

Review

Natural phenanthrenes and their biological activity

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Abstract

The aim of this review is to survey the various naturally occurring phenanthrene compounds that have been isolated from different plants. Only one review has previously been published on this topic. Gorham [Gorham, J., 1989. Stilbenes and phenanthrenes. *Meth. Plant Biochem.* 1, 159–196] reviewed the structures, biosynthesis, separations and spectroscopy of stilbenes and phenanthrenes.

The present study furnishes an overview of the hydroxy or/and methoxy-substituted 9,10-dihydro/phenanthrenes, methylated, prenylated and other monomeric derivatives, dimeric and trimeric phenanthrenes and their biological activities.

A fairly large number of phenanthrenes have been reported from higher plants, mainly in the Orchidaceae family, in the species *Dendrobium*, *Bulbophyllum*, *Eria*, *Maxillaria*, *Bletilla*, *Coelogyna*, *Cymbidium*, *Ephemerantha* and *Epidendrum*. A few phenanthrenes have been found in the Hepaticae class and Dioscoreaceae, Combretaceae and Betulaceae families. Their distribution correlates strongly with the taxonomic divisions.

These plants have often been used in traditional medicine, and phenanthrenes have therefore been studied for their cytotoxicity, antimicrobial, spasmolytic, anti-inflammatory, antiplatelet aggregation, antiallergic activities and phytotoxicity.

On the basis of 120 references, this review covers the phytochemistry and pharmacology of phenanthrenes, describing 252 compounds. This contribution stems from our work on the medicinal plant *Tamus communis*.

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Keywords: Phenanthrenes; Dihydrophenanthrenes; Biological activity; Dimeric phenanthrenes; Phenanthraquinones

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1. Introduction

The phenanthrenes are a rather uncommon class of aromatic metabolites which are presumably formed by oxidative coupling of the aromatic rings of stilbene precursors. Besides these stilbene derived compounds, phenanthrenes most likely originated from diterpenoid precursors are also included in the present review. A large number of differently substituted phenanthrenes have been reported to occur in plants and have been demonstrated to possess various biological activities.

The phenanthrenes isolated so far may be classified into three major groups: monophenanthrenes, diphenanthrenes and triphenanthrenes. Monophenanthrenes are subdivided according to the number and type of the structural moieties, while diphenanthrenes can be classified by the type of connection of the phenanthrene units. Up to present only one compound of the triphenanthrene group was described.

2. Occurrence of phenanthrenes

A fairly large number of phenanthrenes have been reported from higher plants, mainly in the Orchidaceae family, in 49 species: in particular *Dendrobium*, *Bulbophyllum*, *Eria*, *Maxillaria*, *Bletilla*, *Coelogyne*, *Cymbidium*, *Ephemerantha* and *Epidendrum*. A few phenanthrenes have been found in the Hepaticae class and Dioscoreaceae, Combretaceae and Betulaceae families (Table 1). The phenanthrenes were mainly isolated from the whole plants, but in some cases the cortex, tubers or stems were studied and found to contain such compounds. The greatest number of phenanthrenes has been described from the *Juncus* species, but notable numbers have been isolated from *Bletilla striata* and *Bulbophyllum vaginatum*.

3. Structural characteristics of phenanthrenes

3.1. Monomeric phenanthrenes

Most natural phenanthrenes occur in monomeric form; this group consists of about 210 compounds (Tables 2–9). Of these, almost 100 are only hydroxy- and/or methoxy-substituted, and equally 9,10-dihydro- or dehydro derivatives (Tables 2–5). Their great structural diversity stems from the number and position of their oxygen functions. The hydroxy and methoxy moieties number are between 3 and 6, and can usually be found on C-2, C-3, C-5, C-6 or C-7. Homogeneously substituted phenanthrenes are rare; there are only four such compounds among the tri-substituted phenanthrenes bearing only methoxy functionalities (2, 10, 12 and 20). Only two of the tetrasubstituted compounds are all-hydroxy-substituted (29, 58) and three are substituted only with methoxy groups [callosumin (26), 46, callosuminin (57)]. The structures of two com-

pounds [rotundatin (40) and 61] are unusual as they contain a hydroxy or methoxy group on C-9 or C-10. None of the pentasubstituted compounds bears only hydroxy or only methoxy groups. Interestingly, one compound [plicatol-A (97)] contains methoxy functions on both C-9 and C-10. There are only two hexasubstituted monophenanthrenes (98, 99) (Table 5).

Besides hydroxy and methoxy groups, further substituents can be found in monomeric phenanthrenes, such as methyl [stemanthrene A (104)], hydroxymethyl (120), carboxy (123), formyl [dehydroeffusal (153)], prenyl [gancanin U (154), sinensol G (156)] and vinyl (123–128) (Table 6). Compounds, substituted with methyl and vinyl groups can be found in *Micrandropsis*, *Sagotia*, *Stemona*, *Juncus* and *Domohinea* species. Euphorbiaceae family can be characterized by the occurrence of a wide range of diterpenes, thus it can be assumed that methyl and oxymethyl-substituted phenanthrenes in *Micrandropsis*, *Sagotia* and *Domohinea* have diterpenoid origin (de Alvarenga et al., 1976). *Juncus* phenanthrenes obviously also derived from a specific biosynthetic pathway. Glycosides are relatively rare: they have been reported only in *Juncus effusus* [effusides I–V. (157–161)], *Epimedium koreanum* [epimedoicariside A (162)], *Dendrobium chrysanthum* [denchryside A (163)] and *B. striata* (164–167). In *Coelogyne ochracea* a carboxy group [ochrolic acid (168)], in *Micrandropsis scleroxylon* the uncommon *S*-methyl group [micrandrol C (169)], and in *Polysiphonia ferulacea* two bromide groups [polysiphenol (170)] are attached to the phenanthrene skeleton. Yamaki et al. (1993a) isolated a novel type of phenanthrene with a spirolactone ring, blespirol (171), from *B. striata* (Table 7). The structure was proved by X-ray analysis. In general, unusual substitution is somewhat more likely in 9,10-dihydrophenanthrenes.

Another type of monomeric phenanthrenes is the group of phenanthraquinones; altogether 19 compounds belong in this group (Table 8). They are usually hydroxy, methoxy or methyl-substituted, but in *Cremastra appendiculata* a 2-oxopropyl group (184, 185), in *Spiranthes sinensis* a prenyl group [spiranthoquinone (186)], and in *Plectranthus* species a 2-propenyl [plectranthon A, C, D (187, 188, 190)] or 2-acetoxypropyl group (189) can be found in the molecule. Plectantrones A–D (187–190) are 1,4-phenanthraquinones, which biogenetically are derived from the diterpenoid type abietanoic precursors. (Alder et al., 1984). In the 1990s, a new bisbibenzyl derivative, shancilin (246) was isolated from the tubers of the orchid *Pleione bulbocodioides*, and were two 244 and 245 from *Frullania convoluta*. Guo et al. (2006) isolated an unusual molecule, a bibenzyl-dihydrophenanthrene ether, phoyunnanin D (247), from the whole plant of *Pholidota yunnanensis*.

Isolation of monomeric phenanthrenes was carried out in general similarly. Usually, the plant materials are extracted with MeOH, EtOH, CHCl₃, Me₂CO or MeOH–CHCl₃ (1:1). After concentration *in vacuo*, the residue is extracted successively with Et₂O, EtOAc, CHCl₃ or *n*-hexane. Extracts are chromatographed on a silica gel

Table 1
Occurrence of phenanthrenes in plant families

	Latin name	Drug	Compounds	Activity
Berberidaceae	<i>Epimedium koreanum</i>		162	
Betulaceae	<i>Alnus maximowiczii</i>	Herba	20	
Combretaceae	<i>Combretum apiculatum</i>	Cortex	27, 31, 62, 65–70, 76, 78–80, 83, 84	Antitumour
	<i>Combretum caffrum</i>	Cortex	62, 66, 67, 69, 82	
	<i>Combretum molle</i>	Cortex	65, 68–70, 80, 84	
	<i>Combretum psidioides</i>	Cortex	25, 56, 62, 66, 71, 75, 81, 82	
Dioscoreaceae	<i>Dioscorea batatas</i>		53–55	Antifungal
	<i>Dioscorea bulbifera</i>		29, 58	
	<i>Dioscorea decipiens</i>	Radix	74	Antifungal Antitumour, antiviral
	<i>Dioscorea prazeri</i>	Tuber, yam	69	
	<i>Dioscorea rotundata</i>	Tuber, yam	6, 53, 56	
	<i>Tamus communis</i>	Radix	25, 27, 28, 42, 43, 47, 48, 56, 85–93, 182	
Euphorbiaceae	<i>Domohinea perrieri</i>	Stem	108–111, 179	Cytotoxic
	<i>Micrandropsis scleroxylon</i>	Trunk wood	100, 102, 169	
	<i>Sagotia racemosa</i>	Trunk wood	100–103	
Fabaceae	<i>Glycyrrhiza uralensis</i>	Aerial part	154, 155	
Hepaticae	<i>Frullania convoluta</i>		244, 245	
	<i>Marchantia polymorpha</i>	Herba	21, 22, 226–228	
	<i>Plagiochila killarniensis</i>	Aerial part	8–14, 23, 26	
	<i>Plagiochila oresitropa</i>			
Juncaceae	<i>Juncus acutus</i>	Aerial part	112–128, 131, 133–138, 142, 146–148, 152, 236–241	Antialgal
	<i>Juncus effusus</i>	Aerial part	112, 115–118, 121–124, 126–128, 130, 132–135, 139–141, 143–146, 149–151, 153, 157–161	
	<i>Juncus roemerianus</i>	Root	115, 116, 129, 146	Antimicrobial
Lamiaceae	<i>Plectranthus species</i>		187–190	
Orchidaceae	<i>Agrostophyllum callosum</i>	Whole plant	3, 24, 26, 31, 57, 221, 222	Antitumour/antimicrobial
	<i>Agrostophyllum khasiyanum</i>	Whole plant	221, 222	
	<i>Arundina graminifolia</i>	Rhizoma	202	
	<i>Bletilla formosana</i>	Whole plant	41, 192–201, 218	
	<i>Bletilla striata</i>	Tuber	1, 2, 4, 17, 46, 164–167, 171, 191–195, 197, 207, 214–216, 218, 219, 229, 249–252	
	<i>Bulbophyllum gymnopus</i>	Whole plant	62, 75, 85, 96	
	<i>Bulbophyllum leopardium</i>	Whole plant	51	
	<i>Bulbophyllum reptans</i>	Whole plant	1, 19, 62, 75, 85, 96, 214, 223–225	
	<i>Bulbophyllum vaginatum</i>	Whole plant	1, 19, 24, 30, 36, 42–44, 50, 52, 61–64, 75–77, 233	
	<i>Cirrhopetalum andersonii</i>	Whole plant	34, 45	
	<i>Cirrhopetalum maculosum</i>		223	
	<i>Coelogyne cristata</i>	Whole plant	73, 95	
	<i>Coelogyne elata</i>	Whole plant	1	
	<i>Coelogyne flaccida</i>	Whole plant	31	
	<i>Coelogyne ochracea</i>	Whole plant	1, 168, 176, 177	
	<i>Cremastra appendiculata</i>	Tuber	18, 19, 184, 185, 223, 230, 231, 243	Cytotoxic
	<i>Cymbidium aloifolium</i>	Root	1, 24, 180, 181	
	<i>Cymbidium pendulum</i>	Whole plant	86, 99	
	<i>Cypripedium tibeticum</i>		173, 178	
	<i>Dendrobium chrysanthum</i>	Herba	163	
	<i>Dendrobium densiflorum</i>	Stems	4, 15, 86, 173, 175	
	<i>Dendrobium loddigesii</i>	Stems	15	
	<i>Dendrobium moniliforme</i>	Stem	172, 183	
	<i>Dendrobium moscatum</i>		15	
	<i>Dendrobium nobile</i>	Aerial part	4, 172	
	<i>Dendrobium plicatile</i>	Stems	4, 15, 36, 40, 43, 97, 174, 213	Antitumour
	<i>Dendrobium rotundatum</i>	Whole plant	40, 42, 62, 75	Cytotoxic
	<i>Dendrobium thyrsiflorum</i>	Stems	86, 220, 242	
	<i>Ephemerantha fimbriata</i>		38, 50, 94	
	<i>Ephemerantha lonchophylla</i>	Stems	35–37, 43, 48, 172, 174	

Table 1 (continued)

	Latin name	Drug	Compounds	Activity
	<i>Epidendrum rigidum</i>	Whole plant	35, 94	Phytotoxic
	<i>Eria carinata</i>	Whole plant	42	
	<i>Eria confusa</i>	Whole plant	85, 98	
	<i>Eria flava</i>	Whole plant	1, 19, 37, 43, 214	
	<i>Eria stricta</i>	Whole plant	42	
	<i>Eulophia nuda</i>	Tuber	1, 32, 33, 42, 43, 59, 60, 86, 232	
	<i>Eulophia petersii</i>	Root	1, 4, 16, 32, 59	
	<i>Gymnadenia conopsea</i>	Tuber	1, 7, 194, 195, 210, 211, 214, 217	Antiallergic
	<i>Loroglossum hircinum</i>		5, 6	Antifungal
	<i>Lusia indivisa</i>	Whole plant	4, 16	
	<i>Lusia volucris</i>		234	
	<i>Maxillaria densa</i>	Whole plant	36, 39, 42, 49, 94, 96	Phytotoxic, spasmolytic
	<i>Nidema boothii</i>	Whole plant	4, 37, 43, 72, 86, 174	Spasmolytic
	<i>Orchis militaris</i>		3	Antifungal
	<i>Pholidota yunnanensis</i>	Whole plant	247, 248	NO production inhibitory
	<i>Pleione bulbocodioides</i>		1, 4, 195, 207, 246	
	<i>Scaphyglottis livida</i>	Whole plant	1, 43, 86	Spasmolytic/aorta dilatatory
	<i>Spiranthes sinensis</i>	Aerial part	156, 186, 202–206, 208, 209, 235	Cytotoxic
	<i>Thunia alba</i>	Whole plant	4, 43, 86, 214, 223	
Rhodomelaceae	<i>Polysiphonia ferulacea</i>		170	
Stemonaceae	<i>Stemona collinsae</i>		104–107	
	<i>Stemona pierrei</i>		104–107	
	<i>Stemona tuberosa</i>		104–107	

column or on Sephadex LH-20 or subjected to preparative TLC and HPLC. Majumder et al. (1982) developed a special method for the isolation of phenanthrenes. The plant materials were soaked in MeOH for three weeks. The MeOH extract was then drained off, concentrated under reduced pressure, and diluted with H₂O, and the liberated solids were exhaustively extracted with Et₂O. The Et₂O extract was fractionated into acidic and non-acidic fractions with 2 M aqueous NaOH. The aqueous alkaline solution was acidified in the cold with conc. HCl, and the liberated solids were extracted with Et₂O, the extract was washed with H₂O and dried, and the solvent was removed.

3.2. Dimeric phenanthrenes and a triphenanthrene

The nearly 40 dimeric phenanthrenes include 9,10-dihydro- and dehydro derivatives (Tables 10 and 11). The monomers are mostly 1-1'-linked, but 1-3', 1-8' and 3-3' linkages also occur in the natural compounds. The compounds are usually hydroxy and methoxy-substituted. In 2003, DellaGreca et al. isolated five dimeric 9,10-dihydrophenanthrenoids with interesting hepta- or octacyclic structures (237–241) from the rhizome of *Juncus acutus*. From the stems of *Dendrobium thyrsiflorum*, a derivative of phenanthrene–phenanthraquinone, denthyrsinone (242), was obtained (Zhang et al., 2005). Investigation of the tubers of *B. striata* led to the isolation of four unusual bis(dihydrophenanthrene)ethers (249–252), in which phenanthrene monomers are coupled through ether bridge. The structures of blestrin C (251) and D (252) were confirmed by X-ray analysis (Yamaki et al., 1992) (see Table 11).

The only triphenanthrene (243) described so far was isolated from the tubers of an orchidaceous plant, *C. appendiculata* (Xue et al., 2006).

4. Biological activities

4.1. Anticancer effects of phenanthrenes

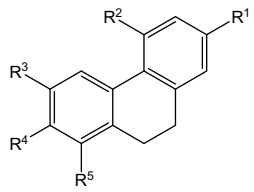
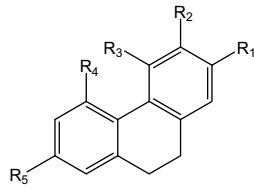
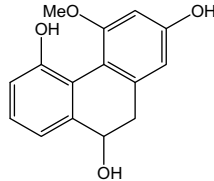
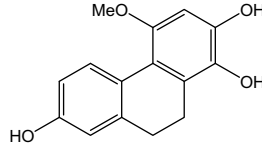
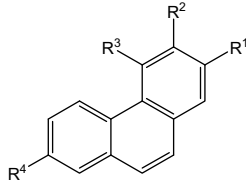
In 1979, Pettit et al. began a study of cancer cell growth inhibitors present in the African willow tree *Combretum caffrum* which resulted in the isolation and structural determination of a series of active phenanthrenes, dihydrophenanthrenes and stilbenes. The cell growth inhibitory activities of phenanthrenes from *C. caffrum* (62, 66, 69, 82) were tested on murine P388 lymphocytic leukaemia cell lines; the IC₅₀ values were 2.2, 2.8, 2.6 and 2.0 µg/ml, respectively. A series of publications by other researchers reported similar effects of phenanthrenes (Pettit et al., 1988, and references cited therein).

Lusianthridin (4) and denbinobin (172) isolated from *Dendrobium nobile* were found to exert cytotoxic effects both *in vitro* and *in vivo*. The significant activities of these compounds on A549 human lung carcinoma [ED₅₀: 7.7 µg/ml (4); 1.3 µg/ml (172)]; SK-OV-3 human ovary adenocarcinoma [ED₅₀: 9.4 µg/ml (4); 3.5 µg/ml (172)] and HL-60 human promyelocytic leukaemia [ED₅₀: 9.8 µg/ml (4); 0.11 µg/ml (172)] cell lines were also demonstrated. Lusianthridin (4) appears to be less effective than denbinobin (172). Their methylated derivatives did not exhibit activities, suggesting that a free phenolic hydroxy group

Table 2
Trisubstituted dihydro/phenanthrenes with hydroxy- or/and methoxy-substitution

	1 R¹ = OH, R² = OMe, R³ = OH; coelonin	<i>B. reptans</i> (Majumder et al., 1999) <i>B. striata</i> (Yamaki et al., 1991) <i>B. vaginatum</i> (Leong et al., 1997) <i>C. aloifolium</i> (Juneja et al., 1987) <i>C. elata</i> (Majumder et al., 1982) <i>C. ochracea</i> (Majumder et al., 1982) <i>E. flava</i> (Majumder and Banerjee, 1990a) <i>E. nuda</i> (Tuchinda et al., 1988) <i>E. petersii</i> (Blitzke et al., 2000) <i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006) <i>P. bulbocodioides</i> (Bai et al., 1996) <i>S. livida</i> (Estrada et al., 1999a) <i>B. striata</i> (Yamaki et al., 1991) <i>A. callosum</i> (Majumder et al., 1995, 1996) <i>O. militaris</i> (Baller et al., 1957; Fisch et al., 1973) <i>B. striata</i> (Takagi et al., 1983) <i>D. densiflorum</i> (Fan et al., 2001) <i>D. nobile</i> (Lee et al., 1995) <i>D. plicatile</i> (Yamaki and Honda, 1996) <i>E. petersii</i> (Blitzke et al., 2000) <i>L. indivisa</i> (Majumder and Lahiri, 1990d) <i>N. boothii</i> (Hernandez-Romero et al., 2004) <i>P. bulbocodioides</i> (Bai et al., 1996) <i>T. alba</i> (Majumder et al., 1998b)
	2 R¹ = OMe, R² = OMe, R³ = OMe 3 R¹ = OMe, R² = OMe, R³ = OH; orchinol 4 R¹ = OMe, R² = OH, R³ = OH; lusianthrudin	<i>L. hircinum</i> (Fisch et al., 1973) <i>L. hircinum</i> (Fisch et al., 1973) <i>D. rotundata</i> (Coxon et al., 1982)
	5 R¹ = OMe, R² = OMe, R³ = OH, R⁴ = H, R⁵ = H; loroglossol 6 R¹ = OH, R² = OMe, R³ = OH, R⁴ = H, R⁵ = H; hircinol 7 R¹ = OMe, R² = H, R³ = OH, R⁴ = OH, R⁵ = H 8 R¹ = OH, R² = OMe, R³ = H, R⁴ = OMe, R⁵ = H 9 R¹ = OMe, R² = OMe, R³ = H, R⁴ = OH, R⁵ = H 10 R¹ = OMe, R² = OMe, R³ = H, R⁴ = OMe, R⁵ = H 11 R¹ = OH, R² = OMe, R³ = H, R⁴ = H, R⁵ = OMe 12 R¹ = OMe, R² = OMe, R³ = H, R⁴ = H, R⁵ = OMe	<i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006) <i>Plagiochila</i> sp. (Anton et al., 1997) <i>P. killarniensis</i> (Rycroft et al., 1999) <i>Plagiochila</i> sp. (Anton et al., 1997) <i>Plagiochila</i> sp. (Anton et al., 1997) <i>Plagiochila</i> sp. (Anton et al., 1997) <i>Plagiochila</i> sp. (Anton et al., 1997)
	13 R¹ = OH, R² = H 14 R¹ = H, R² = OMe	<i>Plagiochila</i> sp. (Anton et al., 1997) <i>P. killarniensis</i> (Rycroft et al., 1999) <i>Plagiochila</i> sp. (Anton et al., 1997)
	15 R¹ = OH, R² = OMe, R³ = OH, R⁴ = H; plicatol-B, moscatin	<i>D. plicatile</i> (Honda and Yamaki, 2000) <i>D. rotundatum</i> (Majumder and Sen, 1987b; Majumder and Pal, 1992) <i>D. densiflorum</i> (Fan et al., 2001) <i>D. moscatum</i> (Majumder and Sen, 1987b) <i>D. loddigesii</i> (Chen et al., 1994)
	16 R¹ = OMe, R² = OH, R³ = H, R⁴ = OH; lusianthrin 17 R¹ = OMe, R² = OMe, R³ = H, R⁴ = OMe 18 R¹ = OH, R² = OMe, R³ = H, R⁴ = OMe 19 R¹ = OH, R² = OMe, R³ = H, R⁴ = OH; flavanthrinin	<i>E. petersii</i> (Blitzke et al., 2000) <i>L. indivisa</i> (Majumder and Lahiri, 1990d) <i>B. striata</i> (Yamaki et al., 1991) <i>C. appendiculata</i> (Xue et al., 2006) <i>B. reptans</i> (Majumder et al., 1999) <i>B. vaginatum</i> (Leong et al., 1997) <i>E. flava</i> (Majumder and Banerjee, 1990a) <i>C. appendiculata</i> (Xue et al., 2006)
	20 R¹ = OMe, R² = OMe, R³ = OMe, R⁴ = H, R⁵ = H 21 R¹ = OMe, R² = OMe, R³ = H, R⁴ = H, R⁵ = OH 22 R¹ = OH, R² = OMe, R³ = H, R⁴ = H, R⁵ = OH 23 R¹ = OH, R² = OMe, R³ = H, R⁴ = OMe, R⁵ = H	<i>A. maximowiczii</i> (Tori et al., 1995) <i>M. polymorpha</i> (Adam and Becker, 1994) <i>M. polymorpha</i> (Adam and Becker, 1994) <i>Plagiochila</i> sp. (Anton et al., 1997)

Table 3
Tetrasubstituted dihydro/phenanthrenes with hydroxy- or/and methoxy-substitution

	24 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$, $R^5 = \text{H}$; 6-methoxy-coelonin	<i>A. callosum</i> (Majumder et al., 1995, 1996) <i>B. vaginatum</i> (Leong et al., 1997) <i>C. aloifolium</i> (Juneja et al., 1987) <i>C. psidioides</i> (Letcher and Nhamo, 1972b) <i>T. communis</i> (Kovács et al., 2007) <i>A. callosum</i> (Majumder et al., 1996) <i>Plagiochila</i> sp. (Anton et al., 1997) <i>T. communis</i> (Aquino et al., 1985a, 1991; Letcher and Nhamo, 1972a) <i>C. apiculatum</i> (Letcher and Nhamo, 1971) <i>T. communis</i> (Aquino et al., 1985a, 1991) <i>D. bulbifera</i> (Wij and Rangaswami, 1978) <i>B. vaginatum</i> (Leong et al., 1999) <i>A. callosum</i> (Majumder et al., 1995, 1996) <i>C. flaccida</i> (Majumder et al., 1995) <i>C. apiculatum</i> (Letcher and Nhamo, 1971) <i>E. nuda</i> (Tuchinda et al., 1988) <i>E. petersii</i> (Blitzke et al., 2000) <i>E. nuda</i> (Tuchinda et al., 1988)
	25 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$, $R^5 = \text{H}$;	
	26 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OMe}$, $R^5 = \text{H}$; callosumin	
	27 $R^1 = \text{OMe}$, $R^2 = \text{OH}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$, $R^5 = \text{H}$	
	28 $R^1 = \text{OMe}$, $R^2 = \text{OH}$, $R^3 = \text{OMe}$, $R^4 = \text{OMe}$, $R^5 = \text{H}$	
	29 $R^1 = \text{OH}$, $R^2 = \text{OH}$, $R^3 = \text{OH}$, $R^4 = \text{OH}$, $R^5 = \text{H}$	
	30 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{OH}$, $R^4 = \text{OH}$, $R^5 = \text{H}$	
	31 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{OH}$, $R^4 = \text{OMe}$, $R^5 = \text{H}$; callosin	
	32 $R^1 = \text{OMe}$, $R^2 = \text{OH}$, $R^3 = \text{H}$, $R^4 = \text{OMe}$, $R^5 = \text{OH}$; eulophiol	
	33 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{H}$, $R^4 = \text{OMe}$, $R^5 = \text{OH}$	
	34 $R^1 = R^2 = -\text{O}-\text{CH}_2-\text{O}-$, $R^3 = \text{OH}$, $R^4 = \text{H}$, $R^5 = \text{OH}$; cirrhopenanthridin	<i>C. andersonii</i> (Majumder and Basak, 1991a)
	35 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OH}$, $R^4 = \text{H}$, $R^5 = \text{OH}$; ephemeranthal-A	<i>E. lonchophylla</i> (Tezuka et al., 1991) <i>E. rigidum</i> (Hernandez-Romero et al., 2005) <i>B. vaginatum</i> (Leong et al., 1997) <i>D. plicatile</i> (Yamaki and Honda, 1996) <i>E. lonchophylla</i> (Chen et al., 2000; Tezuka et al., 1991) <i>M. densa</i> (Estrada et al., 1999b, 2004; Valencia-Islas et al., 2002) <i>E. lonchophylla</i> (Tezuka et al., 1991) <i>E. flava</i> (Majumder and Banerjee, 1990a) <i>N. boothii</i> (Hernandez-Romero et al., 2004) <i>E. fimbriata</i> (Tezuka et al., 1993)
	36 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{H}$, $R^5 = \text{OH}$; erianthridin	
	37 $R^1 = \text{OMe}$, $R^2 = \text{OH}$, $R^3 = \text{OMe}$, $R^4 = \text{H}$, $R^5 = \text{OH}$; ephemeranthal-B, flavanthridin	<i>M. densa</i> (Estrada et al., 1999b)
	38 $R^1 = \text{OH}$, $R^2 = \text{OH}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$, $R^5 = \text{H}$; ephemeranthal-C	<i>D. plicatile</i> (Honda and Yamaki, 2000) <i>D. rotundatum</i> (Majumder and Pal, 1992)
	40 plicatol-C, rotundatin	
	41	<i>B. formosana</i> (Lin et al., 2005)
	42 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$; nudol	<i>B. vaginatum</i> (Leong et al., 1997) <i>D. rotundatum</i> (Majumder and Pal, 1992) <i>E. carinata</i> (Bhandari et al., 1985) <i>E. stricta</i> (Bhandari et al., 1985) <i>E. nuda</i> (Bhandari et al., 1985; Tuchinda et al., 1988) <i>M. densa</i> (Estrada et al., 1999b, 2004) <i>T. communis</i> (Réthy et al., 2006)

(continued on next page)

Table 3 (continued)

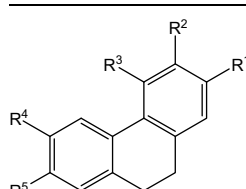
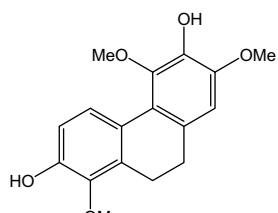
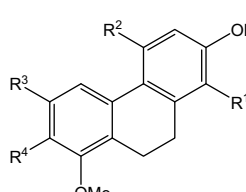
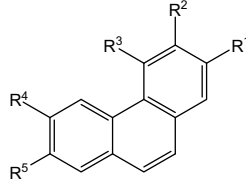
	43 $R^1 = \text{OMe}$, $R^2 = \text{OH}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$;	<i>B. vaginatum</i> (Leong et al., 1997) <i>D. plicatile</i> (Yamaki and Honda, 1996) <i>E. flava</i> (Majumder and Banerjee, 1990a) <i>E. lonchophylla</i> (Chen et al., 2000) <i>E. nuda</i> (Tuchinda et al., 1988) <i>N. boothii</i> (Hernandez-Romero et al., 2004) <i>S. livida</i> (Estrada et al., 1999a; Estrada-Soto et al., 2006) <i>T. alba</i> (Majumder et al., 1998b) <i>T. communis</i> (Réthy et al., 2006) <i>B. vaginatum</i> (Leong et al., 1997, 1999) <i>C. andersonii</i> (Majumder and Basak, 1990b, 1991a)
	44 $R^1 = \text{OH}$, $R^2 = \text{OH}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$	
	45 $R^1 = R^2 = -\text{O}-\text{CH}_2-\text{O}-$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$, cirrhopetalin	
	46 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OMe}$	
	47 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$;	
	48 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OH}$, $R^4 = \text{OH}$; TaVIII.	
	49 $R^1 = \text{OH}$, $R^2 = \text{OMe}$	
	50 $R^1 = \text{OH}$, $R^2 = \text{OH}$; fimbriol-B	
	51 $R^1 = \text{OMe}$, $R^2 = \text{OH}$; bulbophyllanthrin	
	52 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$	
	53 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OH}$, $R^4 = \text{OMe}$; batatasin I	
	54 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OH}$, $R^4 = \text{OH}$	
	55 $R^1 = \text{OH}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$	
	56 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OH}$; TaVI	
	57 $R^1 = \text{OMe}$, $R^2 = \text{OMe}$, $R^3 = \text{OMe}$, $R^4 = \text{OMe}$; callosuminin	
	58	
	59 $R^1 = \text{H}$, $R^2 = \text{OH}$, $R^3 = \text{OMe}$, $R^4 = \text{H}$	
	60 $R^1 = \text{H}$, $R^2 = \text{OMe}$, $R^3 = \text{OH}$, $R^4 = \text{H}$	
	61 $R^1 = \text{OH}$, $R^2 = \text{H}$, $R^3 = \text{H}$, $R^4 = \text{OMe}$	

is essential for inhibitory activity (Lee et al., 1995). Lusianthridin (**4**) isolated from *B. striata* did not exert activity against the leukaemic P388 cell line *in vitro* (Takagi et al., 1983). In contrast, at a dose of 20 µg/kg, lusianthridin (**4**) displayed an antitumour effect, while denbinobin (**172**) was inactive in ICR mice implanted intraperitoneally with 10^6 cells of sarcoma 180 (Takagi et al., 1983).

D. thyrsiflorum has been used in Chinese ethnomedicine. Five phenanthrenes isolated from the stems were assayed against several tumour cell lines by use of the MTT test. Two dimeric phenanthrenes (**220**, **242**) and denthirsinin

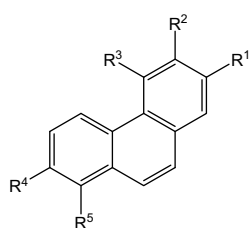
(**86**) displayed significant cytotoxicity against HeLa, K-562 and MCF-7 cells. The IC_{50} values (µM) on these cell lines were: denthirsinol (**220**) 9.3, 1.6 and -, denthirsinone (**242**) 9.9, 6.0 and 3.5, and denthirsinin (**86**) 2.7, 2.3 and 4.8, respectively. Hircinol (**6**) ($\text{IC}_{50} > 100$, 6.3 and > 100 µM) and moscatin (**15**) ($\text{IC}_{50} > 100$, 7.1 and > 100 µM) were less effective in killing HeLa and MCF-7 cells than denthirsinol (**220**). Structure–activity relationship analyses revealed that the dimerization of phenanthrenes is a very important factor for the inhibition of cancer cell growth (Zhang et al., 2005).

Table 4
Pentasubstituted dihydro/phenanthrenes with hydroxy- or/and methoxy-substitution

	62 R ¹ = OH, R ² = OMe, R ³ = OMe, R ⁴ = OMe, R ⁵ = OH	<i>B. gymnopus</i> (de Alvarenga et al., 1976; Majumder and Banerjee, 1988b) <i>B. reptans</i> (Majumder et al., 1999) <i>B. vaginatum</i> (Leong et al., 1997) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>C. caffrum</i> (Pettit et al., 1988) <i>C. psidioides</i> (Letcher and Nhamo, 1972b) <i>D. rotundatum</i> (Majumder and Pal, 1992)
	63 R ¹ = OH, R ² = OH, R ³ = OMe, R ⁴ = OMe, R ⁵ = OH 64 R ¹ = OH, R ² = OH, R ³ = OMe, R ⁴ = OH, R ⁵ = OH 65 R ¹ = OMe, R ² = OMe, R ³ = OH, R ⁴ = OH, R ⁵ = OH	<i>B. vaginatum</i> (Leong et al., 1999) <i>B. vaginatum</i> (Leong et al., 1999) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>C. molle</i> (Letcher et al., 1972) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>C. caffrum</i> (Pettit et al., 1988) <i>C. psidioides</i> (Letcher and Nhamo, 1972b)
	66 R ¹ = OMe, R ² = OMe, R ³ = OMe, R ⁴ = OMe, R ⁵ = OH 67 R ¹ = OH, R ² = OMe, R ³ = OMe, R ⁴ = OMe, R ⁵ = OMe 68 R ¹ = OMe, R ² = OMe, R ³ = OH, R ⁴ = OMe, R ⁵ = OH	<i>C. apiculatum</i> (Pettit et al., 1988) <i>C. caffrum</i> (Pettit et al., 1988) <i>C. apiculatum</i> , (Letcher and Nhamo, 1971; Malan and Swinny, 1993) <i>C. molle</i> (Letcher et al., 1972) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>C. caffrum</i> (Pettit et al., 1988) <i>C. psidioides</i> (Letcher and Nhamo, 1972b)
	69 R ¹ = OMe, R ² = OMe, R ³ = OMe, R ⁴ = OH, R ⁵ = OH; prazerol 70 R ¹ = OH, R ² = OMe, R ³ = OMe, R ⁴ = OH, R ⁵ = OMe 71 R ¹ = OH, R ² = OMe, R ³ = OMe, R ⁴ = OH, R ⁵ = OH	<i>C. apiculatum</i> (Letcher and Nhamo, 1971; Malan and Swinny, 1993) <i>C. molle</i> (Letcher et al., 1972; Malan and Swinny, 1993) <i>D. prazeri</i> (Biswas et al., 1988) <i>C. apiculatum</i> (Letcher and Nhamo, 1971) <i>C. molle</i> (Letcher and Nhamo, 1971; Letcher et al., 1972) <i>C. psidioides</i> (Letcher and Nhamo, 1972b)
	72	<i>N. boothii</i> (Hernandez-Romero et al., 2004)
	73 R ¹ = H, R ² = OH, R ³ = OH, R ⁴ = OMe, coeloganthridin 74 R ¹ = H, R ² = OMe, R ³ = OMe, R ⁴ = OH	<i>C. cristata</i> (Majumder et al., 2001) <i>D. decipiens</i> (Sunder et al., 1978)
	75 R ¹ = OH, R ² = OMe, R ³ = OMe, R ⁴ = OMe, R ⁵ = OH	<i>B. gymnopus</i> (DellaGreca et al., 1993; Majumder and Banerjee, 1988b) <i>B. reptans</i> (Majumder et al., 1999) <i>B. vaginatum</i> (Leong et al., 1997) <i>C. psidioides</i> (Letcher and Nhamo, 1972b) <i>D. rotundatum</i> (Honda and Yamaki, 2000; Majumder and Pal, 1992)
	76 R ¹ = OH, R ² = OH, R ³ = OMe, R ⁴ = OMe, R ⁵ = OH 77 R ¹ = OH, R ² = OH, R ³ = OMe, R ⁴ = OH, R ⁵ = OH 78 R ¹ = OMe, R ² = OH, R ³ = OMe, R ⁴ = OH, R ⁵ = OH 79 R ¹ = OMe, R ² = OH, R ³ = OMe, R ⁴ = OMe, R ⁵ = OH 80 R ¹ = OMe, R ² = OMe, R ³ = OH, R ⁴ = OMe, R ⁵ = OH 81 R ¹ = OH, R ² = OMe, R ³ = OMe, R ⁴ = OH, R ⁵ = OH 82 R ¹ = OMe, R ² = OMe, R ³ = OMe, R ⁴ = OMe, R ⁵ = OH 83 R ¹ = OH, R ² = OMe, R ³ = OMe, R ⁴ = OH, R ⁵ = OMe 84 R ¹ = OMe, R ² = OMe, R ³ = OH, R ⁴ = OH, R ⁵ = OH	<i>B. vaginatum</i> (Leong et al., 1997, 1999) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>B. vaginatum</i> (Leong et al., 1999) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>C. apiculatum</i> (Malan and Swinny, 1993) <i>C. molle</i> (Letcher et al., 1972) <i>C. psidioides</i> (Letcher and Nhamo, 1972b) <i>C. caffrum</i> (Pettit et al., 1988) <i>C. psidioides</i> (Letcher and Nhamo, 1972b) <i>C. apiculatum</i> (Letcher and Nhamo, 1971) <i>C. apiculatum</i> (Letcher and Nhamo, 1971) <i>C. molle</i> (Letcher et al., 1972)

(continued on next page)

Table 4 (continued)



85 R¹ = OH, R² = OMe, R³ = OMe,
R⁴ = OH, R⁵ = OMe; confusarin

86 R¹ = OMe, R² = OH, R³ = OMe,
R⁴ = OH, R⁵ = OMe; denthsyrinin

87 R¹ = OMe, R² = OMe, R³ = OMe,
R⁴ = OH, R⁵ = OMe;

88 R¹ = OMe, R² = OMe, R³ = OMe,
R⁴ = R⁵ = -O-CH₂-O-; TaI

89 R¹ = OMe, R² = OH, R³ = OMe,
R⁴ = R⁵ = -O-CH₂-O-; TaIV

90 R¹ = OMe, R² = R³ = -O-CH₂-O-,
R⁴ = OMe, R⁵ = OMe TaI

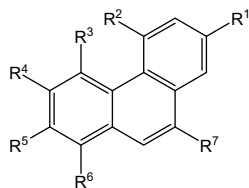
91 R¹ = OMe, R² = R³ = -O-CH₂-O-,
R⁴ = OH, R⁵ = OMe; TaIV

92 R₁ = OMe, R₂ = OMe, R₃ = OMe,
R₄ = OMe, R₅ = OH; TaV

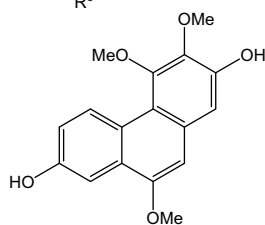
93 R¹ = OMe, R² = OMe, R³ = OH,
R⁴ = OMe, R⁵ = OH; TaIX

94 R¹ = H, R² = OH, R³ = OMe,
R⁴ = OMe, R⁵ = OH, R⁶ = H, R⁷ = OMe; fimbriol-A

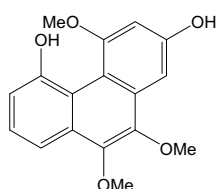
95 R¹ = OH, R² = OH, R³ = H, R⁴ = OH,
R⁵ = OMe, R⁶ = OMe, R⁷ = H; coeloganthrin



96 gymnopusin



97 plicatol-A



B. gymnopus (de Alvarenga et al., 1976;
Majumder and Banerjee, 1988b)
B. reptans (Majumder et al., 1999)
E. confusa (Majumder and Kar, 1987a)
T. communis (Réthy et al., 2006; Bordat et al., 2006)
C. pendulum (Majumder and Sen, 1991b)
D. densiflorum (Fan et al., 2001)
D. thysiflorum (Zhang et al., 2005)
E. nuda (Tuchinda et al., 1988)
N. boothii (Hernandez-Romero et al., 2004)
S. livida (Estrada et al., 1999a)
T. alba (Majumder et al., 1998b)
T. communis (Réthy et al., 2006; Bordat et al., 2006)
T. communis (Kovács et al., 2007)

T. communis (Majumder and Basak, 1991a;
Letcher and Wong, 1978)
T. communis (Majumder and Basak, 1991a;
Letcher and Wong (1979))
T. communis (Aquino et al., 1985b, 1991;
Reisch et al., 1969, 1970)
T. communis (Aquino et al., 1985b, 1991;
Letcher and Wong, 1979; Reisch et al., 1969, 1970)
T. communis (Aquino et al., 1985a,b, 1991;
Letcher and Wong, 1978; Reisch et al., 1970, 1973)
T. communis (Aquino et al., 1985a,b, 1991;
Reisch et al., 1973; Takasugi et al., 1987)

E. fimbriata (Tezuka et al., 1993)
E. rigidum (Hernandez-Romero et al., 2005)
M. densa (Estrada et al., 1999b, 2004)
C. cristata (Majumder et al., 2001)

B. gymnopus (Majumder and Banerjee, 1988b)
B. reptans (Majumder et al., 1999)
M. densa (Estrada et al., 1999b, 2004;
Fisch et al., 1973; Valencia-Islas et al., 2002)

D. plicatile (Honda and Yamaki, 2000)

This was supported by the investigation of mono-, bi-, and triphenanthrenes of *C. appendiculata*. The tuber of this plant has been used in traditional Chinese medicine for the treatment of various cancers. The isolated phenanthrenes (**18**, **19**) were inactive (IC₅₀ > 5 µg/ml) against all the tested cell lines (A549, A2780, Bel7402, BGC-823, HCT-8, MCF-7 and WISH). Biphenanthrenes (**223**, **231**) and the unusual triphenanthrene (**243**) proved to be active compounds in this investigation (Xue et al., 2006).

Many phenanthrenes have been isolated from petroleum ether and chloroform extracts of the rhizomes of *Tamus*

communis through cytotoxic assay guidance. The antitumour effects of eight phenanthrenes and one dihydrophe-nanthrene were tested on the HeLa cell line by Hohmann et al.; the compounds showed high cytotoxic activities with IC₅₀s of 20.18 (**42**), 6.66 (**43**), 13.85 (**47**), 0.97 (**85**), >20 (**86**), 15.86 (**25**), 12.18 (**56**), 8.52 (**87**) and 3.64 µM (**89**) (Réthy et al., 2006; Kovács et al., 2007).

Aquino et al. studied the cytotoxicities of compounds **27**, **28**, **90**, **92** and **93**, isolated from *T. communis* on CER (chicken embryo-related) and HeLa cells. The HeLa cells were found to be generally more susceptible than the

Table 5
Hexasubstituted dihydro/phenanthrenes with hydroxy- or/and methoxy-substitution

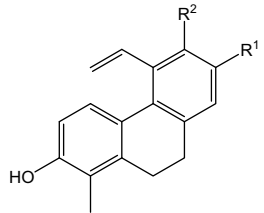
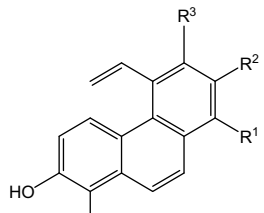
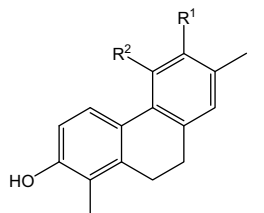
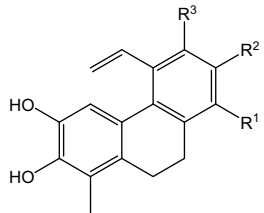
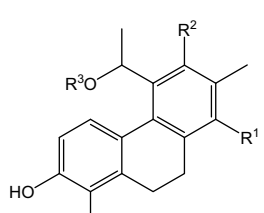
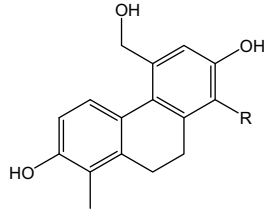
	98 confusaridin	<i>E. confusa</i> (Majumder and Kar, 1987a)
	99 pendulin	<i>C. pendulum</i> (Majumder and Sen, 1991b)

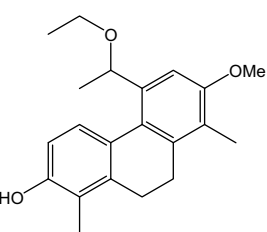
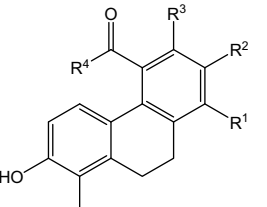
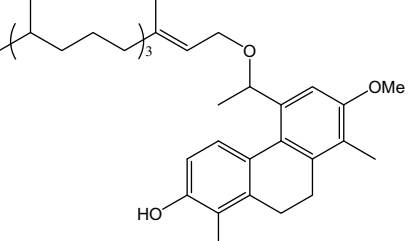
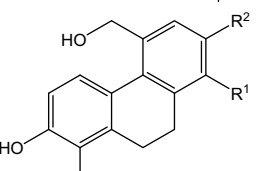
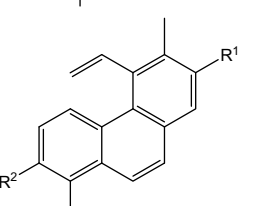
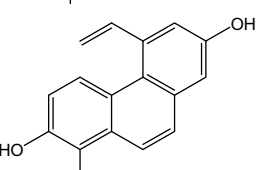
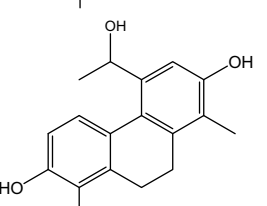
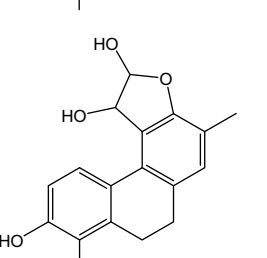
Table 6
Methyl, oxymethyl, vinyl and prenylsubstituted monomeric dihydro/phenanthrenes

	100 R ¹ = Me, R ² = OH; micrandrol-B	<i>M. scleroxylon</i> (de Alvarenga and Gottlieb, 1974)
	101 R ¹ = OMe, R ² = Me; micrandrol-F	<i>S. racemosa</i> (de Alvarenga et al., 1976)
		<i>S. racemosa</i> (de Alvarenga et al., 1976)
	102 R ¹ = Me, R ² = OH; micrandrol-A	<i>M. scleroxylon</i> (de Alvarenga and Gottlieb, 1974)
	103 R ¹ = OMe, R ² = Me; micrandrol-E	<i>S. racemosa</i> (de Alvarenga et al., 1976)
		<i>S. racemosa</i> (de Alvarenga et al., 1976)
	104 R ¹ = H, R ² = OH, R ³ = Me, R ⁴ = OMe; stemanthrene A	<i>S. collinsae</i> (Adams et al., 2005)
	105 R ¹ = H, R ² = OMe, R ³ = Me, R ⁴ = OH; stemanthrene B	<i>S. pierrei</i> (Adams et al., 2005; Kostecki et al., 2004)
		<i>S. tuberosa</i> (Adams et al., 2005)
	106 R ¹ = Me, R ² = OH, R ³ = Me, R ⁴ = OMe; stemanthrene C	<i>S. collinsae</i> (Adams et al., 2005)
		<i>S. pierrei</i> (Adams et al., 2005; Kostecki et al., 2004)
		<i>S. tuberosa</i> (Adams et al., 2005)
	107 R ¹ = Me, R ² = OH, R ³ = H, R ⁴ = OMe; stemanthrene D, racemosol	<i>S. collinsae</i> (Adams et al., 2005)
		<i>S. pierrei</i> (Adams et al., 2005; Kostecki et al., 2004)
		<i>S. tuberosa</i> (Adams et al., 2005)
		<i>S. pierrei</i> (Adams et al., 2005)
		<i>S. tuberosa</i> (Adams et al., 2005)
	108 R ¹ = Me, R ² = Me	<i>D. perrieri</i> (Long et al., 1997)
	109 R ¹ = CH ₂ OH, R ² = Me	<i>D. perrieri</i> (Long et al., 1997)
	110 R ¹ = Me, R ² = CH ₂ OH	<i>D. perrieri</i> (Long et al., 1997)
	111 R ¹ = CH ₂ OH, R ² = CH ₂ OH	<i>D. perrieri</i> (Long et al., 1997)
	112 R ¹ = OH, R ² = H, R ³ = Me	<i>J. acutus</i> (DellaGreca et al., 2002a, 2004)
	113 R ¹ = H, R ² = OH, R ³ = H	<i>J. effusus</i> (DellaGreca et al., 1993)
		<i>J. acutus</i> (DellaGreca et al., 2004)
	114 R ¹ = H, R ² = Me, R ³ = H	<i>J. acutus</i> (DellaGreca et al., 2004)

(continued on next page)

Table 6 (continued)

	115 $R^1 = \text{Me}, R^2 = \text{H}$, juncunol	<i>J. acutus</i> (DellaGreca et al., 2002a, 2004) <i>J. effusus</i> (DellaGreca et al., 1993) <i>J. roemerianus</i> (Sarkar et al., 1988)
	116 $R^1 = \text{OH}, R^2 = \text{Me}$, juncusol	<i>J. acutus</i> (DellaGreca et al., 2002a,b, 2004) <i>J. effusus</i> (DellaGreca et al., 1993; Shima et al., 1991) <i>J. roemerianus</i> (Chapatwala et al., 1981; Sarkar et al., 1988)
	117 $R^1 = \text{Me}, R^2 = \text{OH}$	<i>J. acutus</i> (DellaGreca et al., 2004) <i>J. effusus</i> (DellaGreca et al., 1993)
	118 $R^1 = \text{OH}, R^2 = \text{H}$, effusol	<i>J. acutus</i> (DellaGreca et al., 2004) <i>J. effusus</i> (DellaGreca et al., 1993; Shima et al., 1991)
	119 $R^1 = \text{H}, R^2 = \text{Me}$ 120 $R^1 = \text{OH}, R^2 = \text{CH}_2\text{OH}$ 121 $R^1 = \text{CH}_2\text{OH}, R^2 = \text{H}$	<i>J. acutus</i> (DellaGreca et al., 2004) <i>J. acutus</i> (DellaGreca et al., 2004) <i>J. acutus</i> (DellaGreca et al., 2004) <i>J. effusus</i> (DellaGreca et al., 1997)
	122 $R^1 = \text{H}, R^2 = \text{CH}_2\text{OH}$	<i>J. acutus</i> (DellaGreca et al., 2004) <i>J. effusus</i> (DellaGreca et al., 1997)
	123 $R^1 = \text{COOH}, R^2 = \text{H}, R^3 = \text{H}$	<i>J. acutus</i> (DellaGreca et al., 2004)
	124 $R^1 = \text{H}, R^2 = \text{COOH}, R^3 = \text{H}$	<i>J. effusus</i> (DellaGreca et al., 1993) <i>J. acutus</i> (DellaGreca et al., 2004)
	125 $R^1 = \text{H}, R^2 = \text{H}, R^3 = \text{COOH}$ 126 $R^1 = \text{Me}, R^2 = \text{OH}, R^3 = \text{H}$	<i>J. effusus</i> (DellaGreca et al., 1993) <i>J. acutus</i> (DellaGreca et al., 2004) <i>J. acutus</i> (DellaGreca et al., 2002a, 2004)
	127 $R^1 = \text{OH}, R^2 = \text{H}, R^3 = \text{Me}$ 128 $R^1 = \text{Me}, R^2 = \text{OMe}, R^3 = \text{H}$	<i>J. effusus</i> (DellaGreca et al., 1993) <i>J. acutus</i> (DellaGreca et al., 2004) <i>J. effusus</i> (DellaGreca et al., 1993) <i>J. acutus</i> (DellaGreca et al., 2002a, 2004) <i>J. effusus</i> (DellaGreca et al., 1993)
	129 $R^1 = \text{OH}, R^2 = \text{Ac}$; juncunone 130 $R^1 = \text{OH}, R^2 = \text{H}$	<i>J. roemerianus</i> (Sarkar et al., 1988) <i>J. effusus</i> (DellaGreca et al., 1993)
	131 $R^1 = \text{OH}, R^2 = \text{H}, R^3 = \text{Me}$ 132 $R^1 = \text{H}, R^2 = \text{Me}, R^3 = \text{H}$	<i>J. acutus</i> (DellaGreca et al., 2004) <i>J. effusus</i> (DellaGreca et al., 1993)
	133 $R^1 = \text{H}, R^2 = \text{OH}, R^3 = \text{H}$ 134 $R^1 = \text{H}, R^2 = \text{OH}, R^3 = \text{Me}$ 135 $R^1 = \text{OH}, R^2 = \text{H}, R^3 = \text{H}$	<i>J. acutus</i> (DellaGreca et al., 2002a, 2004) <i>J. effusus</i> (DellaGreca et al., 1993, 1997) <i>J. acutus</i> (DellaGreca et al., 2002a, 2004) <i>J. effusus</i> (DellaGreca et al., 1993) <i>J. acutus</i> (DellaGreca et al., 2002a, 2004) <i>J. effusus</i> (DellaGreca et al., 1993)
	136 $R = \text{H}$ 137 $R = \text{Me}$	<i>J. acutus</i> (DellaGreca et al., 2004) <i>J. acutus</i> (DellaGreca et al., 2004)

	138	<i>J. acutus</i> (DellaGreca et al., 2002a, 2004)
	139 R ¹ = H, R ² = Me, R ³ = OH, R ⁴ = Me 140 R ¹ = Me, R ² = OMe, R ³ = H, R ⁴ = H 141 R ¹ = H, R ² = Me, R ³ = OH, R ⁴ = H	<i>J. effusus</i> (DellaGreca et al., 1993) <i>J. effusus</i> (DellaGreca et al., 1993) <i>J. effusus</i> (DellaGreca et al., 1993)
	142	<i>J. acutus</i> (DellaGreca et al., 2002a, 2004)
	143 R ¹ = Me, R ² = OH 144 R ¹ = Me, R ² = OMe 145 R ¹ = H, R ² = Me	<i>J. effusus</i> (DellaGreca et al., 1997) <i>J. effusus</i> (DellaGreca et al., 1997) <i>J. effusus</i> (DellaGreca et al., 1997)
	146 R ¹ = OH, R ² = OH, dehydrojuncusol 147 R ¹ = H, R ² = OH 148 R ¹ = OMe, R ² = OMe	<i>J. effusus</i> (Shima et al., 1991) <i>J. roemerianus</i> (Sarkar et al., 1988) <i>J. acutus</i> (DellaGreca et al., 2002a, 2004) <i>J. acutus</i> (DellaGreca et al., 2002a, 2004) <i>J. acutus</i> (DellaGreca et al., 2002a, 2004)
	149 dehydroeffusol	<i>J. effusus</i> (Shima et al., 1991)
	150	<i>J. effusus</i> (DellaGreca et al., 1997)
	151	<i>J. effusus</i> (DellaGreca et al., 1997)

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Table 6 (continued)

	152	<i>J. acutus</i> (DellaGreca et al., 2004)
	153 dehydroeffusal	<i>J. effusus</i> (Shima et al., 1991)
	154 R =	<i>G. uralensis</i> (Fukai et al., 1991)
	155 R = H; gancaonin V	<i>G. uralensis</i> (Fukai et al., 1991)
	156 sinensol G	<i>S. sinensis</i> (Lin et al., 2001)

Table 7

Miscellaneous monomeric phenanthrene derivatives

	157 R ¹ = Me, R ² = Glc, R ³ = H, effuside I	<i>J. effusus</i> (DellaGreca et al., 1995)
	158 R ¹ = H, R ² = Glc, R ³ = H, effuside II	<i>J. effusus</i> (DellaGreca et al., 1995)
	159 R ¹ = Glc, R ² = H, R ³ = H, effuside III	<i>J. effusus</i> (DellaGreca et al., 1995)
	160 R ¹ = H, R ² = H, R ³ = Glc, effuside IV	<i>J. effusus</i> (DellaGreca et al., 1995)
	161 R ¹ = Me, R ² = Glc, R ³ = Glc, effuside V	<i>J. effusus</i> (DellaGreca et al., 1995)
	162 epimedoicarisoside A	<i>E. koreanum</i> (Li et al., 1995)
	163 denchryside A	<i>D. chrysanthum</i> (Ye et al., 2003)
	164	<i>B. striata</i> (Yamaki et al., 1993b)
	165	<i>B. striata</i> (Yamaki et al., 1993b)

Table 7 (continued)

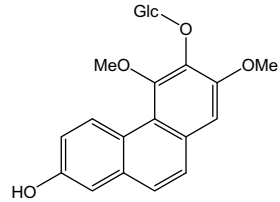
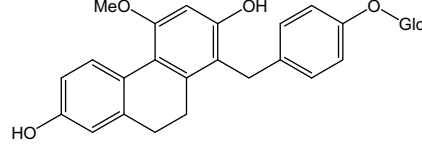
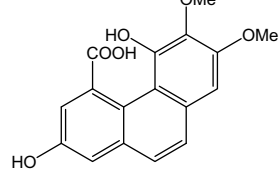
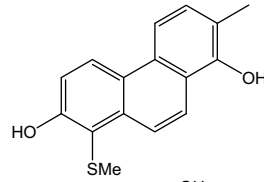
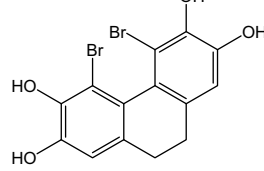
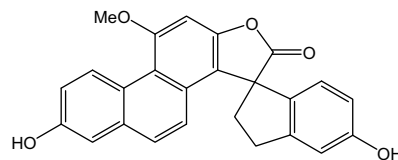
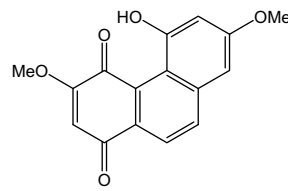
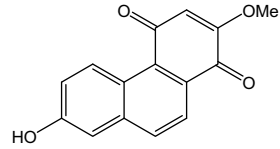
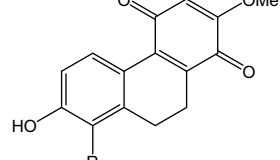
	166	<i>B. striata</i> (Yamaki et al., 1993b)
	167	<i>B. striata</i> (Yamaki et al., 1993b)
	168 ochrolic acid	<i>C. ochracea</i> (Anuradha et al., 1994)
	169 micrandrol C	<i>M. scleroxylon</i> (de Alvarenga and Gottlieb, 1974)
	170 polysiphenol	<i>P. ferulacea</i> (Aknin et al., 1992)
	171 blespirol	<i>B. striata</i> (Yamaki et al., 1993a)

Table 8
Phenanthraquinones

	172 denbinobin	<i>D. moniliforme</i> (Lin et al., 2001) <i>D. nobile</i> (Lee et al., 1995) <i>E. lonchophylla</i> (Chen et al., 2000; Tezuka et al., 1991)
	173 densiflorol B, cypritibetquinone A	<i>C. tibeticum</i> (Liu et al., 2005a) <i>D. densiflorum</i> (Fan et al., 2001)
	174 R = H; ephemeranθοquinone	<i>D. plicatile</i> (Yamaki and Honda, 1996) <i>E. lonchophylla</i> (Tezuka et al., 1991) <i>N. boothii</i> (Hernandez-Romero et al., 2004)
	175 R = OMe; cypripedin	<i>D. densiflorum</i> (Fan et al., 2001)

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Table 8 (continued)

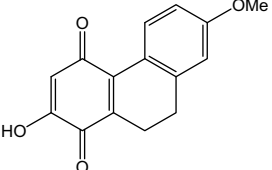
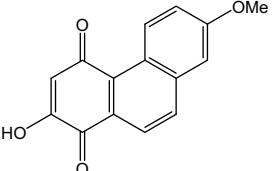
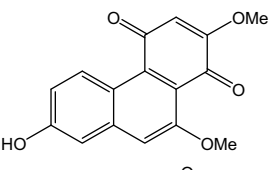
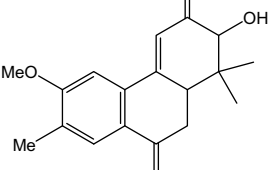
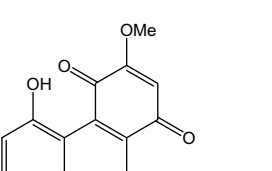
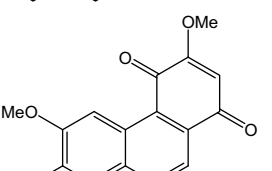
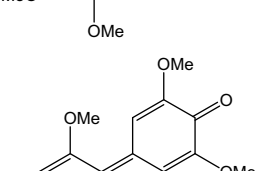
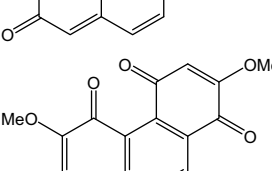
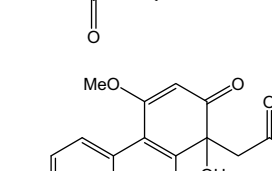
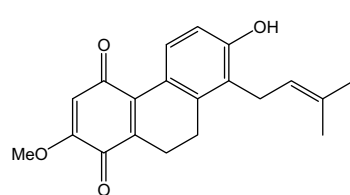
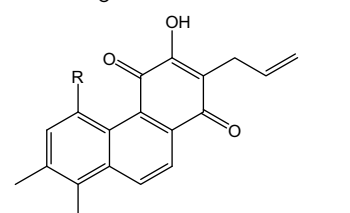
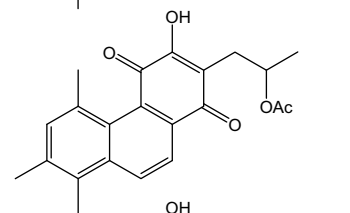
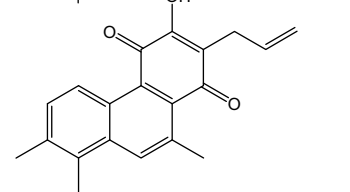
	176 ochrone A	<i>C. ochracea</i> (Bhaskar et al., 1991)
	177 ochrone B	<i>C. ochracea</i> (Bhaskar et al., 1991)
	178 cypritibetquinone B	<i>C. tibeticum</i> (Liu et al., 2005a)
	179 domohinone	<i>D. perrieri</i> (Long et al., 1997)
	180 cymbinodin A	<i>C. aloifolium</i> (Barua et al., 1990)
	181 cymbinodin B	<i>C. aloifolium</i> (Ghosh et al., 1992)
	182 TaII	<i>T. communis</i> (Reisch et al., 1970)
	183 moniliformin	<i>D. moniliforme</i> (Lin et al., 2001)
	184 R = H 185 R = Me	<i>C. appendiculata</i> (Xue et al., 2006) <i>C. appendiculata</i> (Xue et al., 2006)

Table 8 (continued)

	186 spiranthoquinone	<i>S. sinensis</i> (Tezuka et al., 1990)
	187 R = Me, plectranthon A 188 R = H, plectranthon C	<i>Plectranthus</i> sp. (Alder et al., 1984) <i>Plectranthus</i> sp. (Alder et al., 1984)
	189 plectranthon B	<i>Plectranthus</i> sp. (Alder et al., 1984)
	190 plectranthon D	<i>Plectranthus</i> sp. (Alder et al., 1984)

CER cells to the toxic action of these compounds, which were toxic to the cells at concentrations above 4–20 µg/ml, with the exception of **90** (100 µg/ml), the only compound in which hydroxy groups are missing. This is a further indication that free phenolic hydroxy groups are essential for the inhibitory activity (Aquino et al., 1991).

Compounds from *Domohinea perrieri* were screened for *in vitro* cytotoxicity against a number of cancer cell lines. Compounds **108** and **109** were found to demonstrate significant cytotoxic responses against several lines, with some cell-type selectivity. Compound **108** was more active against drug-resistant KB cells, while **109** was active against HT (fibrosarcoma) and U373 (glioma) cell lines. **110**, **111** and **179** were not significantly active against any of the cell lines tested. Compounds with a hydroxymethyl group on C-7 were not active, suggesting that an unsubstituted methyl group on C-7 is important for the activity (Long et al., 1997).

Hydroxybenzyl-phenanthrenes [sinensol A–F (**202–206** and **208**)] from *S. sinensis* proved to be active against the MS-G2 cell line and were cytotoxic at 20 µg/ml, but showed no anti-hepatitis B virus e antigen (HBeAg) effect at non-cytotoxic (5 or 10 µg/ml) doses (Lin et al., 2000).

4.2. Antimicrobial effects

The accumulation of phytoalexins in plants is a response to infection by pathogenic fungi. Phytoalexins are utilized

by plants to stop the growth of the attacking fungus. Orchid phytoalexins are phenanthrenes and dihydrophenanthrenes, as exemplified by orchinol (**3**) from *Orchis militaris* and hircinol (**6**) from *Loroglossum hircinum*. Their antifungal activities, together with those of loroglossol (**5**), were investigated on *Candida lipolitica* in 1973. Loroglossol was inactive, while orchinol (**3**) (at either 50 or 100 ppm) was considerably more active than hircinol (**6**). Orchinol (**3**) at 100 ppm inhibited the growth of the cells completely for the first 6 days, whereas hircinol (**6**) or the control did so for only 3 days (Fisch et al., 1973).

The tubers of *B. striata* were investigated, because this has been used in traditional medicine in China to treat pneumonorrhagia and pneumonophthisis. The methanol extracts of *B. striata* and lusianthridin (**4**) were mainly active against Gram-positive bacteria, but weakly active against certain fungi. Biphenanthrenes [blestriareneA–C (**214**, **218**, **229**)] were active against the Gram-positive bacteria *Staphylococcus aureus* and *Streptococcus nutans*. Blestriarene B (**218**) exhibited the most potent activity against both test organisms (Yamaki et al., 1989).

The dihydrophenanthrene stemanthrene D (**107**) from *Stemona collinsae* demonstrated a weak activity against the fungi: *Fusarium avenaceum*, *Cladosporium herbarium* and *Pyricularia grisea*, with EC₅₀ values >200 µg/ml. The antifungal properties of stemanthrenes A–D (**104–107**) from *Stemona pierrei* were also investigated. In this study

Table 9

Monomeric phenanthrenes with hydroxybenzyl substitution

	191 $R^1 = \text{H}$, $R^2 = \text{hydroxybenzyl}$, $R^3 = \text{H}$ 192 $R^1 = \text{hydroxybenzyl}$, $R^2 = \text{H}$, $R^3 = \text{hydroxybenzyl}$ 193 $R^1 = \text{H}$, $R^2 = \text{hydroxybenzyl}$, $R^3 = \text{hydroxybenzyl}$ 194 $R^1 = \text{H}$, $R^2 = \text{H}$, $R^3 = \text{hydroxybenzyl}$	<i>B. striata</i> (Yamaki et al., 1990) <i>B. formosana</i> (Lin et al., 2005) <i>B. striata</i> (Yamaki et al., 1990) <i>B. formosana</i> (Lin et al., 2005) <i>B. striata</i> (Bai et al., 1993) <i>B. formosana</i> (Lin et al., 2005) <i>B. striata</i> (Bai et al., 1993; Yamaki et al., 1990) <i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006) <i>B. formosana</i> (Lin et al., 2005) <i>B. striata</i> (Yamaki et al., 1990) <i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006) <i>P. bulbocodioides</i> (Bai et al., 1996) <i>B. formosana</i> (Lin et al., 2005) <i>B. formosana</i> (Lin et al., 2005) <i>B. striata</i> (Bai et al., 1991)
	195 $R^1 = \text{H}$, $R^2 = \text{hydroxybenzyl}$ 196 $R^1 = \text{OMe}$, $R^2 = \text{hydroxybenzyl}$ 197 $R^1 = \text{hydroxybenzyl}$, $R^2 = \text{hydroxybenzyl}$	<i>B. formosana</i> (Lin et al., 2005) <i>B. striata</i> (Yamaki et al., 1990) <i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006) <i>P. bulbocodioides</i> (Bai et al., 1996) <i>B. formosana</i> (Lin et al., 2005) <i>B. formosana</i> (Lin et al., 2005) <i>B. striata</i> (Bai et al., 1991)
	198 $R^1 = \text{H}$, $R^2 = \text{OH}$, $R^3 = \text{hydroxybenzyl}$, $R^4 = \text{OMe}$, $R^5 = \text{hydroxybenzyl}$ 199 $R^1 = \text{H}$, $R^2 = \text{OMe}$, $R^3 = \text{H}$, $R^4 = \text{OMe}$, $R^5 = \text{H}$ 200 $R^1 = \text{OMe}$, $R^2 = \text{OH}$, $R^3 = \text{H}$, $R^4 = \text{OMe}$, $R^5 = \text{H}$ 201 $R^1 = \text{hydroxybenzyl}$, $R^2 = \text{OH}$, $R^3 = \text{H}$, $R^4 = \text{OMe}$, $R^5 = \text{H}$	<i>B. formosana</i> (Lin et al., 2005) <i>B. formosana</i> (Lin et al., 2005) <i>B. formosana</i> (Lin et al., 2005) <i>B. formosana</i> (Lin et al., 2005)
	202 $R_1 = \text{H}$, $R^2 = \text{OMe}$; arundinaol, sinensol A 203 $R^1 = \text{CH}_2=\text{CHCH}_3$; $R^2 = \text{OMe}$; sinensol B 204 $R^1 = \text{CH}_2=\text{CHCH}_3$; $R^2 = \text{H}$; sinensol C	<i>A. graminifolia</i> (Liu et al., 2005b) <i>S. sinensis</i> (Lin et al., 2000) <i>S. sinensis</i> (Lin et al., 2000) <i>S. sinensis</i> (Lin et al., 2000)
	205 sinensol D	<i>S. sinensis</i> (Lin et al., 2000)
	206 sinensol E	<i>S. sinensis</i> (Lin et al., 2000)
	207 $R^1 = \text{H}$, $R^2 = \text{H}$; shancidin 208 $R^1 = \text{CH}_2=\text{CHCH}_3$; $R^2 = \text{hydroxybenzyl}$; sinensol F 209 $R^1 = \text{hydroxybenzyl}$, $R^2 = \text{hydroxybenzyl}$; sinensol H	<i>B. striata</i> (Takagi et al., 1983) <i>P. bulbocodioides</i> (Bai et al., 1996) <i>S. sinensis</i> (Lin et al., 2000) <i>S. sinensis</i> (Lin et al., 2001)

Table 9 (continued)

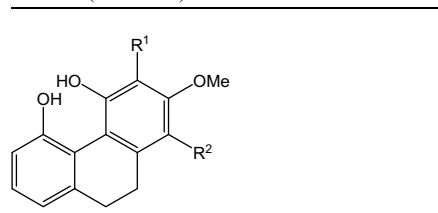
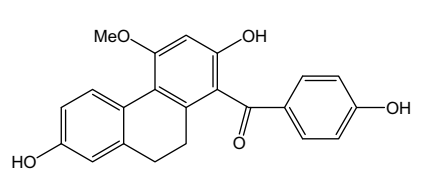
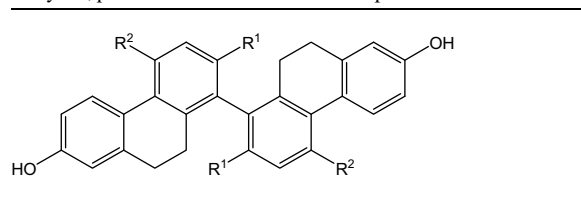
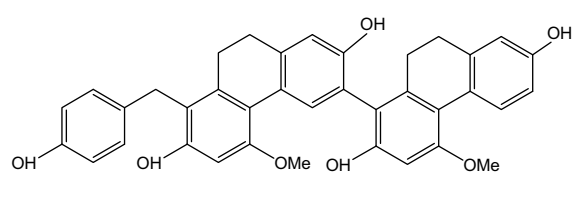
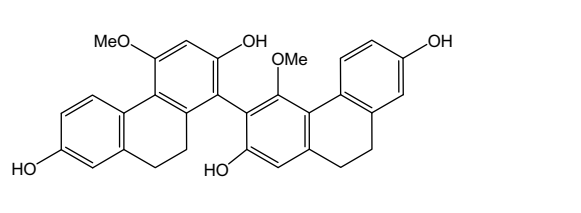
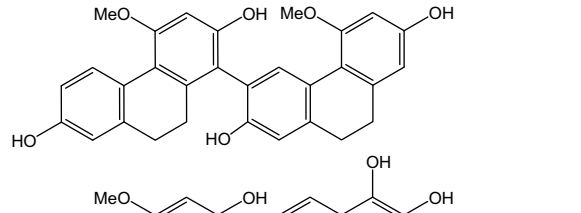
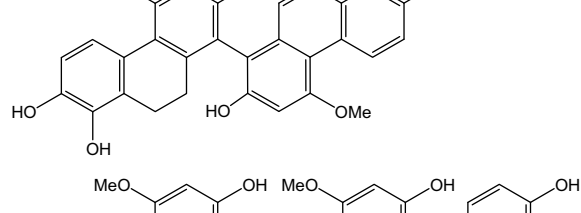
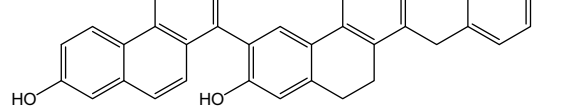
	210 R¹ = H, R² = hydroxybenzyl; gymconopin A 211 R¹ = hydroxybenzyl, R² = H; gymconopin B	<i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006) <i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006)
	212	<i>B. striata</i> (Bai et al., 1993)

Table 10

Dihydro/phenanthrene dimers and a triphenanthrene

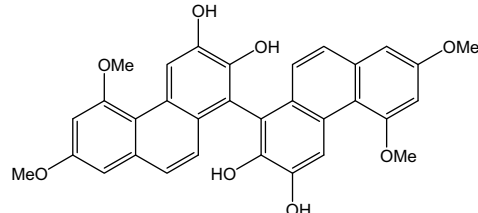
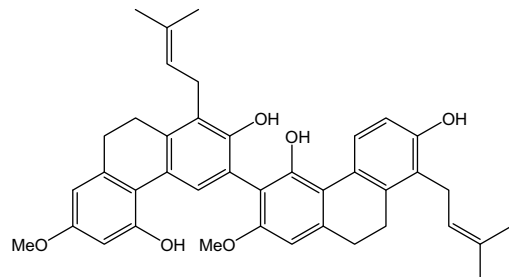
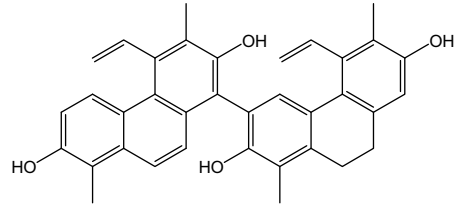
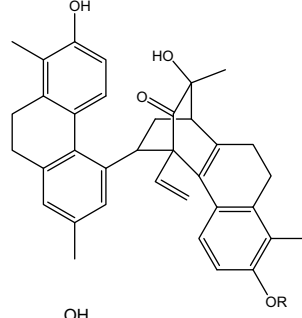
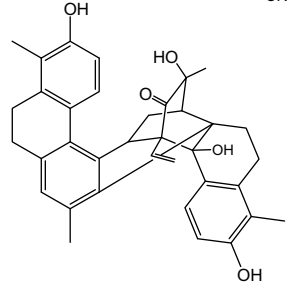
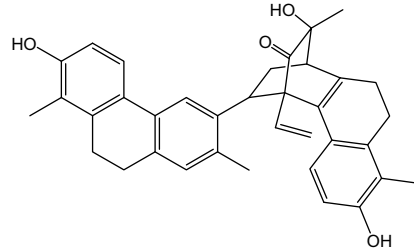
	213 R¹ = OMe, R² = OH 214 R¹ = OH, R² = OMe; blestriarene A, flavanthrin	<i>D. plicatile</i> (Yamaki and Honda, 1996) <i>B. reptans</i> (Majumder et al., 1999) <i>B. striata</i> (Yamaki et al., 1989) <i>E. flava</i> (Majumder and Banerjee, 1988a, 1990a) <i>G. conopsea</i> (Matsuda et al., 2004; Morikawa et al., 2006) <i>T. alba</i> (Majumder et al., 1998b)
	215 blestrianol B	<i>B. striata</i> (Bai et al., 1991)
	216 blestrianol A	<i>B. striata</i> (Bai et al., 1991)
	217 gymconopin C	<i>G. conopsea</i> (Matsuda et al., 2004)
	218 blestriarene B	<i>B. striata</i> (Yamaki et al., 1989) <i>B. formosana</i> (Lin et al., 2005)
	219 blestrianol C	<i>B. striata</i> (Bai et al., 1991)

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Table 10 (continued)

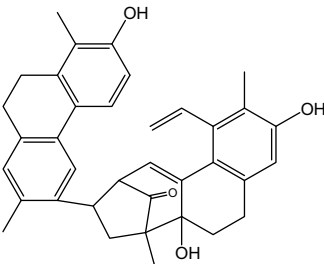
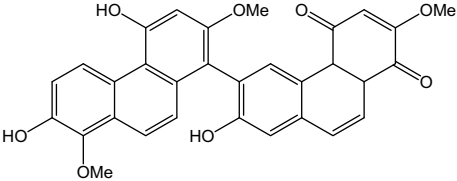
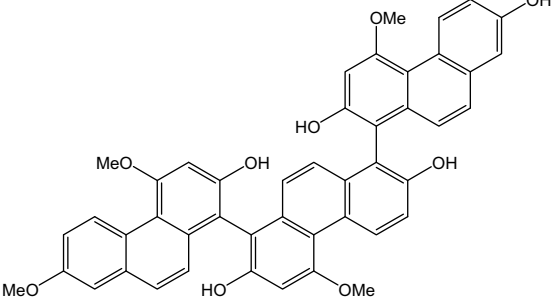
	220 denthyrsinol	<i>D. thyrsiflorum</i> (Zhang et al., 2005)
	221 R ¹ = OMe, R ² = H; agrostinin	<i>A. khasiyanum</i> (Majumder et al., 1998a)
	222 R ¹ = OH, R ² = Me; agrostonidin	<i>A. callosum</i> (Majumder et al., 1998a) <i>A. khasiyanum</i> (Majumder et al., 1998a) <i>A. callosum</i> (Majumder et al., 1998a)
	223 R ¹ = H, R ² = H; cirrhoptalanthrin	<i>C. maculosum</i> (Majumder et al., 1990e) <i>B. reptans</i> (Majumder et al., 1999) <i>T. alba</i> (Majumder et al., 1998b) <i>C. appendiculata</i> (Xue et al., 2006)
	224 R ¹ = OMe, R ² = OMe; reptanthrin	<i>B. reptans</i> (Majumder et al., 1999)
	225 isoreptanthrin	<i>B. reptans</i> (Majumder et al., 1999)
	226 R ¹ = Me, R ² = Me 227 R ¹ = Me, R ² = H 228 R ¹ = H, R ² = H	<i>M. polymorpha</i> (Adam and Becker, 1994) <i>M. polymorpha</i> (Adam and Becker, 1994) <i>M. polymorpha</i> (Adam and Becker, 1994)
	229 blestriarene C	<i>B. striata</i> (Yamaki et al., 1989)
	230 R ¹ = Me, R ² = H, R ³ = H 231 R ¹ = Me, R ² = Me, R ³ = H 232 R ¹ = H, R ² = H, R ³ = OMe	<i>C. appendiculata</i> (Xue et al., 2006) <i>C. appendiculata</i> (Xue et al., 2006) <i>E. nuda</i> (Tuchinda et al., 1988)
	233	<i>B. vaginatum</i> (Leong and Harrison, 2004)

Table 10 (continued)

	234 volucrin	<i>L. volucris</i> (Majumder and Lahiri, 1990c)
	235 spiranthesol	<i>S. sinensis</i> (Tezuka et al., 1990)
	236	<i>J. acutus</i> (DellaGreca et al., 2003)
	237 R = H 238 R = Me	<i>J. acutus</i> (DellaGreca et al., 2003)
	239	<i>J. acutus</i> (DellaGreca et al., 2003)
	240	<i>J. acutus</i> (DellaGreca et al., 2003)

(continued on next page)

Table 10 (continued)

	241	<i>J. acutus</i> (DellaGreca et al., 2003)
	242 denthyrsinone	<i>D. thyrsiflorum</i> (Zhang et al., 2005)
	243	<i>C. appendiculata</i> (Xue et al., 2006)

dihydrophenanthrenes exerted a weak activity, similarly as in previous studies (Kostecki et al., 2004; Pacher et al., 2002).

The microbiological effects of juncusol (**116**) have been tested on several species. *Bacillus* species were inhibited at all concentrations, while *Plannococcus* species were inhibited only at the highest concentration. *Pseudomonas* species, *Mycobacterium smegmatis*, *Enterobacter aerogenes* and *Escherichia coli* were not inhibited at any of the concentrations used (Chapatwala et al., 1981).

The virus replication inhibitory effects of phenanthrenes of *T. communis* (**27**, **28**, **90**, **91**, **92**, **93**) have been tested on RNA enveloped virus: vesicular stomatitis virus (VSV) and human rhinovirus serotype 1B (HRV 1B). The results of the screening revealed marked inhibitory action on plaque formation against VSV (**27**), with an IC_{50} of 9 μ g/ml. On HRV, these compounds produced a low decrease in viral multiplication (Aquino et al., 1991).

4.3. Spasmolytic effects

Spasmolytic effects have been investigated in case of phenanthrenes isolated from *Scaphyglottis livida*, *Maxillaria densa* and *Nidema boothii*. *S. livida* and *M. densa* are used by indigenous people in the tropical forests of Mexico. The ground herb of *S. livida* is applied to eliminate ectoparasites. The decoction is used for the treatment of stomach aches and to avoid abortion. *M. densa* is utilized for the same purposes.

Estrada et al. investigated the spasmolytic action of compounds of *S. livida* (Estrada et al., 1999a). Bioactiv-

ity-guided fractionation of the active extract resulted in the isolation of lusianthridin (**4**), **43** and denthirsinin (**86**). Compound **43** significantly antagonized the histamine-induced contractions of the rat ileum, in contrast with lusianthridin (**4**), and denthirsinin (**86**), which were inactive. The contractions evoked by $BaCl_2$ were inhibited slightly by **43** and denthirsinin (**86**), but lusianthridin (**4**) enhanced the contractions elicited by $BaCl_2$. The relaxatory response elicited by natural products is probably mediated by the neuronal release of NO. Compounds of *S. livida* induced the production of NO in ileal tissue, which in turn provoked relaxation of the ileal muscles by elevating the cyclic GMP content. Later, the vasorelaxing effect of **43** was studied on intact and denuded rat aorta rings. Compound **43** and denthirsinin (**86**) provoked the inhibition of NA-evoked contractions in the endothelium and appeared to induce a dose-response vasorelaxation by more than one mechanism (Estrada et al., 1999a, 2006). Phenanthrenes [erianthridin (**36**), **39**, nudol (**42**), **49** and gymnopusin (**96**)] isolated from *M. densa* provoked a concentration-dependent inhibition of the spontaneous contractions of the rat ileum induced by histamine, $BaCl_2$ and L-NAME. All these compounds antagonized the contractions, but they exerted a weaker smooth muscle relaxant activity than the extract; this could be due to a synergistic effect of the isolated compounds (Estrada et al., 2004).

Bioassay-guided fractionation of the active extract of *E. boothii* led to the identification of a new dihydrophenanthrene (**72**) and numerous known stilbenoids

Table 11
Dihydro/phenanthrenes with unusual structure

	244 R = H 245 R = OH	<i>F. convoluta</i> (Flegel et al., 1999) <i>F. convoluta</i> (Flegel et al., 1999)
	246 shancilin	<i>P. bulbocodioides</i> (Bai et al., 1996)
	247 phoyunnanin D	<i>P. yunnanensis</i> (Guo et al., 2006)
	248 phoyunnanin E	<i>P. yunnanensis</i> (Guo et al., 2006)
	249 R ¹ = OMe, R ² = H, R ³ = OH; blestrin A 250 R ¹ = H, R ² = OH, R ³ = OMe; blestrin B	<i>B. striata</i> (Bai et al., 1990) <i>B. striata</i> (Bai et al., 1990)
	251 R ¹ = OMe, R ² = H; blestrin C 252 R ¹ = H, R ² = OMe; blestrin D	<i>B. striata</i> (Yamaki et al., 1992) <i>B. striata</i> (Yamaki et al., 1992)

[lusianthridin (**4**), flavanthridin (**37**), **43**, denthirsinin (**86**) and **174**]. Denthirsinin (**86**) and **72** induced noteworthy concentration-dependent inhibition of the spontaneous contractions of the guinea-pig ileum (Hernandez-Romero et al., 2004).

4.4. Antiallergic and anti-inflammatory activities

The tubers of *Gymnadenia conopsea* have been used in traditional Chinese medicine for the treatment of asthma, neurasthenia and chronic hepatitis. The methanolic

extract of the tubers was found to show an antiallergic effect on the ear passive cutaneous anaphylaxis reaction in mice. Column chromatography of the methanolic extract afforded a fraction which inhibited the antigen-induced release of β -hexosaminidase, a marker of degranulation, in RBL-2H3 cells sensitized with anti-DNP IgE. From the active fraction, numerous phenanthrenes were isolated, but these compounds were not investigated (Matsuda et al., 2004).

Denbinobin (**172**), a phenanthraquinone from *Dendrobium moniliforme*, showed *in vitro* anti-inflammatory activity. This compound, at 1 μ M, stimulated with 1 μ g/ml of lipopolysaccharide, significantly inhibited the formation of tumour necrosis factor α and prostaglandin E2 in RAW 264.7 and N9 cells (Lin et al., 2001).

Various species from the genus *Stemona* have long been used in traditional Asian medical practices for the treatment of inflammation-related diseases, such as asthma. Phenanthrenes of the *Stemona* species were tested in an *ex vivo* leukotriene biosynthesis inhibition assay, using human neutrophil granulocytes. Stemanthrene A (**104**) and D (**107**) displayed clear activity in a dose-dependent manner, with IC₅₀ values of 8.5 μ M and 4.8 μ M, respectively. Stemanthrene B (**105**) and C (**106**) initially caused very high inhibition (100%) at 25 μ M, but because of the degradation of the compounds during storage the activity was lost. The potency of phenanthrenes in this test system suggests that these substances might be the anti-inflammatory and antiasthmatic principles of the *Stemona* species (Adams et al., 2005).

In 2006, four compounds were isolated from the rhizomes of *T. communis* (**47**, **85**, **86** and **92**) and their anti-inflammatory activities were analysed. The activity of **86** was evaluated from the production of prostaglandin PG6KF1- α , induced in keratinocytes by the stimulation of arachidonic acid and calcium ionophore A23187 (Bordat et al., 2006). The compounds showed a significant anti-inflammatory activity at 1 μ g/ml, 3 μ g/ml and 10 μ g/ml with the inhibition percent of the release of PG6KF1- α of 25%, 59% and 90%, respectively.

4.5. Antiplatelet aggregation, phytotoxicity and antialgal activity

Ephemerantha lonchophylla was used in traditional Chinese medicine as a health tonic, to regulate the body fluid balance, and as an antipyretic. An ethanolic extract of the stems of *E. lonchophylla* exhibited antiplatelet aggregation activity. Chen et al. isolated erianthridin (**36**), **43** and denbinobin (**172**) from the stems of this plant. The *in vitro* antiplatelet effects of these compounds were evaluated on washed rabbit platelets against aggregation induced by either thrombin, arachidonic acid (AA), collagen or PAF. At high concentration (100 μ g/ml) the isolated compounds displayed significant inhibitory effects against the aggregation caused by AA, collagen and PAF. Further dose-response analyses indicated that inhibition against

AA-induced aggregation was effective, erianthridin (**36**) proving to be the most potent compound, with an IC₅₀ of about 9 μ M, while for **43** IC₅₀ was 24 μ M. The antiplatelet effects may be due to the inhibition of thromboxane A₂ formation because the platelet aggregation induced by AA or collagen was most readily inhibited (Chen et al., 2000).

Dendrobium loddigesii is used with the same aims as *E. lonchophylla* in China. The active principle, moscatin (**15**), was isolated by using bioassay-guided fractionation by Chen et al. This compound strongly inhibited both AA and collagen-induced platelet aggregation. The antiplatelet effects of this compound may be due to the inhibition of thromboxane A₂ formation (Chen et al., 1994).

The phytotoxicities of compounds obtained from *M. densa* and *Epidendrum rigidum* were examined on *Amaranthus hypochondriacus*. Gymnopusin (**96**) and erianthridin (**36**) from *M. densa* inhibited the radical elongation of *A. hypochondriacus* seedlings, with IC₅₀ values of 330 and 58.2 μ M, respectively. Both phenanthrene derivatives exhibited moderate cytotoxicity towards all mammalian cells tested (Valencia-Islas et al., 2002). Compounds ephemeranthol-A (**35**) and fimbriol A (**94**) isolated from *E. rigidum* also demonstrated substantial phytotoxicity against *A. hypochondriacus*, with IC₅₀ values of 0.12 and 5.9 μ M, respectively (Hernandez-Romero et al., 2005).

The antialgal activities of 41 monomeric and 5 dimeric phenanthrenes were investigated against *Selenastrum capricornutum* by DellaGreca et al. in numerous studies. (DellaGreca et al., 1993, 1995, 1997, 2002a,b, 2003). The antialgal activities of the dimeric phenanthrenes were higher than those of the 9,10-dihydrophenanthrenes. As already observed in monomeric 9,10-dihydrophenanthrenes, a reduction of the polarity in related compounds causes a decrease in activity.

5. Conclusions

Numerous phenanthrenes and their derivatives have been found, mainly in higher plants, and their biological activities have been studied. The phenanthrenes are a promising and expanding group of biologically active natural compounds whose potential has not yet been investigated sufficiently thoroughly, and which have not been exploited by the pharmaceutical industry.

Many phenanthrene-containing plants have been used in traditional medicine throughout the world, but mainly in China, and phytochemical–pharmacological investigations which have resulted in the identification of phenanthrenes as their active principles have provided support for the use of these plants in ethnomedical practice. On the other hand, the mechanisms of action and the structure–activity relationships of these compounds have been reported only rarely and are worthy of future investigations.

References

- Adam, K.P., Becker, H., 1994. Phenanthrenes and other phenolics from *in vitro* cultures of *Marchantia polymorpha*. *Phytochemistry* 35, 139–143.
- Adams, M., Pacher, T., Greger, H., Bauer, R., 2005. Inhibition of leukotriene biosynthesis by stilbenoids from *Stemona* species. *J. Nat. Prod.* 68, 83–85.
- Aknin, M., Samb, A., Mirailles, J., Costantino, V., Fattorusso, E., Mangoni, A., 1992. Polysiphenol, a new brominated 9,10-dihydrophenanthrene from the Senegalese red alga *Polysiphonia ferulacea*. *Tetrahedron Lett.* 33, 555–558.
- Alder, A.C., Rüedi, P., Eugster, C.H., 1984. Plectranthone A, B, C und D. Diterpenoide phenanthren-1,4-dione aus Blattdrüsen einer *Plectranthus* sp. (Labiatae). *Helv. Chim. Acta* 67, 1003–1011.
- Anton, H., Kraut, L., Mues, R., Morales, Z.M.I., 1997. Phenanthrenes and bibenzyls from a *Plagiochila* species. *Phytochemistry* 46, 1069–1075.
- Anuradha, V., Rao, N.S.P., Bhaskar, M.U., 1994. Ochroleic acid, a precursor to phenanthropyrones, from *Coelogyne ochracea*. *Phytochemistry* 36, 1515–1517.
- Aquino, R., Behar, I., de Simone, F., Pizza, C., 1985a. Natural dihydrophenanthrene derivatives from *Tamus communis*. *J. Nat. Prod.* 48, 811–813.
- Aquino, R., Behar, I., de Simone, F., Pizza, C., Senatore, F., 1985b. Phenanthrene derivatives from *Tamus communis*. *Biochem. Syst. Ecol.* 13, 251–252.
- Aquino, R., Conti, C., de Simone, F., Orsi, N., Pizza, C., Stein, M.L., 1991. Antiviral activity of constituents of *Tamus communis*. *J. Chemother.* 3, 305–309.
- Bai, L., Yamaki, M., Inoue, K., Takagi, S., 1990. Blestrin A and B, bis(dihydrophenanthrene)ethers from *Bletilla striata*. *Phytochemistry* 29, 1259–1260.
- Bai, L., Kato, T., Inoue, K., Yamaki, M., Takagi, S., 1991. Blestrinol A, B and C, biphenanthrenes from *Bletilla striata*. *Phytochemistry* 30, 2733–2735.
- Bai, L., Kato, T., Inoue, K., Yamaki, M., Takagi, S., 1993. Stilbenoids from *Bletilla striata*. *Phytochemistry* 33, 1481–1483.
- Bai, L., Yamaki, M., Takagi, S., 1996. Stilbenoids from *Pleione bulbocodioides*. *Phytochemistry* 42, 853–856.
- Baller, A., Corrodi, H., Gaumann, E., Hardegger, E., Kern, H., Winterhalter-Wild, N., 1957. Wilting agents and antibiotics. XX. Induced defensive substances in the Orchidaceae. 1. *Helv. Chim. Acta* 40, 1062–1066.
- Barua, A.K., Ghosh, B.B., Ray, S., Patra, A., 1990. Cymbinodin-A, a phenanthraquinone from *Cymbidium aloifolium*. *Phytochemistry* 29, 3046–3047.
- Bhandari, S.R., Kapadi, A.H., Majumder, P.L., Joardar, M., Shoolery, J.N., 1985. Nudol, a phenanthrene of the orchids *Eulophia nuda*, *Eria carinata* and *Eria stricta*. *Phytochemistry* 24, 801–804.
- Bhaskar, M.U., Rao, L.J.M., Rao, N.S.P., Rao, P.R.M., 1991. Ochrone A, a novel 9,10-dihydro-1,4-phenanthraquinone from *Coelogyne ochracea*. *J. Nat. Prod.* 54, 386–389.
- Biswas, M., Som, U.K., Ghosh, P.K., Dutta, C.P., Banerji, A., 1988. Prazerol, a new 9,10-dihydrophenanthrene derivative isolated from *Dioscorea prazeri*. *Tetrahedron* 44, 4871–4876.
- Blitzke, T., Masaoud, M., Schmidt, J., 2000. Constituents of *Eulophia petersii*. *Fitoterapia* 71, 593–594.
- Bordat, P., Tarroux, R., Charveron, M., David, B., 2006. Phenanthrene derivatives, their synthesis, anti-inflammatory activity, and use in treating inflammatory skin diseases. *FRXXBL FR 2882357 A1* 20060825.
- Chapatwala, K.D., de la Cruz, A.A., Miles, D.H., 1981. Antimicrobial activity of juncosol, a novel 9,10-dihydrophenanthrene from the marsh plant *Juncus roemerianus*. *Life Sci.* 29, 1997–2001.
- Chen, C.-C., Wu, L.-G., Ko, F.-N., Teng, C.-M., 1994. Antiplatelet aggregation principles of *Dendrobium loddigesii*. *J. Nat. Prod.* 57, 1271–1274.
- Chen, C.-C., Huang, Y.-L., Teng, C.-M., 2000. Antiplatelet aggregation principles from *Ephemerantha lonchophylla*. *Planta Med.* 66, 372–374.
- Coxon, D.T., Ogundana, S.K., Dennis, C., 1982. Antifungal phenanthrenes in yam tubers. *Phytochemistry* 21, 1389–1392.
- de Alvarenga, M.A., Gottlieb, O.R., 1974. Methyl- and methylthio-phenanthrenes from *Micrandropsis scleroxylon*. *Phytochemistry* 13, 1283–1288.
- de Alvarenga, M.A., Gottlieb, O.R., Magalhaes, M.T., 1976. Methylphenanthrenes from *Sagotia racemosa*. *Phytochemistry* 15, 844–845.
- DellaGreca, M., Fiorentino, A., Mangoni, L., Molinaro, A., Monaco, P., Previtera, L., 1993. Cytotoxic 9,10-dihydrophenanthrenes from *Juncus effusus* L. *Tetrahedron* 49, 3425–3432.
- DellaGreca, M., Fiorentino, A., Monaco, P., Previtera, L., Zarrelli, A., 1995. Effusides I–V: 9,10-dihydrophenanthrene glucosides from *Juncus effusus*. *Phytochemistry* 40, 533–535.
- DellaGreca, M., Monaco, P., Previtera, L., Zarrelli, A., Pollio, A., Pinto, G., Fiorentino, A., 1997. Minor bioactive dihydrophenanthrenes from *Juncus effusus*. *J. Nat. Prod.* 60, 1265–1268.
- DellaGreca, M., Fiorentino, A., Isidori, M., Lavorgna, M., Monaco, P., Previtera, L., Zarrelli, A., 2002a. Phenanthrenoids from the wetland *Juncus acutus*. *Phytochemistry* 60, 633–638.
- DellaGreca, M., Fiorentino, A., Monaco, P., Previtera, L., Zarrelli, A., 2002b. A new dimeric 9,10-dihydrophenanthrenoid from the rhizome of *Juncus acutus*. *Tetrahedron Lett.* 43, 2573–2575.
- DellaGreca, M., Fiorentino, A., Monaco, P., Previtera, L., Temussi, F., Zarrelli, A., 2003. New dimeric phenanthrenoids from the rhizomes of *Juncus acutus*. Structure determination and antialgal activity. *Tetrahedron* 59, 2317–2324.
- DellaGreca, M., Isidori, M., Lavorgna, M., Monaco, P., Previtera, L., Zarrelli, A., 2004. Bioactivity of phenanthrenes from *Juncus acutus* on *Selenastrum capricornutum*. *J. Chem. Ecol.* 30, 867–879.
- Estrada, S., Rojas, A., Mathison, Y., Israel, A., Mata, R., 1999a. Nitric oxide/cGMP mediates the spasmolytic action of 3,4'-dihydroxy-5,5'-dimethoxybibenzyl from *Scaphyglottis livida*. *Planta Med.* 65, 109–114.
- Estrada, S., Toscano, R.A., Mata, R., 1999b. New phenanthrene derivatives from *Maxillaria densa*. *J. Nat. Prod.* 62, 1175–1178.
- Estrada, S., López-Guerrero, J.J., Villalobos-Molina, R., Mata, R., 2004. Spasmolytic stilbenoids from *Maxillaria densa*. *Fitoterapia* 75, 690–695.
- Estrada-Soto, S., López-Guerrero, J.J., Villalobos-Molina, R., Mata, R., 2006. Endothelium-independent relaxation of aorta rings by two stilbenoids from the orchids *Scaphyglottis livida*. *Fitoterapia* 77, 236–239.
- Fan, C., Wang, W., Wang, Y., Qin, G., Zhao, W., 2001. Chemical constituents from *Dendrobium densiflorum*. *Phytochemistry* 57, 1255–1258.
- Fisch, M.H., Flick, B.H., Arditti, J., 1973. Structure and antifungal activity of hircinol, loroglossol and orchinol. *Phytochemistry* 12, 437–441.
- Flegel, M., Adam, K.-P., Becker, H., 1999. Sesquiterpene lactones and bisbibenzyl derivatives from the neotropical liverwort *Frullania convoluta*. *Phytochemistry* 52, 1633–1638.
- Fukai, T., Wang, Q.-H., Nomura, T., 1991. Six prenylated phenols from *Glycyrrhiza uralensis*. *Phytochemistry* 30, 1245–1250.
- Ghosh, B.B., Ray, S., Bhattacharyya, P., Datta, P.K., Mukherjee, B.B., Patra, A., Banerjee, A.K., Barua, A.K., 1992. Cymbinodin B, a phenanthraquinone from *Cymbidium aloifolium*. *Indian J. Chem.* 31B, 557–558.
- Gorham, J., 1989. Stilbenes and phenanthrenes. *Meth. Plant Biochem.* 1, 159–196.
- Guo, X.-Y., Wang, J., Wang, N.-L., Kitanaka, S., Liu, H.-W., Yao, X.-S., 2006. New stilbenoids from *Pholidota yunnanensis* and their inhibitory effects on nitric oxide production. *Chem. Pharm. Bull.* 54, 21–25.
- Hernandez-Romero, Y., Rojas, J.-I., Castillo, R., Rojas, A., Mata, R., 2004. Spasmolytic effects, mode of action, and structure–activity relationships of stilbenoids from *Nidema boothii*. *J. Nat. Prod.* 67, 160–167.

- Hernandez-Romero, Y., Acevedo, L., de Sanchez, M., Shier, W.T., Abbas, H.K., Mata, R., 2005. Phytotoxic activity of bibenzyl derivatives from the orchid *Epidendrum rigidum*. J. Agric. Food Chem. 53, 6276–6280.
- Honda, C., Yamaki, M., 2000. Phenanthrenes from *Dendrobium plicatile*. Phytochemistry 53, 987–990.
- Juneja, R.K., Sharma, S.C., Tandon, J.S., 1987. Two substituted bibenzyls and a dihydrophenanthrene from *Cymbidium aloifolium*. Phytochemistry 26, 1123–1125.
- Kostecki, K., Engelmeier, D., Pacher, T., Hofer, O., Vajrodaya, S., Greger, H., 2004. Dihydrophenanthrenes and other antifungal stilbenoids from *Stemona cf. pierrei*. Phytochemistry 65, 99–106.
- Kovács, A., Forgo, P., Zupkó, I., Réthy, B., Falkay, Gy., Szabó, P., Hohmann, J., 2007. Phenanthrenes and a dihydrophenanthrene from *Tamus communis* and their cytotoxic activity. Phytochemistry 33, 687–692.
- Lee, Y.H., Park, J.D., Baek, N.I., Kim, S.I., Ahn, B.Z., 1995. *In vitro* and *in vivo* antitumoral phenanthrenes from the aerial parts of *Dendrobium nobile*. Planta Med. 61, 178–180.
- Leong, Y.-W., Kang, C.-C., Harrison, L.J., Powell, A.D., 1997. Phenanthrenes, dihydrophenanthrenes and bibenzyls from the orchid *Bulbophyllum vaginatum*. Phytochemistry 44, 157–165.
- Leong, Y.-W., Harrison, L.J., Powell, A.D., 1999. Phenanthrene and other aromatic constituents of *Bulbophyllum vaginatum*. Phytochemistry 50, 1237–1241.
- Leong, Y.-W., Harrison, L.J., 2004. A biphenanthrene and a phenanthro[4,3-*b*]furan from the orchid *Bulbophyllum vaginatum*. J. Nat. Prod. 67, 1601–1603.
- Letcher, R.M., Nhamo, L.R.M., 1971. Chemical constituents of the Combretaceae. Part I. Substituted phenanthrenes and 9,10-dihydrophenanthrenes from the heartwood of *Combretum apiculatum*. J. Chem. Soc. (C), 3070–3076.
- Letcher, R.M., Nhamo, L.R.M., 1972a. A revised structure for the tetra-substituted phenanthrene from *Tamus communis*. Tetrahedron Lett. 48, 4869–4870.
- Letcher, R.M., Nhamo, L.R.M., 1972b. Chemical constituents of the Combretaceae. Part III. Substituted phenanthrenes, 9,10-dihydrophenanthrenes, and bibenzyls from the heartwood of *Combretum psidioides*. J. Chem. Soc., Perkin Trans. I, 2941–2946.
- Letcher, R.M., Nhamo, L.R.M., Gumiro, I.T., 1972. Chemical constituents of the Combretaceae. Part II. Substituted phenanthrenes and 9,10-dihydrophenanthrenes and a substituted bibenzyl from the heartwood of *Combretum molle*. J. Chem. Soc., Perkin Trans. I, 206–211.
- Letcher, R.M., Wong, K.-M., 1978. Structure and synthesis the phenanthrenes TaI and TaV from *Tamus communis*. J. Chem. Soc., Perkin Trans. I, 739–742.
- Letcher, R.M., Wong, K.-M., 1979. Structure and synthesis of the phenanthrenes TaIV and TaVIII from *Tamus communis*. J. Chem. Soc., Perkin Trans. I, 2449–2450.
- Li, W.-K., Pan, J.-Q., Lü, M.-J., Zhang, R.-Y., Xiao, P.-G., 1995. A 9,10-dihydrophenanthrene derivative from *Epimedium koreanum*. Phytochemistry 39, 231–233.
- Lin, T.-H., Chang, S.-J., Chen, C.-C., Wang, J.-P., Tsao, L.-T., 2001. Two phenanthraquinones from *Dendrobium moniliforme*. J. Nat. Prod. 64, 1084–1086.
- Lin, Y.-L., Huang, R.-L., Don, M.-J., Kuo, Y.-H., 2000. Dihydrophenanthrenes from *Spiranthes sinensis*. J. Nat. Prod. 63, 1608–1610.
- Lin, Y.-L., Wang, W.-Y., Kuo, Y.-H., Liu, Y.-H., 2001. Homocyclotirucallane and two dihydrophenanthrenes from *Spiranthes sinensis*. Chem. Pharm. Bull. 49, 1098–1101.
- Lin, Y.-L., Chen, W.-P., Macabalan, A.D., 2005. Dihydrophenanthrenes from *Bletilla formosana*. Chem. Pharm. Bull. 53, 1111–1113.
- Liu, D., Ju, J., Zou, Z., Lin, G., Yang, J., 2005a. Isolation and structure determination of cypritetquinone A and B, two new phenanthraquinones from *Cypripedium tibeticum*. Yaoxue Xuebao. Acta Pharm. Sin. 40, 255–257.
- Liu, M.-F., Han, Y., Xing, D.-M., Wang, W., Xu, L.-Z., Du, L.-J., Ding, Y., 2005b. One new benzylidihydrophenanthrene from *Arundina graminifolia*. J. Asian Nat. Prod. Res., 767–770.
- Long, L., Lee, S.K., Chai, H.-B., Rasoanaivo, P., Gao, Q., Navarro, H., Wall, M.E., Wani, M.C., Farnsworth, N.R., Cordell, G.A., Pezzuto, J.M., Kinghorn, A.D., 1997. Novel bioactive phenanthrene derivatives from *Domohinea perrieri*. Tetrahedron 53, 15663–15670.
- Majumder, P., Laha, S., Datta, N., 1982. Coelonin, a 9,10-dihydrophenanthrene from the orchids *Coelogyne ochracea* and *Coelogyne elata*. Phytochemistry 21, 478–480.
- Majumder, P.L., Kar, A., Shoolery, J.N., 1985. Bulbophyllanthrin, a phenanthrene of the orchid *Bulbophyllum leopardium*. Phytochemistry 24, 2083–2087.
- Majumder, P.L., Kar, A., 1987a. Confusarin and confusarinidin, two phenanthrene derivatives of the orchid *Eria confusa*. Phytochemistry 26, 1127–1129.
- Majumder, P.L., Sen, R.C., 1987b. Structure of moscatin – a new phenanthrene derivative from *Dendrobium rotundatum*. Indian J. Chem. 26B, 18–20.
- Majumder, P.L., Banerjee, S., 1988a. Structure of flavanthrin, the first dimeric 9,10-dihydrophenanthrene derivative from the orchid *Eria flava*. Tetrahedron 44, 7303–7308.
- Majumder, P.L., Banerjee, S., 1988b. A ring-B oxygenated phenanthrene derivative from the orchid *Bulbophyllum gymnopus*. Phytochemistry 27, 245–248.
- Majumder, P.L., Banerjee, S., 1990a. Two stilbenoids from the orchid *Eria flava*. Phytochemistry 29, 3052–3055.
- Majumder, P.L., Basak, M., 1990b. Cirrhopenalin, a phenanthrene derivative from *Cirrhopenatum andersonii*. Phytochemistry 29, 1002–1004.
- Majumder, P.L., Lahiri, S., 1990c. Volucrin, a new dimeric phenanthrene derivative from the orchid *Lusia volucris*. Tetrahedron 46, 3621–3626.
- Majumder, P.L., Lahiri, S., 1990d. Lusianthrin and lusianthridin, two stilbenoids from the orchid *Lusia indivisa*. Phytochemistry 29, 621–624.
- Majumder, P.L., Pal, A., Joardar, M., 1990e. Cirrhopenalanthrin, a dimeric phenanthrene derivative from the orchid *Cirrhopenatum maculosum*. Phytochemistry 29, 271–274.
- Majumder, P.L., Basak, M., 1991a. Two stilbenoids from the orchid *Cirrhopenatum andersonii*. Phytochemistry 30, 3429–3432.
- Majumder, P.L., Sen, R.C., 1991b. Pendulin, a polyoxygenated phenanthrene derivative from the orchid *Cymbidium pendulum*. Phytochemistry 30, 2432–2434.
- Majumder, P.L., Pal, S., 1992. Rotundatin, a new 9,10-dihydrophenanthrene derivative from *Dendrobium rotundatum*. Phytochemistry 31, 3225–3228.
- Majumder, P.L., Banerjee, S., Maiti, D.C., Sen, S., 1995. Stilbenoids from the orchids *Agrostophyllum callosum* and *Coelogyne flaccida*. Phytochemistry 39, 649–653.
- Majumder, P.L., Banerjee, S., Sen, S., 1996. Three stilbenoids from the orchid *Agrostophyllum callosum*. Phytochemistry 42, 847–852.
- Majumder, P.L., Banerjee, S., Lahiri, S., Mukhoti, N., Sen, S., 1998a. Dimeric phenanthrenes from two *Agrostophyllum* species. Phytochemistry 47, 855–860.
- Majumder, P.L., Roychowdhury, M., Chakraborty, S., 1998b. Thunalbene, a stilbene derivative from the orchid *Thunia alba*. Phytochemistry 49, 2375–2378.
- Majumder, P.L., Pal, S., Majumder, S., 1999. Dimeric phenanthrenes from the orchid *Bulbophyllum reptans*. Phytochemistry 50, 891–897.
- Majumder, P.L., Sen, S., Majumder, S., 2001. Phenanthrene derivatives from the orchid *Coelogyne cristata*. Phytochemistry 58, 581–586.
- Malan, E., Swinny, E., 1993. Substituted bibenzyls, phenanthrenes and 9,10-dihydrophenanthrenes from the heartwood of *Combretum apiculatum*. Phytochemistry 34, 1139–1142.

- Matsuda, H., Morikawa, T., Xie, H., Yoshikawa, M., 2004. Antiallergic phenanthrenes and stilbenes from the tubers of *Gymnadenia conopsea*. *Planta Med.* 70, 847–855.
- Morikawa, T., Xie, H., Matsuda, H., Wang, T., Yoshikawa, M., 2006. Bioactive constituents from Chinese natural medicines. XVII. Constituents with radical scavenging effect and new glucosyloxybenzyl 2-isobutylmalates from *Gymnadenia conopsea*. *Chem. Pharm. Bull.* 54, 506–513.
- Pacher, T., Seger, C., Engelmeier, D., Vajrodaya, S., Hofer, O., Greger, H., 2002. Antifungal stilbenoids from *Stemona collinsae*. *J. Nat. Prod.* 65, 820–827.
- Pettit, G.R., Singh, S.B., Niven, M.L., Schmidt, J.M., 1988. Cell growth inhibitory dihydrophenanthrene and phenanthrene constituents of the african tree *Combretum caffrum*. *Can. J. Chem.* 66, 406–413.
- Reisch, J., Báthory, M., Szendrei, K., Minker, E., Novák, I., 1969. Stickstoff-freie Phenanthren-derivate aus dem Rhizom von *Tamus communis* L. *Tetrahedron Lett.* 2, 67–68.
- Reisch, J., Báthory, M., Novák, I., Szendrei, K., 1970. Természetes fenantrén-vegyületek szerkezete és szintézise. *Herba Hung.* 9, 43–47.
- Reisch, J., Báthory, M., Szendrei, K., Novák, I., Minker, E., 1973. Weitere Phenanthrene aus dem Rhizom von *Tamus communis*. *Phytochemistry* 12, 228–229.
- Réthy, B., Kovács, A., Zupkó, I., Forgo, P., Vasas, A., Falkay, Gy., Hohmann, J., 2006. Cytotoxic phenanthrenes from the rhizomes of *Tamus communis*. *Planta Med.* 72, 767–770.
- Rycroft, D.S., Cole, W.J., Aslam, N., Lamont, Y.M., Gabriel, R., 1999. Killarniensolide, methyl orsellinates and 9,10-dihydrophenanthrenes from the liverwort *Plagiochila killarniensis* from Scotland and the Azores. *Phytochemistry* 50, 1167–1173.
- Sarkar, H., Zerezhgi, M., Bhattacharyya, J., 1988. Dehydrojuncosol, a constituent of the roots of *Juncus roemerianus*. *Phytochemistry* 27, 3006–3008.
- Shima, K., Toyota, M., Asakawa, Y., 1991. Phenanthrene derivatives from the medullae of *Juncus effusus*. *Phytochemistry* 30, 3149–3151.
- Sunder, R., Rangaswami, S., Reddy, G.C.S., 1978. A new dihydrophenanthrene from *Dioscorea decipiens*. *Phytochemistry* 17, 1067.
- Takagi, S., Yamaki, M., Inoue, K., 1983. Antimicrobial agents from *Bletilla striata*. *Phytochemistry* 22, 1011–1015.
- Takasugi, M., Kawashima, S., Monde, K., Katsui, N., Masamune, T., Shirata, A., 1987. Antifungal compounds from *Dioscorea batatas* inoculated with *Pseudomonas cichorii*. *Phytochemistry* 26, 371–375.
- Tezuka, Y., Ji, L., Hirano, H., Ueda, M., Nagashima, K., Kikuchi, T., 1990. Studies on the constituents of orchidaceous plants. IX. Constituents of *Spiranthes sinensis* (Pers.) Ames var. *amoena* (M. Biebersson) Hara. (2). Structures of spiranthesol, spiranthoquinone, spiranthol-C, and spirasineol-B, new isopentenylidihydrophenanthrenes. *Chem. Pharm. Bull.* 38, 629–635.
- Tezuka, Y., Hirano, H., Kikuchi, T., Xu, G.J., 1991. Constituents of *Ephemerantha lonchophylla*: isolation and structure elucidation of new phenolic compounds, ephemeranthol-A, ephemeranthol-B, and ephemeranthoquinone, and of a new diterpene glucoside, ephemeranthoside. *Chem. Pharm. Bull.* 39, 593–598.
- Tezuka, Y., Yoshida, Y., Kikuchi, T., Xu, G.J., 1993. Constituents of *Ephemerantha fimbriata*. Isolation and structure elucidation of two new phenanthrenes, fimbriol-A and fimbriol-B, and a new dihydrophenanthrene, ephemeranthol-C. *Chem. Pharm. Bull.* 41, 1346–1349.
- Tori, M., Hashimoto, A., Hirose, K., Asakawa, Y., 1995. Diarylheptanoids, flavonoids, stilbenoids, sesquiterpenoids and a phenanthrene from *Alnus maximowiczii*. *Phytochemistry* 40, 1263–1264.
- Tuchinda, P., Udchachon, J., Khumtaveeporn, K., Taylor, W.C., Engelhardt, L.M., White, A.H., 1988. Phenanthrenes of *Eulophia nuda*. *Phytochemistry* 27, 3267–3271.
- Valencia-Islas, N.A., Paul, R.N., Shier, W.T., Mata, R., Abbas, H.K., 2002. Phytotoxicity and ultrastructural effects of gymnopusin from the orchid *Maxillaria densa* on duckweed (*Lemna paucicostata*) frond and root tissues. *Phytochemistry* 61, 141–148.
- Wij, M., Rangaswami, S., 1978. Chemical components of *Dioscorea bulbifera*: isolation and structure of a new dihydrophenanthrene (2,4,6,7-tetrahydroxy-9,10-dihydrophenanthrene) and a new phenanthrene (2,4,5,6-tetrahydroxyphenanthrene). *Indian J. Chem.* 16B, 643–644.
- Xue, Z., Li, S., Wang, S., Wang, Y., Yang, Y., Shi, J., He, L., 2006. Mono-, bi-, and triphenanthrenes from the tubers of *Cremastra appendiculata*. *J. Nat. Prod.* 69, 907–913.
- Yamaki, M., Bai, L., Inoue, K., Takagi, S., 1989. Biphenanthrenes from *Bletilla striata*. *Phytochemistry* 28, 3503–3505.
- Yamaki, M., Bai, L., Inoue, K., Takagi, S., 1990. Benzylphenanthrenes from *Bletilla striata*. *Phytochemistry* 29, 2285–2287.
- Yamaki, M., Kato, T., Bai, L., Inoue, K., Takagi, S., 1991. Methylated stilbenoids from *Bletilla striata*. *Phytochemistry* 30, 2759–2760.
- Yamaki, M., Bai, L., Kato, T., Inoue, K., Takagi, S., Yamagata, Y., Tomita, K.-I., 1992. Bisphenanthrene ethers from *Bletilla striata*. *Phytochemistry* 31, 3985–3987.
- Yamaki, M., Bai, L., Kato, T., Inoue, K., Takagi, S., Yamagata, Y., Tomita, K.-I., 1993a. Blespirol, a phenanthrene with a spiroactone ring from *Bletilla striata*. *Phytochemistry* 33, 1497–1498.
- Yamaki, M., Kato, T., Bai, L., Inoue, K., Takagi, S., 1993b. Phenanthrene glucosides from *Bletilla striata*. *Phytochemistry* 34, 535–537.
- Yamaki, M., Honda, C., 1996. The stilbenoids from *Dendrobium plicatile*. *Phytochemistry* 43, 207–208.
- Ye, Q.-H., Zhao, W.-M., Qin, G.-W., 2003. New fluorenone and phenanthrene derivatives from *Dendrobium chrysanthum*. *Nat. Prod. Res.* 17, 201–205.
- Zhang, G.-N., Zhong, L.-Y., Bligh, S.W.A., Guo, Y.-L., Zhang, C.-F., Zhang, M., Wang, Z.-T., Xu, L.-S., 2005. Bi-bicyclic and bi-tricyclic compounds from *Dendrobium thyrsiflorum*. *Phytochemistry* 66, 1113–1120.



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determination of biologically active diterpenoids from Euphorbiaceae