Zhang, T.J.; Yan, L.L. Two new  $\alpha$ ,  $\beta$ -unsaturated butyrolactone derivatives from *Pleione bulbocodioides*. *Chin. Chem. Lett.* **2007**, *18*, 1075–1077. [[CrossRef](#)]
50. Chen, Y.; Xu, J.; Yu, H.; Qing, C. Cytotoxic phenolics from *Bulbophyllum odoratissimum*. *Food Chem.* **2008**, *107*, 169–173. [[CrossRef](#)]
51. Yan, Y.L.; Wan, Q.; Zhou, J.S.; Zhou, Y.H.; Ye, H. Advances in research on anti-tumor mechanism of *Pseudobulbus Cremastrae* seu *Pleiones*. *Guangdong Med. J.* **2016**, *37*, 3468–3469. [[CrossRef](#)]
52. Hou, Y.L.; Ding, X.; Hou, W.R.; Song, B.; Yan, X.H. Structure elucidation and antitumor activity of a new polysaccharide from Maerkang *Tricholoma matsutake*. *Int. J. Biol. Sci.* **2017**, *13*, 935–948. [[CrossRef](#)] [[PubMed](#)]
53. Li, M.; Wang, Y.F.; Ma, B.; Liu, G.T.; Zhang, J.J. Effect and mechanism of *Coeloglossum viride* var. *bracteatum* extract onscopolamine-induced deficits of learning and memory behavior of rodents. *Acta Pharm. Sin.* **2009**, *40*, 468–472. [[CrossRef](#)]
54. Zhang, D.; Liu, G.T.; Shi, J.G.; Zhang, J.J. Effects of *Coeloglossum viride* var. *bracteatum* extract on memory deficits and pathological changes in senescent mice. *Basic. Clin. Pharmacol. Toxicol.* **2006**, *98*, 55–60. [[CrossRef](#)] [[PubMed](#)]
55. Zeng, X.H.; Zhang, S.M.; Zhang, L.; Zhang, K.P. A study of the neuroprotective effect of the phenolic glucoside gastrodin during cerebral ischemia in vivo and in vitro. *Planta Medica* **2006**, *72*, 1359–1365. [[CrossRef](#)] [[PubMed](#)]
56. Zhang, D.; Liu, G.T.; Shi, J.G.; Zhang, J.J. *Coeloglossum viride* var. *bracteatum* extract attenuates D-galactose and NaNO<sub>2</sub> induced memory impairment in mice. *J. Ethnopharmacol.* **2006**, *104*, 250–256. [[CrossRef](#)] [[PubMed](#)]
57. Cathlee, C.; Abdellah, M.; Tamara, R.K.; Mary, L.B.; John, J.L.; Dominique, P.; Hartmut, J. Peroxynitrite-induced mitochondrial and endonuclease-mediated nuclear DNA damage in acetaminophen hepatotoxicity. *J. Pharmacol. Exp. Ther.* **2005**, *315*, 879–887. [[CrossRef](#)]
58. Jaeschke, H.; McGill, M.R.; Williams, C.D.; Ramachandran, A. Current issues with acetaminophen hepatotoxicity-A clinically relevant model to test the efficacy of natural products. *Life Sci.* **2011**, *88*, 737–745. [[CrossRef](#)]
59. Michael, P.M. How mitochondria produce reactive oxygen species. *Biochem. J.* **2009**, *417*, 1–13. [[CrossRef](#)]
60. Majumder, P.L.; Pal, A.; Lahiri, S. Structure of Polidotin, a new triterpene from orchids *Pholidota rubra* and *Cirrhopetalum elatum*. *Indian J. Chem. B* **1987**, *26*, 297–300.



© 2019 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).