Mycological Progress (2022) 21: 38
https://doi.org/10.1007/s11557-022-01790-4

DGfM

REVIEW

Fungal perylenequinones

Afra Khiralla[1] · Aisha Ohag Mohammed[2] · Sakina Yagi[3]

Received: 30 September 2021 / Revised: 6 February 2022 / Accepted: 7 February 2022 / Published online: 4 April 2022

Abstract

Perylenequinones (PQs) are aromatic polyketides with an oxidized pentacyclic core that make up a family of natural compounds. Naturally occurring PQs mostly are produced by phytopathogenic fungi, with few aphides, crinoids, and plants. PQs, also known as photosensitizers, absorb light energy which empowers them to produce reactive oxygen species that damage host cells. Therefore, PQs gained a considerable interest in pharmaceutical application notably in photodynamic therapy. This review presents a comprehensive overview of fungal PQs. Their occurrence, categorization, biosynthesis, structures, and bioactivities are all discussed in detail. After that, an analysis outlines their distribution across the kingdom of fungi. A total of 66 fungal PQs have been described from 22 ascomycete genera (*Alternaria, Aspergillus*, *Bulgaria*, *Cenococcum*, *Cercospora*, *Cladosporium*, *Curvularia*, *Daldinia*, *Elsinoë*, *Hypocrella*, *Hypomyces*, *Parastagonospora*, *Phaeosphaeria*, *Phylacia*, *Pyrenochaeta*, *Rhopalostroma*, *Rubroshiraia, Setophoma, Shiraia*, *Stemphylium*, *Stagonospora*, and *Thamnomyces*). *Dothideomycetes* account for the majority of documented fungal PQs (82%), followed by *Sordariomycetes* (14%), *Leotiomycetes* (3%), and *Eurotiomycetes* (1%). Herein, five families *Pleosporaceae*, *Phaeosphaeriaceae*, *Cladosporiaceae*, *Shiraiaceae*, and *Hypoxylaceae* are highlighted as potential sources of novel PQs due to their diversity. The review intends to pique bioprospectors' interest in fungal PQs. Indeed, the pharmaceutical and agrochemical industries might gain greatly by exploiting fungal perylenequinones.

Keywords Fungal natural products · Perylenequinones · Photodynamic therapy · *Dothideomycetes* · *Sordariomycetes*

Introduction

Fungal natural products have received a considerable attention. Several studies unveiled their amazing assortment. Perylenequinones (PQs) are members of natural products' family characterized by an oxidized pentacyclic core represented by the parent perylenequinone 4,9-dihydroxyperylene -3,l0-quinone (**25**). Fungi are the best source for PQs as 85% of all known PQs are reported from fungi, compared to 12% for *Animalia*, and only 3% for *Plantae*. PQ pigments are produced by a wide variety of molds, the most of which are phytopathogens, with few marine sponge-derived, endolichenic, and endophytic fungi (Weiss et al. 1987; Pang et al. 2018; Tantry et al. 2018). Insects are an alternative source of PQs, such as rodoaphin, which is synthetized by aphids. In addition, the stalked crinoid *Gymnocrinus richeri* produced gymnochromes. PQs are also found in few plant species, such as scutiaquinones A and B were discovered in the root of *Scutia myrtina*. Besides, hypericin is one of *Hypericum's* principal active constituents (Weiss and Altland 1965; Miskovsky 2002; Ayers et al. 2007). Moreover, PQs have been extracted from aquatic sediments and soil matter. 4,9-dihydroxyperylene-3,l0-quinone (**25**) and its derivatives were recovered from Japanese Andosols and Cambisol (Hanke et al. 2019; Kobayashi et al. 2019).

Perylenequinones are anticipated to be some of the most promising photodynamic therapy (PDT) agents (Olivo and Ali-Seyed 2007). PDT is a cancer and non-malignant condition treatment that comprises the delivery of a photosensitizing

Section Editor: Marc Stadler

✉ Afra Khiralla
aafraa21@hotmail.com

[1] Botany Department, Faculty of Science and Technology, Shendi University, P.O. Box 142, Shendi, Sudan

[2] Department of Biology, Faculty of Science Al-Zulfi, Majmaah University, Al-Zulfi, Saudi Arabia

[3] Botany Department, Faculty of Science, University of Khartoum, Khartoum, Sudan

chemical such as PQs, followed by exposure of the tissue to non-thermal visible light (400–760 nm). When the molecule is stimulated by light of the appropriate wavelength, the photosensitizer is activated. This produces a series of molecular energy transfers leading to the release of singlet oxygen, a highly reactive and cytotoxic species, resulting in apoptosis. Drug uptake in malignant tissues combined with selective light treatment has the potential to give an effective cancer therapy with efficient cytotoxicity and minimal impairment to surrounding normal tissue (Ackroyd et al. 2001). PDT also provides several advantages over other standard clinical therapies, including more efficiency, greater safety, and decreased toxicity for surrounding normal tissues due to increasing accumulation of photosensitizers and irradiation on diseased targets (Yano et al. 2011). As compared to other photosensitizers investigated, such as porphyrin and phthalocyanine-like photosensitizers, PQs virtually exhibit all of the characteristics of ideal photosensitizers (Li et al. 2015). Hypocrellins A–B (**50–51**) have many advantages that might make them fascinating sensitizers for PDT. They are readily obtained, simply purified, very stable, low in toxicity, and do not form aggregates which would decrease their photodynamic activity. Although hypocrellin A (**50**) is phototoxic, it is rapidly removed from live organisms, usually within 24 h. Its photosensitizing side effects in PDT are considerably reduced as a result of this. In addition, hypocrellin A (**50**) is non-toxic in the absence of light (Diwu and William 1990). Several investigations have been conducted on the apoptotic and cytotoxic effects of some fungal PQs, including calphostin C (**42**), elsinochromes A (**45**), C (**47**), hypocrellin (**49**), and hypocrellin A (**50**). These studies highlighted their potential as promising anticancer medications and explored their application in cancer therapy (Dubauskas et al. 1998; Fang et al. 2006; Olivo and Ali-Seyed 2007; So et al. 2018; Tantry et al. 2018; Mastrangelopoulou et al. 2019). Furthermore, Sharma et al. (2013) have invented a patent (US 8,506,931 B2), that contains hypocrellin derivatives. These compounds can be particularly useful as photosensitizers or sononsensitizers in photodynamic or sonodynamic therapy. Also useful as therapeutic agents for treating various hyperproliferative disorders. Since two decades, the antiviral activity of various PQs has been studied (Hudson et al. 1997; Krishnamoorthy et al. 2005; Wiehe et al. 2019). Hudson and associates discovered a correlation between singlet oxygen ($^1O_2$) quantum yield and antiviral activity (Hudson et al. 1997). Other remarkable biological properties of PQs have been noted, such as the prevention of skin diseases caused by fungal infections, antileishmanial, antimalarial, antimicrobial properties, and mutagenicity (Wang and Bao 1985; Stack and Prival 1986; Diwu 1995; Ma et al. 2004; Fang et al. 2006; Tantry et al. 2018).

PQs were exploited in agriculture field as fungicides. In 2005, a patent (US 6,936,571 B2) was invented by Zhnag and Liu. The active constituents of the fungicide are selected perylenequinone derivatives including cercosporin (**30**), phleichrome (**31**), cladochromes A–D (**33-36**), elsinochromes A–C (**45–47**), hypocrellins A–B (**50–51**), and hypomycins A–B (**53–54**) (Zhnag and Liu 2005). PQs, on the other hand, have a promising environmental role as pesticides, due to their rapid degradation. Ahonsi et al. (2005) stated that, elsinochrome A (**45**) degrades rapidly in such conditions. They advocated for the release of elsinochrome A (**45**) into the environment, particularly in exposed niches such as spraying biocontrol product on plant surfaces, or release from shed diseased leave. This review gathers a comprehensive compilation of published findings on fungal PQs. The taxonomy of PQs and their biosynthesis come first in the introduction. Then, the review is divided into two sections, the first of which highlights a bibliography of fungal PQs and illustrates their structures. The distribution of PQ-producing fungi within the kingdom of fungi is the subject of section two, and the findings are summarized in a brief conclusion.

Classification of perylenequinones

Natural PQs have been categorized into three broad classes (Fig. 1), according to Weiss et al. (1987).

A. Class A: C_{20} compounds without carbon substituents

Class A consists of the simple PQs including the parent perylenequinone 4,9-dihydroxyperylene-3,l0-quinone (**25**), which is found in *Daldinia* and other fungal taxa. Eleven genera (Table 1) produced partially reduced perylenequinones of class A.

B. Class B: PQs carrying carbon substituents

Class B is derived from the unit of cercosporin (**30**) and phleichrome (**31**), with or without additional alicyclic rings. It appears that PQs of class B are enriched in many phytopathogenic strains and have a role in plant pathogenicity. PQs of class B are produced via 11 genera (Table 1). 4,9-Dihydroxyperylene-3, l0-quinone (**25**) is an achiral planar substance. In most fungal perylenequinones, structural elements such as the two bulky methoxy groups or a strained seven-membered ring in positions 6 and 7, together with two C_3 side chains in positions 1 and 12, are the source of enough steric interruption to force the pentacyclic perylenequinone system into a nonplanar helical shape (Weiss et al. 1987; Mulrooey et al. 2012; Hu et al. 2019). This helicity generates an element of asymmetry, the axial chirality M or P of the perylenequinone molecule (Fig. 2). More information concerning stereochemistry of PQs are available (Weiss et al. 1987). Class B was divided into three subclasses (Fig. 1) based on the core structures: (1) Perylenequinone core

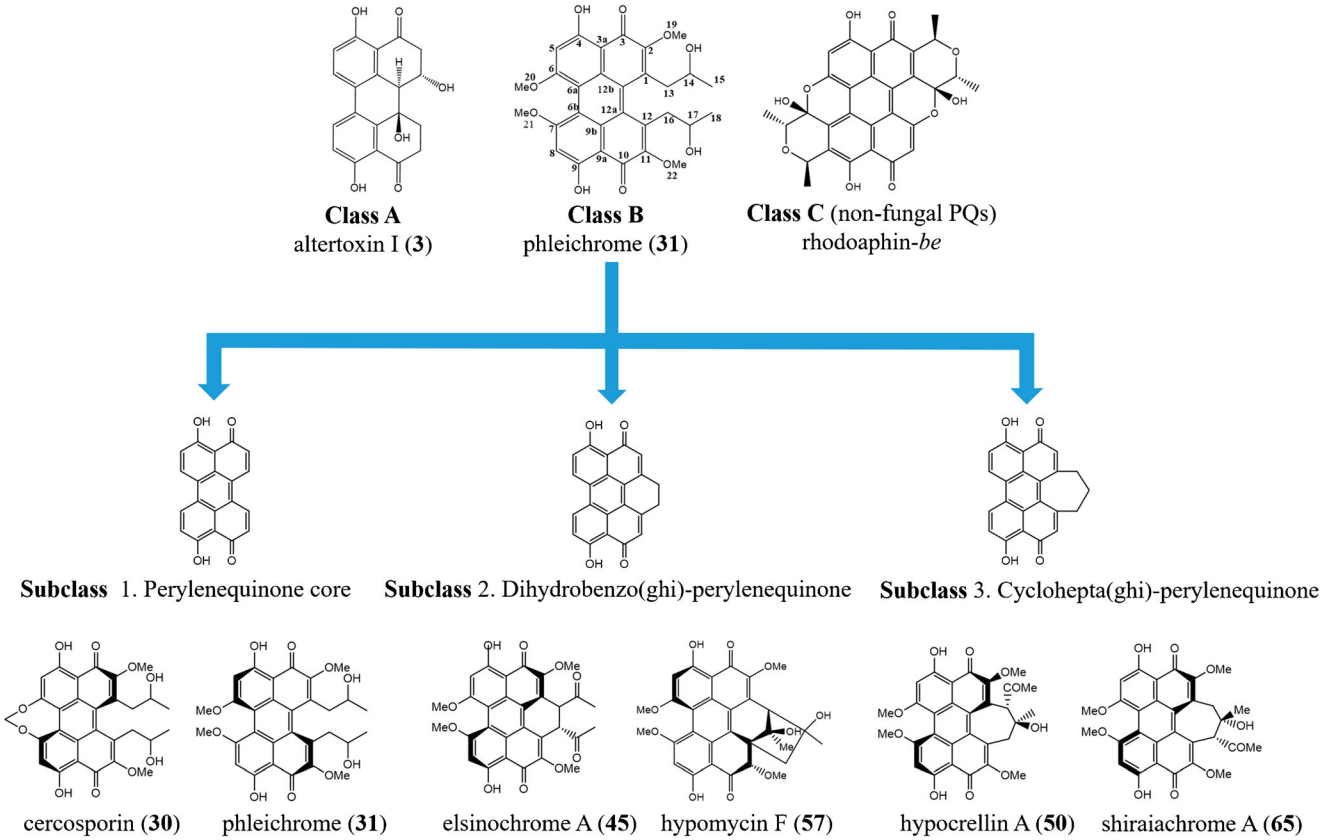


Fig. 1 Classification of perylenequinones

includes cercosporin, phleichrome, cladochromes, and calphostins (2) Dihydrobenzo (ghi)perylenequinone contains: elsinochromes, hypomycins, and phaeosphaerins (3) Cyclohepta(ghi)perylenequinone involves hypocrellins and shiraiachromes (Hu et al. 2019).

C. Class C

The parent perylenequinone 4,9-dihydroxyperylene-3, l0-quinone (**25**) with extra alicyclic rings is classified as class C. Other non-fungal species, such as aphids, crinoids, and plants formed PQs of class C, e.g., rhodoaphin-*be*, erythrouphins-*fb* and *–sl*, gymnochromes, scutiaquinones A and B (Weiss and Altland 1965; Miskovsky 2002; Ayers et al. 2007). The classification of fungal perylenequinones is shown in Fig. 1.

Biosynthesis of fungal perylenequinones

PQs captivated biologists with their role in fungal virulence, potent biological activities, as well as chemists due to their interesting axial chirality and photochemical characteristics (Diwu and Lown 1993; Mulrooey et al. 2010; Daub et al. 2013; So et al. 2018). Therefore, the biosynthetic gene clusters (BGCs) of some fungal PQs like cercosporin (**30**), elsinochrome C (**47**), and hypocrellin A (**50**) have been identified.

Cercosporin (**30**) has a typical pentacyclic perylenequinone core; however, it is distinguished by the presence of an asymmetric 1,3-dioxepine moiety. Cercosporin (**30**) was discovered in *Cercospora kikuchii*, the pathogenic fungus that causes soy bean purple speck disease (Kuyama and Tamura 1957). *CTB* cluster for biosynthesis of cercosporin (**30**) from *Cercospora nicotianae* was the first BGC to be found (Chen et al. 2007; Newman and Townsend 2016; Hu et al. 2019). Elsinochromes (**45–48**) are characterized by the hexacyclic dihydrobenzo(ghi)perylenequinone core. 1n 2017, Chooi and coworkers discovered the *elc* cluster for biosynthesis of elsinochrome C (**47**) in *Parastagonospora nodorum,* that causes septoria nodorum blotch in wheat, which has been proven to be important for its pathogenicity (Chooi et al. 2017). Three bamboo parasitic fungi produced hypocrellins, *Hypocrella bambusae*, *Shiraia bambusicola*, and *Rubroshiraia bambusae*. Hypocrellins (**49–52**) are considered by the hexacyclic cyclohepta(ghi)perylenequinone core, they are notorious to be present in traditional Chinese medicine (Yu et al. 1993). Based on gene expression correlation, the *HYP* cluster for hypocrellin A (**50**) production was discovered in *Shiraia* sp. Slf14 (Yang et al. 2014), and subsequently verified by targeted gene deletion, the monooxygenase-

Table 1 List of PQ-producing genera

Perylenequinone classes	Genera	References
Class A	*Alternaria*	(Idris et al. 2015)
	Aspergillus	(Zhang et al. 2017)
	Bulgaria	(Xian et al. 2006)
	Cenococcum	(Peter et al. 2016)
	Curvularia	(Cruz et al. 2020)
	Daldinia	(Anderson and Murray 1956)
	Phylacia	(Wendt et al. 2018)
	Rhopalostroma	(Stadler et al. 2010)
	Setophoma	(Bazioli et al. 2020)
	Stemphylium	(Podlech et al. 2014)
	Thamnomyces	(Wendt et al. 2018)
Class B	*Cercospora*	(Mastrangelopoulou et al. 2019)
	Cladosporium	(Pettit 2011)
	Elsinoë	(Jiao et al. 2019)
	Hypocrella	(Li et al. 2021)
	Hypomyces	(Liu et al. 2001b, a)
	Parastagonospora	(Chooi et al. 2017)
	Phaeosphaeria	(Li et al. 2012)
	Pyrenochaeta	(Kurobane et al. 2006)
	Rubroshiraia	(Dai et al. 2019)
	Shiraia	(Fang et al. 2006)
	Stagonospora	(Ahonsi et al. 2005)

encoding gene (Mono) which is located in the hypocrellin gene cluster of *Shiraia* sp. (Deng et al. 2018).

Biosynthesis of fungal PQs has been extensively investigated and revised several times to disclose the ambiguity. The *CTB*, *elc*, and *HYP* gene clusters contain multiple shared homologs (Fig. 3) (Chen et al. 2007; Yang et al. 2014; Newman and Townsend 2016; Chooi et al. 2017; Deng et al. 2018; Hu et al. 2019). The phylogenetic analysis of *elcA* and allied fungal non-reducing PKSs revealed that *elcA* is more closely related to *Shiraia* sp. *HYP1* than to *C. nicotianae CTB1*. The *elc* gene cluster shares more homologues with *HYP* gene cluster compared with *CTB* cluster as well. Due to their structures, both hypocrellin A (**50**) and elsinochrome A (**45**) have a hexacyclic system while cercosporin (**30**) is pentacyclic, the additional homologous genes shared between *elc* and *HYP* gene clusters but not *CTB* could be responsible for the formation of the additional ring (Chooi et al. 2017).

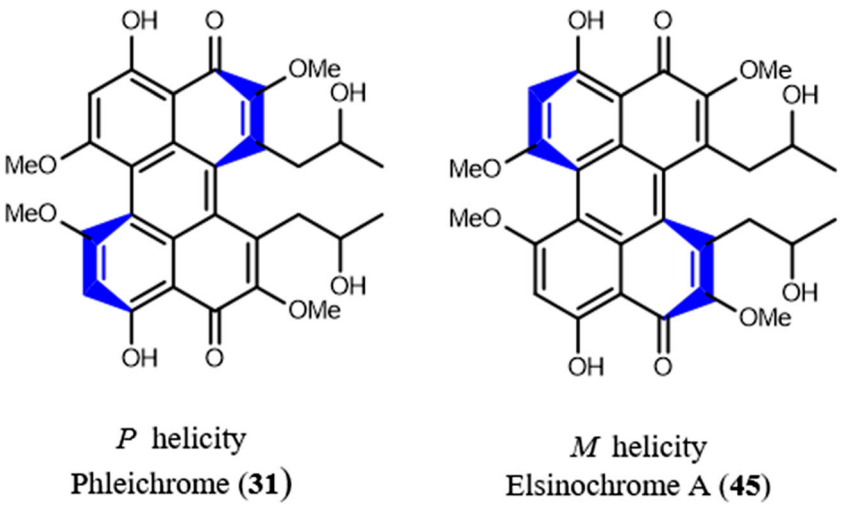


Fig. 2 Axial chirality *P* and *M* of perylenequinones

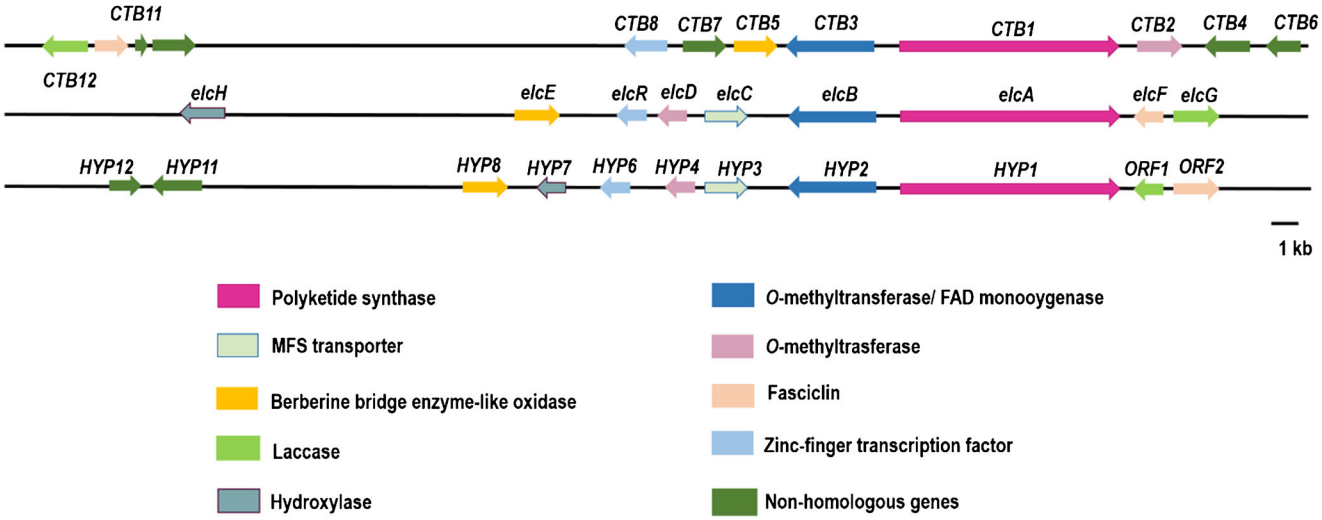


Fig. 3 The biosynthetic gene clusters of cercosporin *CTB*, elsinochrome A (**45**) *elc*, and hypocrellin A (**50**) *HYP*. Modified from Chooi et al. (2017) and Hu et al. (2019)

The most recent biosynthesis of perylenequinones was proposed by Hu et al. (2019) (Fig. 4). A common aromatic polyketide precursor serves as the starting point for biosynthesis, nor-toralactone **I**, which is synthesized by the non-reducing polyketide synthase (PKS) *CTB1*/*elcA*/*HYP1*. The subsequent step was achieved by bifunctional enzyme *CTB3*/*elcB*/*HYP2* homolog, which possesses fused *O*-methyltransferase and Favin-dependent monooxygenase domains. This enzyme is responsible for methylation, hydroxylation, ring opening, decarboxylation of nor-toralactone **I** to afford toralactone **II**, then naphthol intermediate **III**. The *O*-methyltransferase *CTB2*/*elcD*/*HYP4* is proposed to methylate the nascent OH-6 of intermediate **III**, blocking further oxidation at this site and yielding compound **IV**. The oxidative coupling steps to generate the pentacyclic core was elusive. Hu and collaborators have revealed the vagueness by demonstrating a heterologous biosynthesis, that cognate pairing of both Berberine Bridge Enzyme-like Oxidase (BBEO) *elcE*/*CTB5* and Laccase-like Multi Copper Oxidase (LMCO) *elcG*/*CTB12* for the double coupling step of two naphthol intermediates to afford the perylenequinone core **V**. Elsinochrome A (**45**) is synthesized via a radical process triggered by a single electron transfer from an enolate at the side chain to the FAD in *elcH* via the putative perylenequinone intermediate **V**. In the absence of *elcH*, hypocrellins (**49**–**50**) are formed, suggesting that they are most likely derived from the putative intermediate **V** via a transannular aldol reaction (Newman and Townsend 2016; Deng et al. 2018; Hu et al. 2019). *CTB5*, *6*, *7*, *9*, and *10* afford cercosporin (**30**) through different reactions including reduction and homodimerization of the intermediates. The Zinc finger transcription factor *CTB8* co-regulates expression of the cluster, while the Major Facilitator Superfamily (MFS) transporter *CTB4* exports the final metabolite (Chen et al. 2007; Choquer et al. 2007; Newman and Townsend 2016).

Stimulation of PQs' production

Light is an essential factor that regulates several physiological activities of fungi such as growth, reproduction, and biosynthesis of metabolites (Corrochano 2007). Conversely to plants, fungi use light as a source of information rather than energy (Tisch and Schmoll 2010). There is a strong evidence that light influences the synthesis of certain PQs. A significant increase in hypocrellin A (**50**) yield was observed, when *Shiraia* spp. were cultured under light-dark shift and red light (Sun et al. 2018; Ma et al. 2019a). The role of light in formation of cercosporin and elsinochromes by *Cercospora nicotianae*, C. *kikuchii*, and *Elsinoë fawcettii* was emphasized (Ehrenshaft and Upchurch 1991; Choquer et al. 2007). Light, on the other hand, is not required for biosynthesis of all PQs. Light seemed not to induce the synthesis of elsinochrome C (**47**) by *Parastagonospora nodorum* (Liao and Chung 2008). Several other factors, such as media, nutrition, growth conditions, and environmental variables, have an impact on PQs production. The synthesis of hypocrellin (**49**) increased on rice medium compared to Cheerios or oatmeal medium in solid-fermentation cultures (Al Subeh et al. 2020). The use of Triton X-100 and low-intensity ultrasound irradiation resulted in a significant increase in hypocrellin A (**50**) production (Lei et al. 2017; Sun et al. 2017). The formation of different PQs was boosted by co-cultivation of a hypocrellin-producing fungus with bacteria (Ma et al. 2019b).

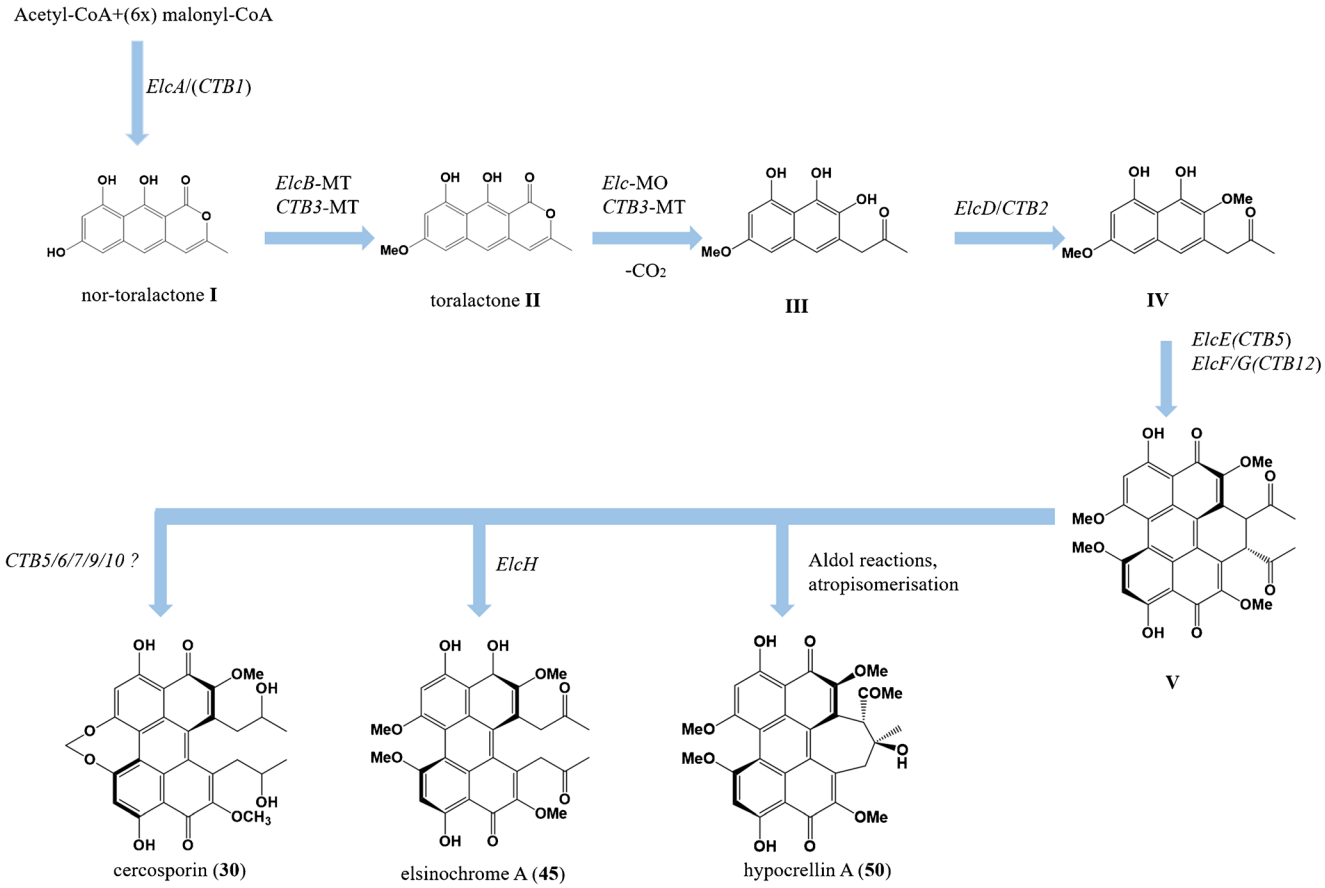


Fig. 4 Proposed biosynthetic pathway for three perylenequinones of class B: cercosporin (**30**), elsinochrome A (**45**), and hypocrellin (**50**). Modified from Hu et al. (2019)

Section one: fungal perylenequinones

Fungal PQs fall into two classes (A and B) of perylenequinones. This section includes the bibliography of known PQs between 1956 and 2021, as well as their structures and biological activities. A total of 66 fungal PQs have been found in 22 fungal genera. Table 2 shows a list of fungal PQs as well as their producers.

Class A perylenequinones

Eleven ascomycete genera (Table 1) have been reported to produce 29 PQs of class A (Figs. 5 and 6). Most of them (24 compounds) are synthetized by *Alternaria* spp. Class A perylenequinones displayed diverse biological properties such as cytotoxicity, antiviral, antimicrobial, antileishmanial, and antimalarial activities.

Alternaria Nees ex Fr

The genus *Alternaria* (*Pleosporaceae*, *Pleosporales*) contains 366 accepted and recognizable species. Some species cause pre-harvest and post-harvest damage to cereal grains, fruits, and vegetables (Patriarca and Pinto 2018; Wijayawardene et al. 2020). *Alternaria* spp. produced several toxins including PQs. A total of 24 perylenequinones were recovered from *Alternaria* species. Recently, two dark PQ pigments, were isolated from the endophyte *Alternaria* sp. associated with *Pinus ponderosa*, identified as 3,6,6a,9,10-pentahydroxy-7,8-epoxy-4-oxo-4,5,6,6a,6b,7,8,9-octahydroperylene (**1**), and 3,6,6a,7,10-pentahydroxy-4,9-dioxo-4,5,6,6a,6b,7,8,9-octahydroperylene (**2**). Compound (**1**) and (**2**) displayed antileishmanial activity against *Leishmania donovani* with IC_{50} values of 2.55 and 4.40 μg/mL, respectively. Also compound (**2**) revealed antimalarial activity against both chloroquine sensitive (D6) (IC_{50} 4.24 μg/mL) and chloroquine resistant (W2) clones of *Plasmodium falciparum* (3.65 μg/mL), as well as cytotoxicity against mammalian kidney fibroblasts (VERO cells) with IC_{50} value of 3.59 μg/mL (Tantry et al. 2018). Altertoxins I–III (**3**–**5**) were described from *Alternaria alternata*. Mutagenicity of compounds (**3**–**5**) was investigated using the Ames test with *Salmonella typhimurium*; these compounds were mutagenic to *Salmonella typhimurium* TA98, TA100, and TA1537 with and without metabolic activation (Stack and Prival 1986). Five perylenequinones (**3**, **6**–**9**) were recovered from *Alternaria* sp. (DC401) an endophyte associated with *Pinus ponderosa*, altertoxin I (**3**), 6-methoxy-3,6a,7,10-tetrahydroxy-4,9-dioxo-4,5,6,6a,6b,7,8,9-

Table 2 List of fungal PQs that have been discovered and their producers

PQs' class	Perylenequinone	Producer	Source	Reference
Class A	1) 3,6,6a,9,10-pentahydroxy-7,8-epoxy-4-oxo-4,5,6,6a,6b,7,8,9-octahydroperylene	*Alternaria* sp.	Endophytic fungus from *Pinus ponderosa*	(Tantry et al. 2018)
	2) 3,6,6a,7,10-pentahydroxy-4,9-dioxo-4,5,6,6a,6b,7,8,9-octahydroperylene			(Tantry et al. 2018)
	3) altertoxin I	*Alternaria alternata*	–	(Stack and Prival 1986)
	4) altertoxin II			
	5) altertoxin III			
	6) 6-methoxy-3,6a,7,10-tetrahydroxy-4,9-dioxo-4,5,6,6a,6b,7,8,9-octahydroperylene	*Alternaria* sp.	Endophytic fungus from *Pinus ponderosa*	(Idris et al. 2015)
	7) 3,6a,9,10-tetrahydroxy-7,8-epoxy-4-oxo-4,5,6,6a,6b,7,8,9-octahydroperylene			
	8) 6-methoxy-3,6a,9,10-tetrahydroxy-7,8-epoxy-4-oxo-4,5,6,6a,6b,7,8,9-octahydroperylene			
	9) dehydroaltertoxin I			
	altertoxin I (**3**)			
	10) altertoxin VII	*Alternaria* sp. SCSIO41014	Sponge-derived fungus	(Pang et al. 2018)
	11) butyl xanalterate			
	12) alterlosin I	*Alternaria alternata*	Pathogenic fungus from *Centaurea maculosa*,	(Stierle et al. 1989)
	13) alterlosin II			
	14) 8β-chloro-3,6aα,7β,9β,10-pentahydroxy-9,8,7,6 atetrahydroperylen-4(6aH)-one	*Alternaria* sp. M6	Halotolerant fungus	(Zhang et al. 2012)
		Aspergillus fumigatus D	Endophytic of *Edgeworthia chrysantha*.	(Zhang et al. 2017)
	15) alterperylenol			
	16) dihydroalterperylenol			
	17) , 7-*epi*-8-hydroxyaltertoxin I	*Alternaria alternata*	Marine endophytic fungus from algal species of the genus *Laurencia*.	(Gao et al. 2009; Bazioli et al. 2020)
	18) 6-*epi*- stemphytriol	*Setophoma* sp.		
	19) stemphyperylenol			
	altertoxin I (**3**)			
	20) alteichin	*Alternaria eichhorniae*	Phytopathogenic fungus	(Robeson et al. 1984)
	21) stemphyltoxin III	*Alternaria alternata*	–	(Davis and Stack 1991)
	22) 1,4,6b,7,10-pentahydroxy-1,2,6b,7,8,12b-hexahydroperylene-3,9-dione	*Alternaria tenuissima* SS77	Endophytic fungus	(Chagas et al. 2016)
	23) 1,4,9,12a-tetrahydroxy-12-methoxy-1,2,11,12,12a,12b-hexahydroperylene-3,10-dione			
	24) 1,4,9-trihydroxy-1,2-dihydroperylene-3,10-dione			
	25) 4,9-dihydroxyperylene-3, l0-quinone	*Bulgaria inquinans* *Daldinia concentrica* *Thamnomyces* sp. *Phylacia* sp. *Cenococcum geophilum* *Rhopalostroma* sp.	–	(Anderson and Murray 1956; Weiss et al. 1987; Stadler et al. 2004; Itoh et al. 2012; Wendt et al. 2018)
	26) 4,9-dihydroxy-1,2,11,12-tetrahydroperylene-3,10-quinone	*Bulgaria inquinans*	–	(Xian et al. 2006)
	27) methylated 12-*epi*-stemphytriol	*Curvularia lunata* LBQM-04	–	(Cruz et al. 2020)
	alterperylenol (**15**)			
	dihydroalterperylenol (**16**)			
	28) stemphyltoxin I	*Stemphylium botryosum*	–	(Podlech et al. 2014)
	29) stemphyltoxin IV			

Table 2 (continued)

PQs' class	Perylenequinone	Producer	Source	Reference
	altertoxin II (**4**) stemphyltoxin III (**21**)			
Class B	30) cercosporin	*Cercospora kikuchii* *C. hayii*	–	(Kuyama and Tamura 1957; Mumma et al. 1973; Mastrangelopoulou et al. 2019)
	31) phleichrome	*Cladosporium phlei*	Pathogenic fungus of *Phleum pretense*	(Seto et al. 2005)
	32) *ent*-isopheichrome	*Cladosporium cucumerinum*	Pathogen	(Arnone et al. 1988)
	33) cladochrome A 34) cladochrome B 35) cladochrome C 36) cladochrome D 37) cladochrome E	*Cladosporium cladosporioides*	–	(Arnone et al., 1990)
	38) cladochrome F 39) cladochrome G	*Cladosporium* spp.	–	(Williams et al. 2008; Pettit 2011)
	40) calphostin A	*Cladosporium cladosporioides*	–	(Iida et al. 2012)
	41) calphostin B 42) calphostin C 43) calphostin D 44) calphostin I	*Phaeosphaeria* sp.		(Li et al. 2012)
	45) elsinochrome A 46) elsinochrome B 47) elsinochrome C 48) elsinochrome D	*Elsinoë annonae* *Stagonospora convolvuli* *Parastagonospora nodorum* *Pyrenochaeta terrestris* *Shiraia* sp. *Phaeosphaeria* sp.	Pathogen	(Weiss et al. 1987; Meille et al. 1989; Kurobane et al. 2006; Li et al. 2012; Chooi et al. 2017; Al Subeh et al. 2020)
	49) hypocrellin 50) hypocrellin A 51) hypocrellin B 52) hypocrellin D	*Hypocrella bambusae* *Rubroshiraia bambusae* *Shiraia* sp.	Pathogen	(Wu et al. 1989; Ma et al. 2004; Dai et al. 2019; Al Subeh et al. 2020; Li et al. 2021)
	53) hypomycin A 54) hypomycin B 55) hypomycin C 56) hypomycin E 57) hypomycin F 58) hypomycin D	*Hypomyces* sp. *Shiraia* sp.	–	(Liu et al. 2001b, a; Shen et al. 2003; Al Subeh et al. 2020)
	59) phaeosphaerin A 60) phaeosphaerin B 61) phaeosphaerin C 62) phaeosphaerin D 63) phaeosphaerin E 64) phaeosphaerin F	*Phaeosphaeria* sp.	Endolichenic fungus from *Heterodermia obscurata*	(Li et al. 2012)
	65) shiraiachrome A 66) *ent*-shiraiachrome A	*Shiraia bambusicola*	Pathogenic fungus of bamboos	(Mulrooey et al. 2012)

octahydroperylene (**6**), 3,6a,9,10-tetrahydroxy-7,8-epoxy-4-oxo-4,5,6,6a,6b,7,8,9-octahydroperylene (**7**), 6-methoxy-3,6a,9,10-tetrahydroxy-7,8-epoxy-4-oxo-4,5,6,6a,6b,7,8,9-octahydroperylene (**8**), and dehydroaltertoxin I (**9**) (Idris et al. 2015). In 2018, two dark red pigments (PQs' derivatives) altertoxin VII (**10**) and butyl xanalterate (**11**) were purified from a culture of the sponge-derived fungus, *Alternaria* sp. SCSIO41014. Compound (**10**) exhibited potent cytotoxicity against human gastric carcinoma cells (SGC-7901) (IC_{50} 8.75 ± 0.13 μg/mL), hepatocellular carcinoma cells (BEL-7402) (13.11 ± 0.95 μg/mL), and human erythroleukemia (K562) (26.58 ± 0.80 μg/mL) (Pang et al. 2018). Two toxins identified as PQs, alterlosins I–II (**12**–**13**) were recovered from *Alternaria alternata*, a pathogen of spotted knapweed *Centaurea maculosa*. Compound (**13**) showed phytotoxicity (Stierle et al. 1989).

A monochloridated perylenequinone named 8β-chloro-3,6aα,7β,9β,10-pentahydroxy-9,8,7,6 atetrahydroperylen-4(6aH)-one (**14**), besides, two further PQs named alterperylenol (**15**), and dihydroalterperylenol (**16**) were isolated from a halotolerant *Alternaria* sp. M6 obtained from the solar salt field at the beach of Bohai Bay in China (Zhang et al. 2012). Four PQs, altertoxin I (**3**), 7-*epi*-8-hydroxyaltertoxin I (**17**), 6-*epi*-stemphytriol (**18**), and stemphyperylenol (**19**) were isolated from *Alternaria alternata*, a marine endophytic fungus derived from an unidentified algal species of the genus *Laurencia*. The antimicrobial activity of compounds (**17**) and (**19**) against *Staphylococcus aureus*, *Escherichia coli*, and *Aspergillus niger* was evaluated, but neither showed obvious activity (Gao et al. 2009). Alteichin (**20**) was recovered from liquid cultures of *Alternaria eichhorniae* Nag Raj & Ponnappa, a phytopathogen that attacks water hyacinth (Robeson et al. 1984). Stemphyltoxin III (**21**) was reported from *Alternaria alternata.* Compound (**21**) was tested for mutagenicity in the Ames *Salmonella typhimurium* plate incorporation assay with and without Aroclor 1254-induced rat S-9 metabolic activation. A positive response was noted in *S. typhimurium* TA98 and TA1537, also marginal response in strain TA100 (Davis and Stack 1991). Three yellow and yellow brownish PQs, 1,4,6b,7,10-pentahydroxy-1,2,6b,7,8,12b-hexahydroperylene-3,9-dione (**22**), 1,4,9,12a-tetrahydroxy-12-methoxy-1,2,11,12,12a,12b-hexahydroperylene-3,10-dione (**23**), and 1,4,9-trihydroxy-1,2-dihydroperylene-3,10-dione (**24**) were obtained from cultures of the endophytic fungus *Alternaria tenuissima* SS77 (Chagas et al. 2016).

Aspergillus P. Micheli ex Haller

The genus *Aspergillus* (*Aspergillaceae*, *Eurotiales*) has a significant economic and social impact. It comprises 428 species. *Aspergillus* spp. occur worldwide in various habitats such as food producing mycotoxins and are frequently reported as human and animal pathogens (Samson et al. 2014; Wijayawardene et al. 2020). Only one PQ is reported from the genus *Aspergillus*. Bioassay-guided fractionation of the crude extract of the salty broth of *Aspergillus fumigatus* D, an endophyte associated with *Edgeworthia chrysantha* led to the isolation of a chlorated perylenequinone, 8-chloro-3,6a,7,9,10-pentahydroxy-9,8,7,6a-tetrahydroperylen-4(6aH)-one (**14**). Compound (**14**) revealed strong antimicrobial effects against *Escherichia coli* (MIC 0.78 μM) and *Candida albicans* (1.56 μM). Also exhibited moderate antiproliferative activity against human lung cancer cell line A549 (IC_{50} 12.79 ± 0. 33 μM) (Zhang et al. 2017).

Bulgaria Fr.

The genus *Bulgaria* (*Phacidiaceae*, *Phacidiales*) consists of 12 species (Wijayawardene et al. 2020). *Bulgaria inquinans* is a saprophyte that grows on felled oak trunks and fallen branches, and less frequently on ash. 4,9-dihydroxyperylene-3,10-quinone (**25**), and 4,9-dihydroxy-1,2,11,12-tetrahydroperylene-3,10-quinone (**26**), were described from the ethanolic extract of *B. inquinans* fruiting bodies (Weiss et al. 1987; Xian et al. 2006).

Cenococcum Moug. & Fr.

There are five species of the genus *Cenococcum* (*Gloniaceae*, *Gloniales*). The most common and globally abundant ectomycorrhizal fungus is *Cenococcum geophilum*. This fungus often dominates the root systems of trees in extreme environments (Peter et al. 2016; Wijayawardene et al. 2020). Sclerotia of *Cenococcum geophilum* were abundant in compound (**25**) which interpreted the existence of compound (**25**) in sediment samples from Lake Biwa (Itoh et al. 2012; Hanke et al. 2019).

Curvularia Boedijn

The genus *Curvularia* (*Pleosporaceae*, *Pleosporales*) is commonly found in plants and soil of tropical and subtropical regions. There are 119 recognized species of *Curvularia* (Khiralla et al. 2019; Wijayawardene et al. 2020). In 2020, three PQs, the methylated 12-*epi*-stemphytriol (**27**), (**15**), and (**16**) were reported for the first time from malt extract broth of *C. lunata* (LBQM-04) (Cruz et al. 2020).

Daldinia Ces. & De Not.

The genus *Daldinia* (*Hypoxylaceae*, *Xylariales*) comprises 67 species. *Daldinia concentrica* is an inedible wood-rotting fungus (Lee et al. 2006; Wijayawardene et al. 2020). 4,9-dihydroxyperylene-3,10-quinone (**25**) was the first perylenequinone discovered by Anderson and Murray (1956). They isolated compound (**25**) from the large black fruiting bodies of *D. concentrica*.

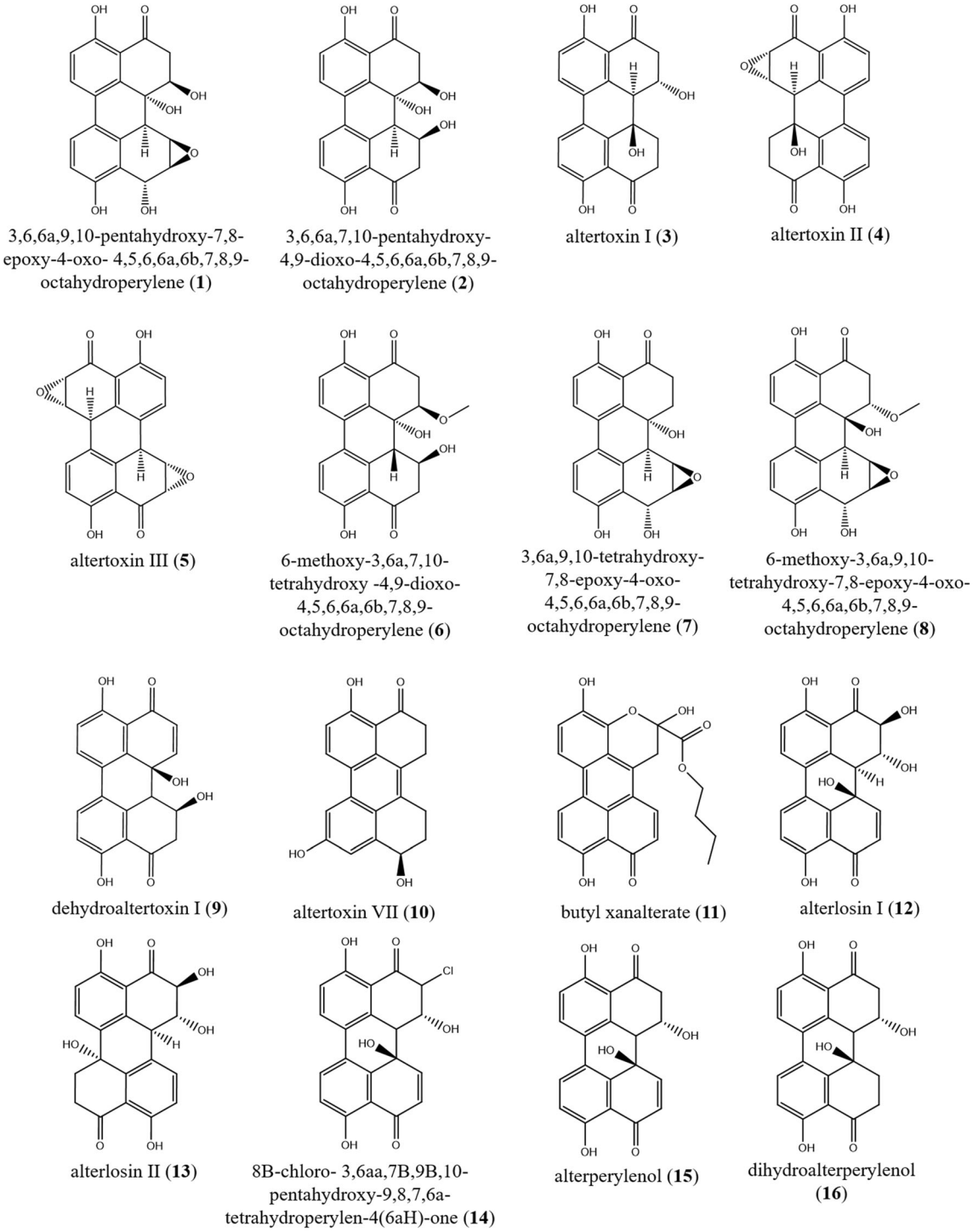


Fig. 5 Perylenequinones described from the genera *Alternaria* and *Setophoma*

Phylacia Lév.

The genus *Phylacia* (*Hypoxylaceae*, *Xylariales*) was collected from different tropical countries such as Colombia, Brazil, Mexico and French Guiana. Twelve species are documented of the genus *Phylacia* (Fournier and Lechat 2015; Wijayawardene et al. 2020). Several members of *Hypoxylaceae* including *Phylacia* spp. were examined. Compound (**25**) was frequently encountered in stromata of *Phylacia* spp. (Wendt et al. 2018).

Rhopalostroma D. Hawksw.

The genus *Rhopalostroma* (*Hypoxylaceae*, *Xylariales*) contains currently 11 species. *Rhopalostroma* spp. have been collected exclusively from Africa and Asia (Daranagama et al.

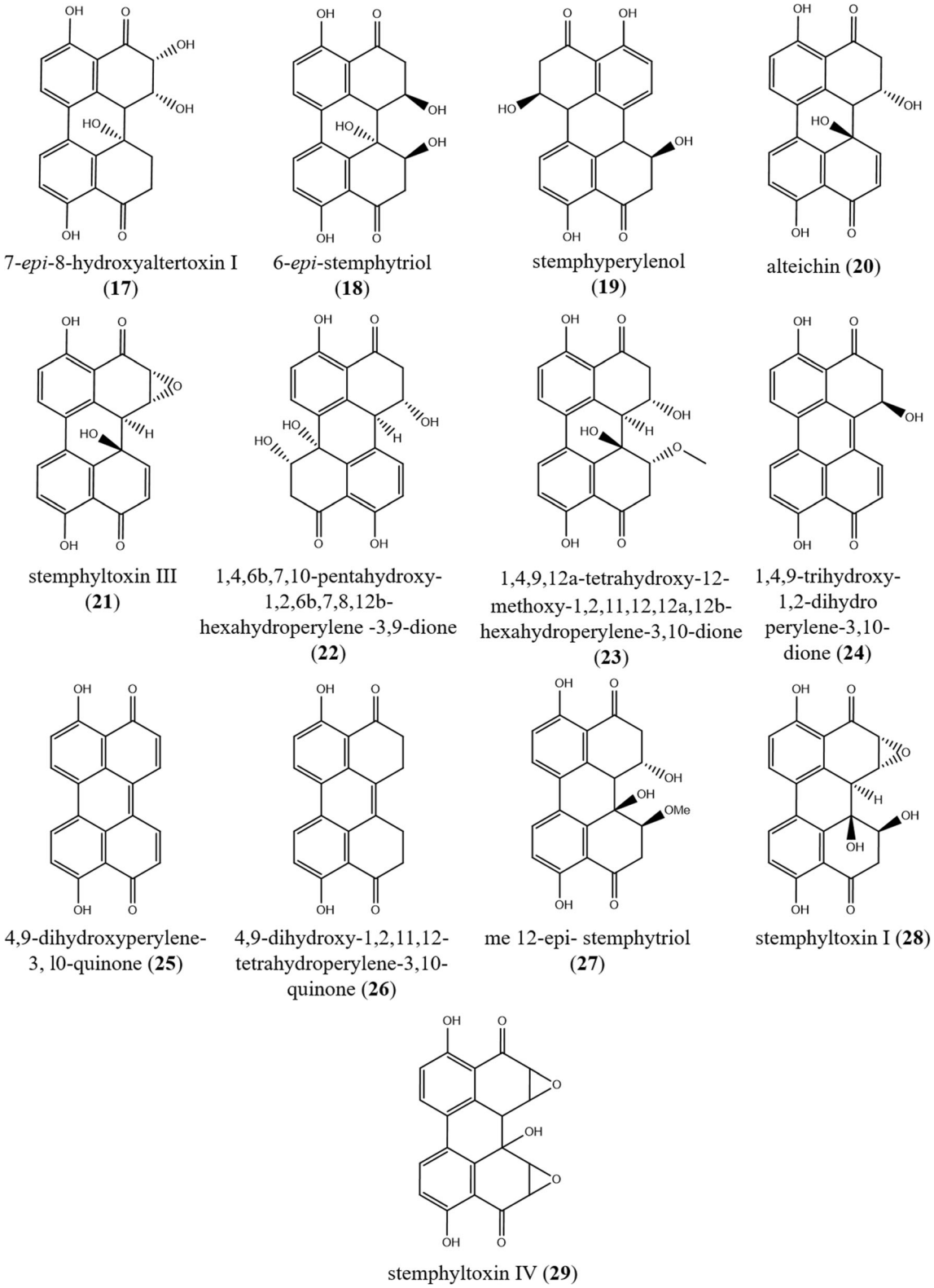


Fig. 6 Reported perylenequinones from the genera *Alternaria, Aspergillus*, *Bulgaria*, *Cenococcum*, *Curvularia*, *Daldinia*, *Phylacia*, *Rhopalostroma*, *Setophoma*, *Stemphylium*, and *Thamnomyces*

2015; Wijayawardene et al. 2020). Stromata extracts of several *Rhopalostroma* spp. were screened using high-performance liquid chromatography with diode array and mass spectrometric detection (HPLC-DAD-MS). The pigment, 4,9-dihydroxyperylene-3,l0-quinone (**25**) was detected (Stadler et al. 2010).

Setophoma Gruyter, Aveskamp & Verkley

Wijayawardene et al. (2020) accepted six species of the genus *Setophoma* (*Phaeosphaeriaceae*, *Pleosporales*). The production of some PQs by *Setophoma* was reported (Bazioli et al. 2020). Stemphyperylenol (**19**) and derivatives were recovered from *Setophoma* sp., compound (**19**) displayed antifungal effects against *Aspergillus fumigatus*, *Pencillium brasilianum*, and *P. digitatum*.

Stemphylium Wallr.

Some species of *Stemphylium* are pathogens of several important crops including onion, alfalfa, sugar beet, and asparagus. The genus *Stemphylium* (*Pleosporaceae*, *Pleosporales*) contains 96 species (Wijayawardene et al. 2020). Four perylenequinones, stemphyltoxins I, IV (**28–29**), besides two further (**4**), and (**21**) were recovered from *Stemphylium botryosum* (Podlech et al. 2014).

Thamnomyces Ehrenb.

Thamnomyces (*Hypoxylaceae*, *Xylariales*) is a tropical genus known exclusively from the Neotropics and Africa. Only 11 species are recorded of the genus *Thamnomyces* (Wijayawardene et al. 2020). Compound (**25**) was reported in stromata extracts of *Thamnomyces* spp. (Wendt et al. 2018).

Class B perylenequinones

Thirty-seven fungal PQs of class B have been described to date (Figs. 7, 8, and 9). They are produced by 11 ascomycete genera (Table 1). The majority of them are plant pathogenic strains. Fungal PQs of class B were also investigated for their biological properties, some of them revealed cytotoxicity, antiviral, antimicrobial and antileishmanial activities.

Cladosporium link

The genus *Cladosporium* (*Cladosporiaceae*, *Capnodiales*) is frequently isolated from soil and organic matter; however, some species are pathogens. The genus *Cladosporium* comprises 237 accepted species (Bensch et al. 2018; Wijayawardene et al. 2020). *Cladosporium* spp. are distinguished by producing diverse PQs including cladochromes and calphostins. Phleichrome (**31**) was reported from the pathogenic fungus *Cladosporium phlei* associated with the timothy plant (*Phleum pratense* L.). In the presence of light, compound (**31**) demonstrated antifungal action against *Epichloe typhina* (Seto et al. 2005). *Ent*-isopheichrome (**32**) beside cladochromes A–G (**33–39**) were described from different *Cladosporium* spp. (Arnone et al. 1988, 1990; Williams et al. 2008; Pettit 2011). Calphostins A–D, I (**40–44**) were purified from the fermented broth of *Cladosporium cladosporioides*. Calphostin C (**42**), revealed potent and specific inhibition of protein kinase C, because it was 1000 times more inhibitory to protein kinase C (IC_{50} 0.05 μM) than other protein kinases such as cAMP-dependent protein kinase and tyrosine-specific protein kinase (IC_{50}, >50 μM) (Kobayashi et al. 1989; Iida et al. 2012).

Cercospora Fresen.

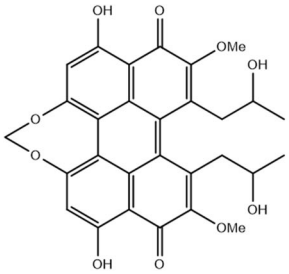
The genus *Cercospora* (*Mycosphaerellaceae*, *Capnodiales*) contains 1125 species. Most *Cercospora* spp. are pathogens (Wijayawardene et al. 2020). In 1957, cercosporin (**30**) was isolated from mycelial cultures of *Cercospora kikuchii*, a pathogen that causes soybean purple speck disease (Kuyama and Tamura 1957). Compound (**30**) demonstrated photocytotoxicity against two glioblastoma multiforme (T98G, U87) and one breast adenocarcinoma (MCF7) human cell lines. However, in the dark compound (**30**) displayed a synergistic cytotoxicity with copper only in the most respiratory cell lines of MCF7 and T98G. Cercosporin (**30**) is a powerful photosensitizer, but with a short activation wave-length, mostly appropriate for superficial PDT treatments (Mastrangelopoulou et al. 2019).

Elsinoë Racib.

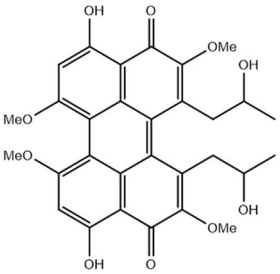
Species of *Elsinoë* are phytopathogens, causing scab and spot anthracnose on several economically important crops. The genus *Elsinoë* (*Elsinoaceae*, *Myriangiales*) contains 40 species (Fan et al. 2017; Wijayawardene et al. 2020). Four PQs were reported from *Elsinoë*. Three bright red pigments, elsinochromes A–C (**45–47**), and one orange named elsinochrome D (**48**) were produced in cultures by *Elsinoë annonae* and its anamorph *Sphaceloma randii* (Weiss et al. 1987; Meille et al. 1989). Elsinochrome phytotoxins are generated also by *E. arachidis*, the responsible fungus of peanut scab. Elsinochrome A (**45**) is distinguished by a superior singlet oxygen quantum yield compared to other kinds of photosensitizes. Elsinochrome A (**45**) could be easily synthesized at present, which makes it an alternative candidate for PDT (Jiao et al. 2019).

Hypocrella Sacc.

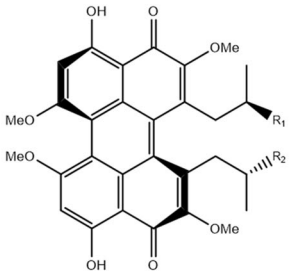
Hypocrella spp. (*Clavicipitaceae*, *Hypocreales*) are common in tropical regions, particularly in moist old-growth forests. There are more than 170 recognized species in the genus *Hypocrella.* Some species of *Hypocrella* are parasites of scale insects and white flies (Mains 1959; Chaverri et al. 2008; Wijayawardene et al. 2020). *H. bambusae*, a parasite of living inflorescence of bamboo, was studied (Dai et al. 2019). Investigations revealed that *H. bambusae* produced several types of PQs: hypocrellins



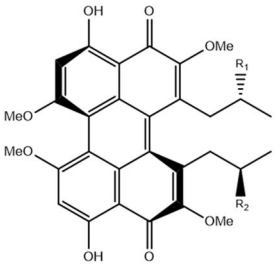
cercosporin (**30**)



phleichrome (**31**)



ent-isophleichrome, R1= R2= OH (**32**)
cladochrome A, R1= R2= beta-hydroxybutyrate (**33**)
cadochrome B, R1= beta-hydroxybutyrate,
R2= benzoate (**34**)
cladochrome C, R1= benzoate,
R2= *p*-hyroxybenzoate (**35**)
caldochrome D, R1= *p*-hydroxyphenylcarbonate,
R2= *p*-hyroxybenzoate (**36**)
cladochrome E, R1= *p*-hydroxyphenylcarbonate,
R2= benzoate (**37**)
cladochrome F, R1= OH, R2= *p*-hyroxybenzoate (**38**)
cladochrome G, R1= OH,
R2= *p*-hydroxyphenylcarbonate (**39**)



calphostin A, R1= R2= benzoate (**40**)
calphostin B, R1= benzoate, R2= OH ((**41**)
calphostin C, R1= benzoate,
R2= *p*-hydroxyphenylcarbonate (**42**)
calphostin D, R1= R2= OH (**43**)
calphostin I, R1= *p*-hyroxybenzoate,
R2= *p*-hydroxyphenylcarbonate (**44**)

Fig. 7 Reported perylenequinones from the genera *Cercospora* and *Cladosporium*

A–B (**49–51**), hypomycins A (**53**), F (**57**), and shiraiachrome A (**65**) (Weiss et al. 1987; Diwu and William 1990; Ma et al. 2004; Cheng et al. 2004; Li et al. 2021). Hypocrellins and shiraiachromes have so close structures. Formerly, there has been much confusion in the naming of the same compounds extracted from different sources, hypocrellin A (**50**) was referred as shiraiachrome B, and hypocrellin B (**51**) was named as either shiraiachrome C or hypocrellin C (Wu et al. 1989; Kishi et al. 1991; Liu et al. 2001a; Ma et al. 2019b). Herein, we followed the structures and nomenclatures (Fig. 8) proposed by Al Subeh et al. (2020).

Hypomyces (Fr.) Tul. & C. Tul.

The genus *Hypomyces* (*Hypocreaceae*, *Hypocreales*) consists exclusively of fungicolous fungi, parasitizing the fruiting bodies of some members of *Agaricales*, *Boletales*, *Helotiales*, *Pezizales*, and *Polyporales*. *Hypomyces* comprises of 150 species widely distributed in Australia, Asia, and Europe (Wijayawardene et al. 2020; Yu et al. 2020). Four perylenequinones, hypomycins A–C, D[1] (**53–55, 58**) were discovered in the mycelia of *Hypomyces* spp. (Liu et al. 2001b, a; Shen et al. 2003).

[1] No information available for hypomycin D structure.

Parastagonospora Quaedvl., Verkley & Crous

Parastagonospora is an important genus in *Phaeosphaeriaceae* that includes pathogens causing leaf and glume blotch on cereal crops. Nineteen species are recognized of the genus *Parastagonospora* (Goonasekara et al. 2019; Wijayawardene et al. 2020). *Parastagonospora nodorum* is a significant pathogen of wheat. The production of elsinochrome C (**47**) by *P. nodorum* was reported by Chooi et al. (2017). They stated that elsinochrome C contributes to the virulence of *P. nodorum* against wheat.

Phaeosphaeria I. Miyake

*Phaeosphaeria*is a member of *Phaeosphaeriaceae*. There are around 96 species of the genus *Phaeosphaeria*. Most of the *Phaeosphaeria* species are parasites of *Poaceae* and grass-like monocot plants (Stchigel et al. 2004; Wijayawardene et al. 2020). Twelve different PQs are produced by *Phaeosphaeria*: phaeosphaerins A–F (**59–64**), five are yellow (phaeosphaerins A–C, E, and F), while one is orange (phaeosphaerin D), as well as calphostin D (**43**) elsinochromes A–C (**45–47**), and hypocrellins A–B (**50–51**). These PQs were purified from an endolichenic fungus *Phaeosphaeria* sp. found

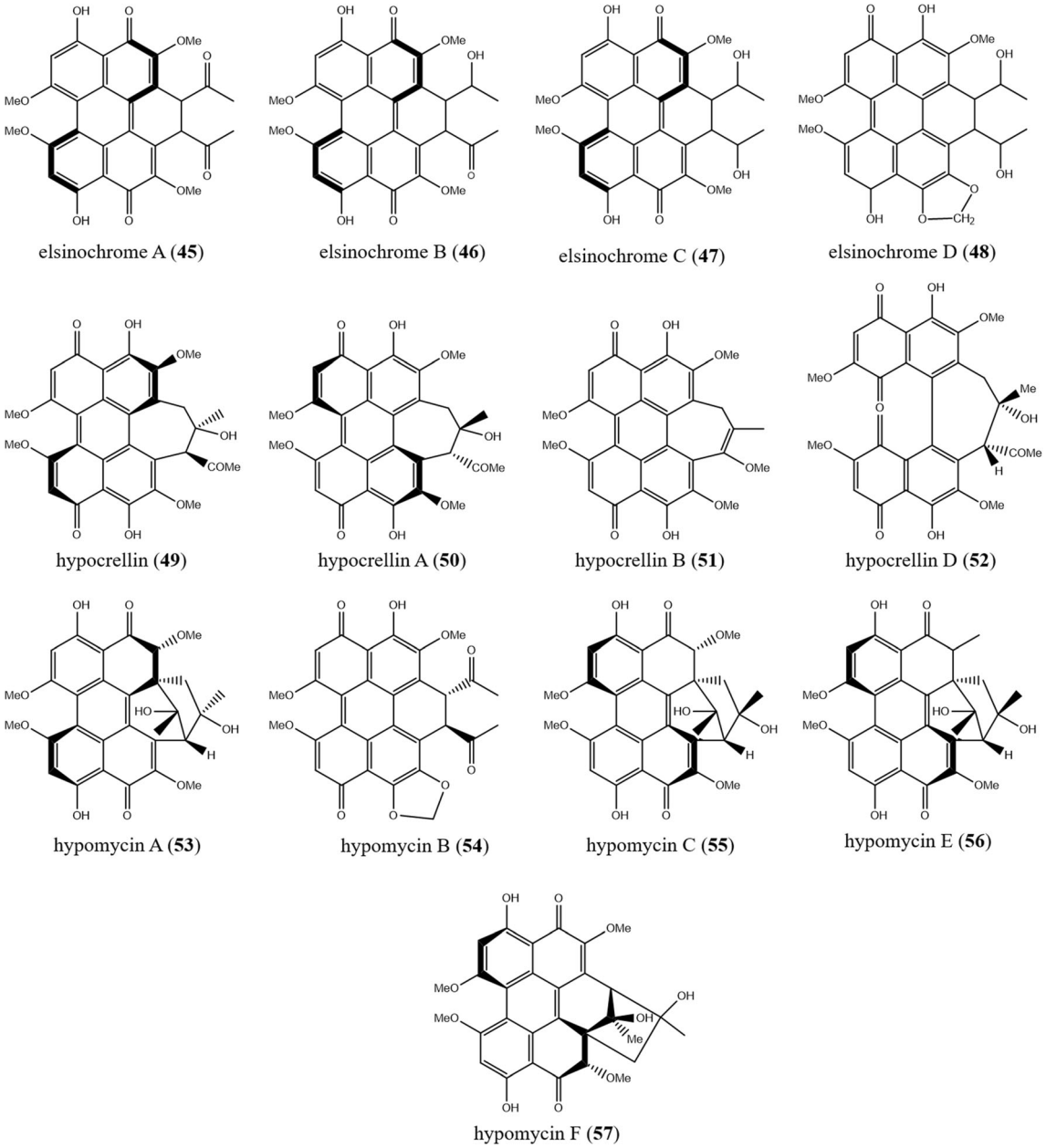


Fig. 8 Produced perylenequinones by the genera *Elsinoë*, *Hypocrella*, *Hypomyces*, *Parastagonospora*, *Pyrenochaeta*, and *Stagonospora*

in the lichen *Heterodermia obscurata*. The unusual α,β-unsaturated ketone moieties present in phaeosphaerins A −F resulted in their yellow coloration. Phaeosphaerins' cytotoxicity against human prostate cancers intensified in the presence of light (Li et al. 2012).

Pyrenochaeta De Not.

Pyrenochaeta spp. (*Pleosporales*) inhabit soil and plant debris and are well-known as pathogen of plants and occasionally humans. The genus *Pyrenochaeta* contains five accepted species (Levic et al. 2013; Yadav et al. 2015; Wijayawardene et al. 2020). *Pyrenochaeta terrestris*, a pathogen that causes onion pink root disease, produced both elsinochrome C (**47**) and D (**48**) (Kurobane et al. 2006).

Rubroshiraia D.Q. Dai & K.D. Hyde

Rubroshiraia (*Shiraiaceae*, *Pleosporales*) contains one species named *Rubroshiraia bambusae* D.Q. Dai & K.D. Hyde, a common pathogen of bamboos. *R. bambusae* is a well-known taxon used in Chinese traditional medicine which is called "Zhuhongjun" (Dai et al. 2019; Wijayawardene et al. 2020). The HPLC profiles of methanol stromata extracts of *R. bambusae* contained high quantities of hypocrellin A and B (**50**–**51**). Stromata extracts of

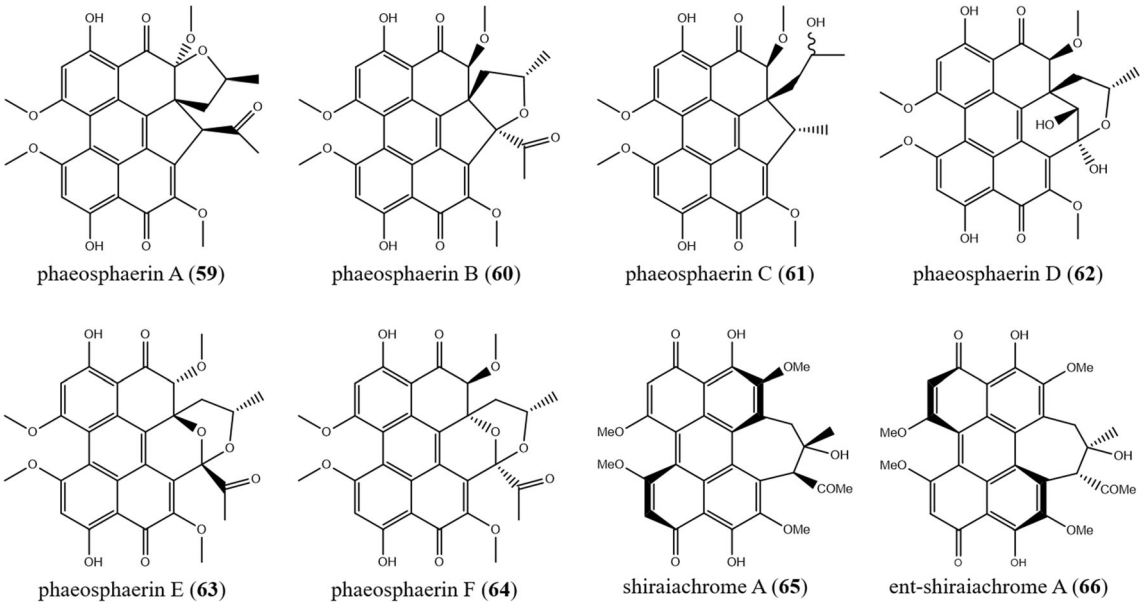


Fig. 9 Described perylenequinones from the genera *Phaeosphaeria* and *Shiraia*

R. bambusae contains almost double the content of hypocrellin A and B compared to *Shiraia bambusicola* (Dai et al. 2019). Hypocrellins have gained much attention due to their light-induced antitumor, antimicrobial, antileishmanial, and antiviral activities (Diwu and William 1990; Hudson et al. 1994; Ma et al. 2004). Some clinical trials showed that hypocrellins have promising treatment for various skin diseases, such as skin cancer and white lesions of the vulva (Wan and Chen 1981; Li et al. 2000).

Shiraia Henn.

The genus *Shiraia* (*Shiraiaceae*, *Pleosporales*) comprises one species. *Shiraia bambusicola* is a pathogen of several genera of bamboos. Large stromata of *S. bambusicola* have been used in folk Chinese medicine (Wu et al. 1989; Wijayawardene et al. 2020). Nine PQs were reported from *S. bambusicola*: elsinochromes A–C (**45**–**47**), hypocrellins A–B, D (**50**–**52**), hypomycin E (**56**), shiraiachrome A (**65**), and *ent*-shiraiachrome A (**66**) (Wu et al. 1989; Fang et al. 2006; Ma et al. 2019b; Al

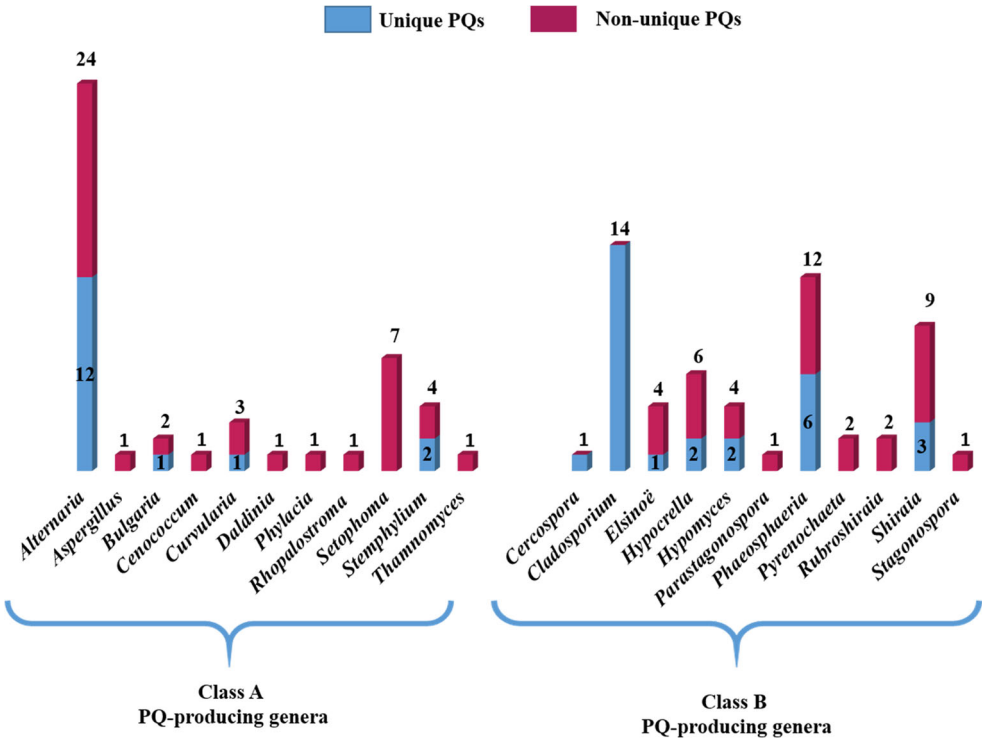


Fig. 10 Number of fungal PQs per genus

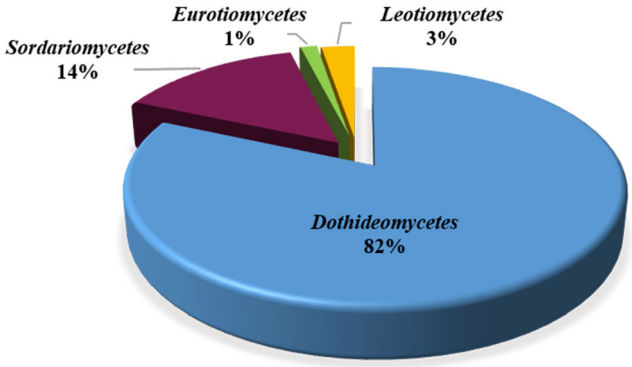


Fig. 11 Distribution of PQs among fungal classes

Subeh et al. 2020; Li et al. 2021). Endophytes, identified as *Shiraia* spp., were also shown to produce hypocrellins on media (Morakotkarn et al. 2008; Shen et al. 2014). Compound (**50**) demonstrated promising antifungal activity against *Candida albicans* (0.65 ± 0.14 μg/mL), and exhibited potent antileishmanial activity (IC_{50} of 0.27 ± 0.03 μg/mL), while compound (**51**) revealed moderate antileishmanial activity (IC_{50} 12.7 ± 2.1 μg/mL). Interestingly, the antileishmanial activity of hypocrellin A was three- and six fold more potent than that of amphotericin B and pentamidine, respectively. Compound (**52**) reduced tumor cell proliferation in Bel-7721 (IC_{50} 1.8 mg/mL), A-549 (8.8 mg/mL), and Anip-973 (38.4 mg/mL) (Fang et al. 2006). Compound (**56**) inhibited pseudotyped SARS-CoV-2 infection in 293T-ACE2 cells (IC_{50} 0.17μM), as well as compound (**66**) (0.038 μM), and both even suppressed live SARS-CoV-2 infection (EC_{50} 0.22 and 0.21μM, respectively) (Li et al. 2021).

Stagonospora (Sacc.) Sacc.

The genus *Stagonospora* (*Massarinaceae*, *Pleosporales*) comprises 220 species. Some species of *Stagonospora* are commonly known as aggressive pathogens of wheat. While other *Stagonospora* spp. have been implicated in bioremediation of aromatic compounds and lignin derivatives (Bergbauer et al. 1992; Zeiner et al. 2016; Wijayawardene et al. 2020). *Stagonospora convolvuli* LA39 is a pathogen of field and hedge bindweeds, and was reported to produce elsinochrome A (**45**). Hence, *S. convolvuli* has been studied as a bindweed biocontrol agent (Ahonsi et al. 2005; Boss et al. 2007).

Section two: distribution of PQ-producing fungi among the kingdom of fungi

This section covers the main information gleaned from the aforementioned fungal PQ reports. In addition, classification of PQ-producing fungi as well as a conclusion.

In this review, 66 fungal PQs were reported from 22 fungal genera between 1956 and 2021. The review revealed that, despite appearances, the synthesis of fungal PQs is not exclusive to phytopathogens. PQ-producing fungi include endophytic, endolichenic, soil, and marine strains. Interestingly, color diversity of fungal PQ pigments was observed to be quite considerable, various colors including red, orange, yellow, and even dark blue are available (Weiss et al. 1987; Meille et al. 1989; Mulrooey et al. 2012; Li et al. 2012; Al Subeh et al. 2020).

Obviously, 29 compounds belonging to class A have been reported from 11 ascomycete genera (Fig. 10). Twenty-four PQs were isolated from *Alternaria* (12 unique), seven from *Setophoma*, four from *Stemphylium* (two unique), three from *Curvularia* (one unique), two from *Bulgaria* (one unique) and one each from *Aspergillus*, *Cenococcum*, *Daldinia*, *Rhopalostroma*, *Thamnomyces*, and *Phylacia*, whereas 37 of

Table 3 List of families and number of PQ-producing genera

Family	Number of genera*	Reference
Aspergillaceae	1	(Zhang et al. 2017)
Cladosporiaceae	1	(Arnone et al., 1990; Williams et al. 2008; Iida et al. 2012)
Clavicipitaceae	1	(Wu et al. 1989; Li et al. 2021)
Elsinoaceae	1	(Jiao et al. 2019)
Gloniaceae	1	(Itoh et al. 2012)
Hypocreaceae	1	(Liu et al. 2001b, a; Shen et al. 2003)
Hypoxylaceae	4	(Anderson and Murray 1956; Stadler et al. 2010)
Massarinaceae	1	(Boss et al. 2007)
Mycosphaerellaceae	1	(Mastrangelopoulou et al. 2019)
Phacidiaceae	1	(Weiss et al. 1987; Xian et al. 2006)
Phaeosphaeriaceae	3	(Li et al. 2012; Chooi et al. 2017; Bazioli et al. 2020)
Pleosporaceae	3	(Kurobane et al. 2006; Tantry et al. 2018; Cruz et al. 2020)
Shiraiaceae	2	(Wu et al. 1989; Al Subeh et al. 2020)

**Pyrenochaeta* (*Pleosporales* genus *incertae sedis*) is excluded from the table

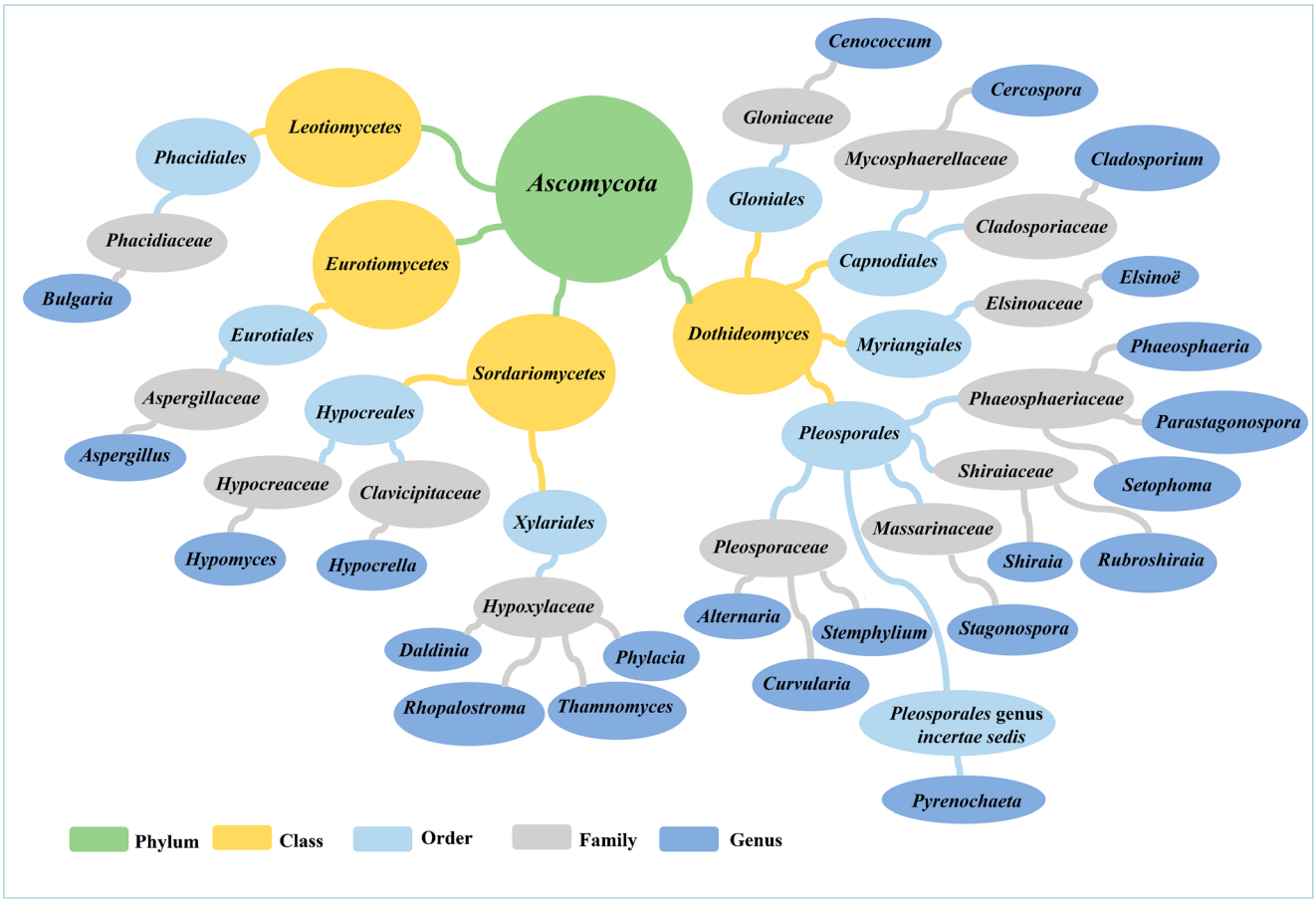


Fig. 12 Outline of PQ-producing fungi

the described fungal PQs belong to class B and were recovered from 11 ascomycete genera (Fig. 10). *Cladosporium* has 14 unique PQs, *Phaeosphaeria* has 12 (six unique), *Shiraia* has nine (three unique), *Hypocrella* has six (two unique), *Elsinoë* has four (one unique), *Hypomyces* has four (two unique), *Pyrenochaeta* and *Rubroshiraia* each has two, *Cercospora* has one unique, *Stagonospora* and *Parastagonospora* each has one PQ.

The genera *Alternaria*, *Cladosporium*, *Phaeosphaeria*, and *Shiraia* have the most distinct PQs (Fig. 10). In comparison to class A, the uniqueness of PQs per genus was higher in class B. Remarkably, all PQ-producing fungi described in this review affiliate with one phylum *Ascomycota*, and only four classes. *Dothideomycetes* (14 genera) accounts for the bulk of the documented PQs 82%, followed by *Sordariomycetes* (six genera) 14%, *Leotiomycetes* (one genus) 3%, and *Eurotiomycetes* (one genus) 1%. The distribution of PQs among fungal genera is summarized in Fig. 11.

Fungal PQs were extracted from cultures, mycelia, stromata, and fruiting bodies, using various solvents including acetone, ethyl acetate, ethanol, and methanol. The tendency of fungal PQs appears to be extracted from cultures over stromata/fruiting bodies. Only 4,9-dihydroxyperylene-3,l0-quinone (**25**) was isolated from stromata/fruiting bodies of *Bulgaria* and *Daldinia* (Weiss et al. 1987; Anderson and Murray, 1956). There is a strong inconsistency in the chemotaxonomy of the PQ-producing fungi. They are described from a total of 13 separate families (Table 3). Fig. 12 shows the classification of PQ-producing fungi based on the recent outline of fungi (Wijayawardene et al. 2020). A chemotaxonomic approach is required to substantiate the hypothesis that members of a specific family could produce PQs. A number of fascinating *Hypoxylaceae* chemotaxonomic studies have been achieved (Helaly et al. 2018; Becker and Stadler 2021; Kuhnert et al. 2021). They documented the occurrence of several secondary metabolites in *Daldinia*, *Phylacia*, *Rhopalostroma*, and *Thamnomyces* stromata, including (**25**). In this review, five families, *Pleosporaceae*, *Phaeosphaeriaceae*, *Cladosporiaceae*, *Shiraiaceae*, and *Hypoxylaceae* are distinguished by their considerable number of PQs and genera. As a consequence, members of these families should be taken into account as potential sources of novel PQs.

Conclusion

Bioprospectors have been captivated by the diversity, novelty, and biological activity of fungal natural products. Perylenequinones (PQs) are naturally occurring aromatic polyketides. They are unique and fascinating compounds because of their chemical and biological properties. Fungi, aphids, crinoids, and plants are the sources of PQs. Fungal PQs have been first discovered in some phytopathogenic species, and it was subsequently recognized that PQs have a role in pathogenicity. Because of their capacity to absorb light and generate reactive oxygen species, fungal PQs possessed different bioactivities including antitumor, antiviral, antileishmanial, antimalarial, and antimicrobial properties, most notably their protein kinase C inhibitory activity. Fungal PQs are divided into two categories: class A simple PQs consists of the parent perylenequinone (4,9-dihydroxyperylene-3, l0-quinone) without carbon substituents. PQs with carbon substituents are compiled in class B. To date, 66 fungal PQs have been described from 22 genera. According to the analysis, fungi are the best source of PQs, accounting for 85 % of all known PQs, whereas only 15 % were obtained from both the kingdoms *Animalia* and *Plantae*. One phylum, *Ascomycota*, and four classes (*Dothideomycetes*, *Sordariomycetes*, *Leotiomycetes*, and *Eurotiomycetes*) are responsible for the documented fungal PQs. *Dothideomycetes* is distinguished by having the greatest diversity of PQ-producing fungi as well as the greatest amount of PQs. The families *Pleosporaceae*, *Phaeosphaeriaceae*, *Cladosporiaceae*, *Shiraiaceae*, and *Hypoxylaceae* could be significant sources of novel PQs. Fungal PQs merit more consideration as PDT agents, due to their advantages over other photosensitizers. Hypocrellins are an excellent example of the application of PQs. Certainly, more investigations are necessary to reveal novel fungal PQs using modern techniques.

Acknowledgements The authors express their sincere gratitude to Prof. Marc Stadler and two anonymous reviewers for their contributions to the manuscript's improvement.

Code availability Not applicable.

Author contribution Conceptualization: Afra Khiralla. Literature search and analysis: Afra Khiralla and Aisha O. Mohammed. Writing and review: Afra Khiralla. Editing and revision: Sakina Yagi.

Data availability Not applicable.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

References

Ackroyd R, Kelty C, Brown N, Reed M (2001) The history of photodetection and photodynamic Therapy. Photochem Photobiol 74:656–669

Ahonsi MO, Maurhofer M, Boss D, Défago G (2005) Relationship between aggressiveness of *Stagonospora* sp. isolates on field and hedge bindweeds, and in vitro production of fungal metabolites cercosporin, elsinochrome A and leptosphaerodione. Eur J Plant Pathol 111:203–215. https://doi.org/10.1007/s10658-004-2878-5

Al Subeh ZY, Raja HA, Monro S et al (2020) Enhanced production and anticancer properties of photoactivated perylenequinones. J Nat Prod 83:2490–2500. https://doi.org/10.1021/acs.jnatprod.0c00492

Anderson JM, Murray J (1956) lsolation of 4,9-dihytlroxy-peryecne-3, 10-quinone from a fungus. Chem Ind 376–376

Arnone A, Assante G, Di Modugno V et al (1988) Perylenequinones from cucumber seedlings infected with *Cladosporium cucumerinum*. Phytochemistry 27:1675–1678. https://doi.org/10.1016/0031-9422(88)80424-2

Arnone A, Assante G, Merlini L, Nasini G (1990) Structure and stereochemistry of cladochrome D and E, novel perylenequinone pigments from *Cladosporium cladosporioides*. Chem Inform 21. https://doi.org/10.1002/chin.199011284

Ayers S, Zink DL, Mohn K et al (2007) Scutiaquinones A and B, perylenequinones from the roots of *Scutia myrtina* with antihelmintic activity. J Nat Prod 70:425–427. https://doi.org/10.1021/np0604937

Bazioli JM, Fill TP, Rocha MC et al (2020) Perylenequinones production induced by co-culturing *Setophoma* sp. and *Penicillium brasilianum*. Phytochem Lett 40:76–83

Becker K, Stadler M (2021) Recent progress in biodiversity research on the *Xylariales* and their secondary metabolism. J Antibiot (Tokyo) 74:1–23. https://doi.org/10.1038/s41429-020-00376-0

Bensch K, Groenewald JZ, Meijer M et al (2018) *Cladosporium* species in indoor environments. Stud Mycol 89:177–301. https://doi.org/10.1016/j.simyco.2018.03.002

Bergbauer M, Eggert C, Kalnowski G (1992) Biotreatment of pulp mill bleachery effluents with the coelomycetous fungus *Stagonospora gigaspora*. Biotechnol Lett 14:317–322

Boss D, Maurhofer M, Schläpfer E, Défago G (2007) Elsinochrome A production by the bindweed biocontrol fungus *Stagonospora convolvuli* LA39 does not pose a risk to the environment or the consumer of treated crops. FEMS Microbiol Ecol 59:194–205. https://doi.org/10.1111/j.1574-6941.2006.00207.x

Chagas FO, Dias LG, Pupo MT (2016) New perylenequinone derivatives from the endophytic fungus *Alternaria tenuissima* SS77. Tetrahedron Lett 57:3185–3189. https://doi.org/10.1016/J.TETLET.2016.06.035

Chaverri P, Liu M, Hodge KT (2008) A monograph of the entomopathogenic genera *Hypocrella*, *Molleriella*, and *Samuelsia* gen. nov. (*Ascomycota*, *Hypocreales*, *Clavicipitaceae*), and their aschersonia-like anamorphs. Stud Mycol 60. https://doi.org/10.3114/sim.2008.60.01

Chen H-Q, Lee M-H, Chung K-R (2007) Functional characterization of three genes encoding putative oxidoreductases required for cercosporin toxin biosynthesis in the fungus *Cercospora nicotianae*. Microbiology 153:2781–2790. https://doi.org/10.1099/mic.0.2007/007294-0

Cheng TF, Jia XM, Ma XH et al (2004) Phylogenetic study on *Shiraia bambusicola* by rDNA sequence analyses. J Basic Microbiol 44:339–350. https://doi.org/10.1002/jobm.200410434

Chooi Y, Zhang G, Hu J et al (2017) Functional genomics-guided discovery of a light-activated phytotoxin in the wheat pathogen *Parastagonospora nodorum* via pathway activation. Environ Microbiol 19:1975–1986. https://doi.org/10.1111/1462-2920.13711

Choquer M, Lee M, Bau H, Chung K (2007) Deletion of a MFS transporter-like gene in *Cercospora nicotianae* reduces cercosporin toxin accumulation and fungal virulence. FEBS Lett 581:489–494. https://doi.org/10.1016/j.febslet.2007.01.011

Corrochano LM (2007) Fungal photoreceptors: sensory molecules for fungal development and behaviour. Photochem Photobiol Sci 6: 725–736

Cruz HJM, Boffo EF, Geris R (2020) Perylenequinones from *Curvularia lunata*. Biochem Syst Ecol 92:104086. https://doi.org/10.1016/j.bse.2020.104086

Dai D, Wijayawardene NN, Tang L et al (2019) *Rubroshiraia* gen. nov., a second hypocrellin-producing genus in *Shiraiaceae* (*Pleosporales*). MycoKeys 58:1–26. https://doi.org/10.3897/mycokeys.58.36723

Daranagama DA, Liu X, Chamyuang S et al (2015) *Rhopalostroma brevistipitatum* sp. nov. from Thailand with an extended generic description for *Rhopalostroma*. Phytotaxa 227:229–242. https://doi.org/10.11646/phytotaxa.227.3.2

Daub ME, Herrero S, Chung K (2013) Reactive oxygen species in plant pathogenesis : the role of perylenequinone photosensitizers. Antioxid Redox Signal 19:970–989. https://doi.org/10.1089/ars.2012.5080

Davis VM, Stack ME (1991) Mutagenicity of stemphyltoxin III, a metabolite of *Alternaria alternata*. Appl Environ Microbiol 57:180–182

Deng H, Gao R, Liao X, Cai Y (2018) Characterisation of a monooxygenase in *Shiraia bambusicola*. Microbiology 164:1180–1188. https://doi.org/10.1099/mic.0.000694

Diwu Z (1995) Novel therapeutic and diagnostic applications of hypocrellins and hypericins. Photochem Photobiol 61:529–539

Diwu Z, Lown JW (1993) Photosensitization with anticancer agents: 15. Perylenequinonoid pigments as potential photodynamic therapeutic agents: Formation of semiquinone radicals and reactive oxygen species on illumination. J Photochem Photobiol B Biol 18:131–143. https://doi.org/10.1016/1011-1344(93)80055-E

Diwu Z, William LJ (1990) Hypocrellins and their use in photosensitization. Photochem Photobiol 52:609–616. https://doi.org/10.1111/j.1751-1097.1990.tb01807.x

Dubauskas Z, Beck TP, Chmura SJ et al (1998) Activated calphostin C cytotoxicity is independent of p53 status and in vivo metastatic potential. Clin Cancer Res 4:2391–2398

Ehrenshaft M, Upchurch RG (1991) Isolation of light-enhanced cDNAs of *Cercospora kikuchii*. Appl Environ Microbiol 57:2671–2676

Fan XL, Barreto RW, Groenewald JZ et al (2017) Phylogeny and taxonomy of the scab and spot anthracnose fungus *Elsinoë* (*Myriangiales*, *Dothideomycetes*). Stud Mycol 87:1–41

Fang LZ, Qing C, Shao HJ et al (2006) Hypocrellin D, a Cytotoxic fungal pigment from fruiting bodies of the ascomycete *Shiraia bambusicola*. J Antibiot (Tokyo) 59:351–354. https://doi.org/10.1038/ja.2006.49

Fournier J, Lechat C (2015) *Phylacia korfii* sp. nov., a new species of *Phylacia* (*Xylariaceae*) from French Guiana, with notes on three other *Phylacia* spp. Ascomycete.org 7:315–319. https://doi.org/10.25664/art-0154

Gao SS, Li XM, Wang BG (2009) Perylene derivatives produced by *Alternaria alternata*, an endophytic fungus isolated from *Laurencia* species. Nat Prod Commun 4:1477–1480

Goonasekara I, Erio C, Bulgakov T et al (2019) Two novel species of *Parastagonospora* (*Phaeosphaeriaceae Pleosporales*) on grasses from Italy and Russia. Asian J Mycol 2:170–182. https://doi.org/10.5943/ajom/2/1/8

Hanke UM, Lima-braun AL, Eglinton TI et al (2019) Significance of perylene for source allocation of terrigenous organic matter in aquatic sediments. Environ Sci Technol 53:8244–8251. https://doi.org/10.1021/acs.est.9b02344

Helaly SE, Thongbai B, Stadler M (2018) Diversity of biologically active secondary metabolites from endophytic and saprotrophic fungi of the ascomycete order *Xylariales*. Nat Prod Rep. https://doi.org/10.1039/C8NP00010G

Hu J, Sarrami F, Li H et al (2019) Heterologous biosynthesis of elsinochrome A sheds light on the formation of the photosensitive. Chem Sci 10:1457–1465. https://doi.org/10.1039/c8sc02870b

Hudson JB, Imperial V, Haugland RP, Diwu Z (1997) Antiviral activities of photoactive perylenequinones. Photochem Photobiol 65:352–354

Hudson JB, Zhou J, Chen J et al (1994) Hypocrellin, from *Hypocrella bambusae*, is phototoxic to human immunodeficiency virus. Photochem Photobiol 60:253–255. https://doi.org/10.1111/j.1751-1097.1994.tb05100.x

Idris A, Tantry MA, Ganai BA et al (2015) Reduced perylenequinone derivatives from an endophytic *Alternaria* sp. isolated from *Pinus ponderosa*. Phytochem Lett 11:264–269

Iida T, Kobayashi E, Yoshida M, Sano H (2012) Calphostins, novel and specific inhibitors of protein kinase C. II. Chemical structures. J Antibiot (Tokyo) 42:1475–1481. https://doi.org/10.7164/antibiotics.42.1475

Itoh N, Sakagami N, Masaki T, Watanabe M (2012) Perylene in Lake Biwa sediments originating from *Cenococcum geophilum* in its catchment area. Geochim Cosmochim Acta 95:241–251

Jiao WL, Liu L, Zhou RJ et al (2019) Elsinochrome phytotoxin production and pathogenicity of *Elsinoë arachidis* isolates in China. PLoS One 14:e0218391. https://doi.org/10.1371/journal.pone.0218391

Khiralla A, Spina R, Saliba S, Laurain-Mattar D (2019) Diversity of natural products of the genera *Curvularia* and *Bipolaris*. Fungal Biol Rev 33:101–122. https://doi.org/10.1016/J.FBR.2018.09.002

Kishi T, Tahara S, Taniguchi N et al (1991) New perylenequinones from *Shiraia bambusicola*. Planta Med 57:376–379. https://doi.org/10.1055/s-2006-960121

Kobayashi E, Nakano H, Morimoto M, Tamaoki T (1989) Calphostin C (UCN-1028C), a novel microbial compound, is a highly potent and specific inhibitor of protein kinase C. Biochem Biophys Res Commun 159:548–553. https://doi.org/10.1016/0006-291X(89)90028-4

Kobayashi T, Rasmussen C, Sumida H (2019) Characterization of the perylenequinone pigments in Japanese Andosols and Cambisol. Soil Sci Plant Nutr 65:1–10. https://doi.org/10.1080/00380768.2018.1536846

Krishnamoorthy G, Webb SP, Nguyen T et al (2005) Synthesis of hydroxy and methoxy perylene quinones , their spectroscopic and computational characterization , and their antiviral activity. Photochem Photobiol Sci 81:924–933. https://doi.org/10.1562/2004-11-23-RA-378

Kuhnert E, Becker K, Stadler M et al (2021) Secondary metabolite biosynthetic diversity in the fungal family *Hypoxylaceae* and *Xylaria hypoxylon*. Stud Mycol 100118:1–43. https://doi.org/10.1016/j.simyco.2021.100118

Kurobane I, Vining LC, McInnes AG et al (2006) Biosynthesis of elsinochromes C and D. Pattern of acetate incorporation determined by ^{13}C and ^{2}H NMR. Can J Chem 59:422–430. https://doi.org/10.1139/v81-063

Kuyama S, Tamura T (1957) Cercosporin. A pigment of *Cercosporina kikuchii* Matsumoto et Tomoyasu. I. Cultivation of fungus, isolation and purification of pigment. J Am Chem Soc 79:5725–5726. https://doi.org/10.1021/ja01578a038

Lee I, Seok S, Kim W, Yun B (2006) Diaporthin and orthosporin from the fruiting body of *Daldinia concentrica*. Mycobiology 34:38–40

Lei XY, Zhang MY, Ma YJ, Wang JW (2017) Transcriptomic responses involved in enhanced production of hypocrellin A by addition of Triton X-100 in submerged cultures of *Shiraia bambusicola*. J Ind Microbiol Biotechnol 44:1–15

Levic JT, Petrovic TM, Stankovic SC, Ivanovic DM (2013) The incidence of *Pyrenochaeta terrestris* in root of different plant species in Serbia. Zb Matice Srp za Prir Nauk 125:21–30. https://doi.org/10.2298/ZMSPN1325021L

Li C, Wang HQ, Xie JL et al (2000) Analysis and comparisons of compounds among three medical fungi of *Hypocreaceae*. Chinese Tradit Herb Drugs 31:250–251

Li G, Wang H, Zhu R et al (2012) Phaeosphaerins A-F, cytotoxic perylenequinones from an endolichenic fungus, *Phaeosphaeria* sp. J Nat Prod 75:142–147. https://doi.org/10.1021/np200614h

Li T, Deng H, Zhao J, Gu Y (2015) Elsinochrome A photosensitizers: alternative drugs for photodynamic therapy. J Innov Opt Health Sci 08:1530001. https://doi.org/10.1142/s1793545815300013

Li YT, Yang C, Wu Y et al (2021) Axial chiral binaphthoquinone and perylenequinones from the stromata of *Hypocrella bambusae* are SARS-CoV-2 entry inhibitors. J Nat Prod 84:436–443. https://doi.org/10.1021/acs.jnatprod.0c01136

Liao HL, Chung KR (2008) Genetic dissection defines the roles of elsinochrome phytotoxin for fungal pathogenesis and conidiation of the citrus pathogen *Elsinoe fawcettii*. Mol Plant-Microbe Interact 21:469–479

Liu WZ, Ma LY, Li C et al (2001a) Structural elucidation of a new perylenequinone. Acta Pharm Sin 36:313–314

Liu WZ, Shen YX, Liu XF et al (2001b) A new perylenequinone from *Hypomyces* sp. Chin Chem Lett 12:431–432

Ma G, Khan SI, Jacob MR et al (2004) Antimicrobial and antileishmanial activities of hypocrellins A and B. Antimicrob Agents Chemother 48:4450–4452. https://doi.org/10.1128/AAC.48.11.4450-4452.2004

Ma YJ, Sun CX, Wang JW (2019a) Enhanced production of hypocrellin A in submerged cultures of *Shiraia bambusicola* by red light. Photochem Photobiol 95:812–822

Ma YJ, Zheng LP, Wang JW (2019b) Inducing perylenequinone production from a bambusicolous fungus *Shiraia* sp . S9 through co-culture with a fruiting body - associated bacterium *Pseudomonas fulva*. Microb Cell Factories 18:1–14. https://doi.org/10.1186/s12934-019-1170-5

Mains EB (1959) Species of *Hypocrella*. Mycopathol Mycol Appl 11: 311–326

Mastrangelopoulou M, Grigalavicius M, Berg K et al (2019) Cytotoxic and photocytotoxic effects of cercosporin on human tumor cell lines. Photochem Photobiol 95:387–396. https://doi.org/10.1111/php.12997

Meille SV, Malpezzi L, Allegra G et al (1989) Structure of elsinochrome A: a perylenequinone metabolite. Acta Crystallogr C 45:628–632. https://doi.org/10.1107/S0108270188012831

Miskovsky P (2002) Hypericin, a new antiviral and antitumor photosensitizer: mechanism of action and interaction with biological macromolecules. Curr Drug Targets. https://doi.org/10.2174/1389450023348091

Morakotkarn D, Kawasaki H, Tanaka K et al (2008) Taxonomic characterization of *Shiraia*-like fungi isolated from bamboos in Japan. Mycoscience 49:258–265. https://doi.org/10.1007/S10267-008-0419-3

Mulrooey CA, Morgan BJ, Li X, Kozlowski MC (2010) Perylenequinone natural products: enantioselective synthesis of the oxidized pentacyclic core. J Organomet Chem 75:16–29. https://doi.org/10.1021/jo9013832

Mulrooey CA, O'Brien EM, Morgan BJ, Kozlowski MC (2012) Perylenequinones: isolation, synthesis, and biological activity. Eur J Org Chem 21:3887. https://doi.org/10.1038/jid.2014.371

Mumma RO, Lukezic FL, Kelly MG (1973) Cercosporin from *Cercospora hayii*. Phytochemistry 12:917–922. https://doi.org/10.1016/0031-9422(73)80703-4

Newman AG, Townsend CA (2016) Molecular characterization of the cercosporin biosynthetic pathway in the fungal plant pathogen *Cercospora nicotianae*. J Am Chem Soc 138:4219–4228. https://doi.org/10.1021/jacs.6b00633.Molecular

Olivo M, Ali-Seyed M (2007) Apoptosis signalling mechanisms in human cancer cells induced by calphostin PDT. Int J Oncol 30:537–548

Pang X, Lin X, Wang P et al (2018) Perylenequione derivatives with anticancer activities isolated from the marine sponge-derived fungus, *Alternaria* sp. SCSIO41014. Mar Drugs 16:1–13. https://doi.org/10.3390/md16080280

Patriarca A, Pinto VF (2018) Alternaria. In: Reference Module in Food Science. Elsevier, pp 1–8. https://doi.org/10.1016/B978-0-08-100596-5.22572-9

Peter M, Kohler A, Ohm RA et al (2016) Ectomycorrhizal ecology is imprinted in the dominant symbiotic fungus *Cenococcum geophilum*. Nat Commun 7. https://doi.org/10.1038/ncomms12662

Pettit RK (2011) Small-molecule elicitation of microbial secondary metabolites. Microb Biotechnol 4:471–478. https://doi.org/10.1111/j.1751-7915.2010.00196.x

Podlech J, Fleck SC, Metzler M et al (2014) Determination of the absolute configuration of perylene quinone-derived mycotoxins by measurement and calculation of electronic circular dichroism spectra and specific rotations. Chem - A Eur J 20:11463–11470. https://doi.org/10.1002/chem.201402567

Robeson D, Strobel G, Matusumoto GK et al (1984) Alteichin: an unusual phytotoxin from *Alternaria eichorniae*, a fungal pathogen of water hyacinth. Experientia 40:1248–1250

Samson RA, Visagie CM, Houbraken J et al (2014) Phylogeny, identification and nomenclature of the genus *Aspergillus*. Stud Mycol 78: 141–173. https://doi.org/10.1016/j.simyco.2014.07.004

Seto Y, Kogami Y, Shimanuki T et al (2005) Production of phleichrome by *Cladosporium phlei* as stimulated by diketopiperadines of *Epichloe typhina*. Biosci Biotechnol Biochem 69:1515–1519

Sharma SK, Woo T, Naicker S (2013) Perylenequinoe drivatives and uses thereof. United States Patent No. US 8,506,931 B2. Quest Pharmatech Inc. https://patents.google.com/patent/US8506931B2/en. Accessed 20 June 2021

Shen XY, Cheng YL, Cai CJ et al (2014) Diversity and antimicrobial activity of culturable endophytic fungi isolated from moso bamboo seeds. PLoS One 9:1–7. https://doi.org/10.1371/journal.pone.0095838

Shen Y, Liu W, Rong X, Sun Y (2003) Studies on the chemical constituents of a fungus producing perylenequinones. Acta Pharm Sin 38: 834–837

So KK, Chun J, Kim DH (2018) Antimicrobial and antitumor photodynamic effects of phleichrome from the phytopathogenic fungus *Cladosporium Phlei*. Mycobiology 46:448–451

Stack ME, Prival MJ (1986) Mutagenicity of the *Alternaria* metabolites altertoxins I, II, and III. Appl Environ Microbiol 52:718–722

Stadler M, Fournier J, Gardt S, Peršoh D (2010) The phylogenetic position of *Rhopalostroma* as inferred from a polythetic approach. Persoonia 25:11–21. https://doi.org/10.3767/003158510X524231

Stadler M, Ju Y, Rogers JD et al (2004) Chemotaxonomy of *Entonaema*, *Rhopalostroma* and other *Xylariaceae*. Mycol Res 108:239–256. https://doi.org/10.1017/S0953756204009347

Stchigel AM, Calduch M, Mac Cormack W, Guarro J (2004) *Phaeosphaeria microscopica* (Karsten) O. Erikss.: first report on *Deschampsia antarctica* Desv. Bol Micol 19:111–115

Stierle AC, Caddlina JH, Strobel GA (1989) Phytotoxins from *Alternaria alternata*, a pathogen of spotted knapweed. J Nat Prod 52:42–47. https://doi.org/10.1021/np50061a003

Sun CX, Ma YJ, Wang JW (2018) Improved hypocrellin A production in *Shiraia bambusicola* by light-dark shift. J Photochem Photobiol B Biol 182:100–107

Sun CX, Ma YJ, Wang JW (2017) Enhanced production of hypocrellin A by ultrasound stimulation in submerged cultures of *Shiraia bambusicola*. Ultrason Sonochem 38:214–224

Tantry MA, Idris AS, Williamson JS et al (2018) Perylenequinones from an endophytic *Alternaria* sp. of *Pinus ponderosa*. Heliyon 4:1–11. https://doi.org/10.1016/j.heliyon.2018.e01046

Tisch D, Schmoll M (2010) Light regulation of metabolic pathways in fungi. Appl Microbiol Biotechnol 85:1259–1277. https://doi.org/10.1007/s00253-009-2320-1

Wan XY, Chen YT (1981) Hypocrellin A, a new drug for photochemotherapy. Chin Sci Bull 26:1040–1042

Wang JB, Bao JN (1985) Clinical analysis and observation of hypocrellin photochemistry in treatment of Lichen amyloidosis in 37 patients. Acta Acad Med Sin 7:349–352

Weiss U, Altland HW (1965) Red pigments of *Dactynotus rudbeckiae* and *D. ambrosiae* [*Homoptera*, *Aphididae*]. Nature 207:1295–1297

Weiss U, Merlini L, Nasini G (1987) Naturally occurring perylenequinones. Prog Chem Org Nat Prod 52:1–71

Wendt L, Sir EB, Kuhnert E et al (2018) Resurrection and emendation of the *Hypoxylaceae*, recognised from a multigene phylogeny of the *Xylariales*. Mycol Prog 17:115–154. https://doi.org/10.1007/s11557-017-1311-3

Wiehe A, O'Brien JM, Senge MO (2019) Trends and targets in antiviral phototherapy. Photochem Photobiol Sci 18:2565–2612

Wijayawardene N, Hyde K, Lkt A et al (2020) Outline of fungi and fungus-like taxa. Mycospere 11:1060–1456. https://doi.org/10.5943/mycosphere/11/1/8

Williams RB, Henrikson JC, Hoover AR et al (2008) Epigenetic remodeling of the fungal secondary metabolome. Org Biomol Chem 6:1895–1997. https://doi.org/10.1039/b804701d

Wu H, Lao XF, Wang QW et al (1989) The shiraiachromes: novel fungal perylenequinone pigments from *Shiraia bambusicola*. J Nat Prod 52:948–951. https://doi.org/10.1021/np50065a006

Xian LP, Jing XN, Meng D, Sha Y (2006) A new perylenequinone from the fruit bodies of *Bulgaria inquinans*. J Asian Nat Prod Res 8:743–746

Yadav S, Agarwal R, Singh S, Goel S (2015) *Pyrenochaeta romeroi* causing subcutaneous phaeohyphomycotic cyst in a diabetic female. Med Mycol Case Rep 8:47–49. https://doi.org/10.1016/j.mmcr.2015.04.001

Yang H, Wang BY, Zhang Z et al (2014) Whole-genome shotgun assembly and analysis of the genome of *Shiraia* sp . strain Slf14, a novel endophytic fungus producing huperzine A and hypocrellin A. Genome Announc 2:e00011–e00014. https://doi.org/10.1128/genomeA.00011-14

Yano S, Hirohara S, Obata M et al (2011) Current states and future views in photodynamic therapy. J Photochem Photobiol C-Photochem Rev 12:46–67

Yu C, Huang T, Ding Z et al (1993) Encyclopedia of Chinese Medicines, vol. 1, item 1187. Chinese Medicinal Science and Technology Press, Beijing, People's Republic of China

Yu F, Jayawardena RS, Liu J et al (2020) *Hypomyces pseudolactifluorum* sp. nov. (*Hypocreales*: *Hypocreaceae*) on *Russula* sp. from Yunnan, PR China. Biodivers Data J 8:1–22. https://doi.org/10.3897/BDJ.8.e53490

Zeiner CA, Purvine SO, Zink EM et al (2016) Comparative analysis of secretome profiles of manganese (II)-oxidizing Ascomycete fungi. PLoS One 11. https://doi.org/10.1371/journal.pone.0157844

Zhang H, Bai X, Wang H (2017) Isolation and identification of an antimicrobial and cytotoxic chlorated perylenequinone from the symbiotic fungus *Aspergillus fumigatus* D. Biochem Pharmacol 139:110. https://doi.org/10.1016/J.BCP.2017.06.066

Zhang SY, Li ZL, Bai J et al (2012) A new perylenequinone from a halotolerant fungus, *Alternaria* sp. M6. Chin J Nat Med 10:68–71. https://doi.org/10.1016/S1875-5364(12)60015-6

Zhnag H, Liu W (2005) Fungicidal composition containing PQDs. United States Patent No. US 6,936,571 B2. https://patents.google.com/patent/US6936571B2/en. Accessed 13 May 2020