Chapter 5
Biodiversity and Industrial Applications of Genus *Chaetomium*

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Contents

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5.1 Introduction

Genus *Chaetomium* was erected by Gustav Kunze as a novel taxon described as C. globosum as a type species (Fig. 5.1). The genus is characterized by superficial ascoma usually covered with appendages (Hawksworth and Wells 1973) (Fig. 5.2); membranaceous peridium, consisting of several pseudoparenchymatous layers; asci either clavate or fusiform (with biseriately arranged ascospores) or rarely cylindrical (with uniseriately arranged ascospores), thin walled, evanescent, and without apical structures; scarce paraphyses that disappear before ascocarps mature (Von Arx et al. 1986); and ascospores that are brown or gray-brown (never opaque or black), one celled, with one or sometimes two germ pores, and exuding as a dark, black, sticky mass (Hess et al. 1967; Millner et al. 1977).

Various investigators, viz. Ames (1963) and Seth (1970), delimited *Chaetomium* species mainly on the different shapes of ascospores and appendages, while Hawksworth and Wells (1973) classified them on the basis of ascomatal setae ornamentation. Other taxonomic criteria such as peridium structure, asci, and ascospore shapes were selected by Sörgel (1960) and Dreyfuss (1975) to delimit species. In 1986, Von Arx et al. (1986) revised the genus in a more comprehensive way through following the previously introduced taxonomic concepts of Sörgel and Dreyfuss and the unpublished thesis by Carter (1982).

Genus *Chaetomium* is a cosmopolitan taxon and considered one of the prevalent components of different ecological habitats in a wide range of biomes (Von Arx et al. 1986; Abdel-Azeem 2020) due to their potential ability to colonize a wide variety of substrata. Large number of *Chaetomium* taxa are dung inhabitants (coprophilous) (Abdel-Azeem and Salem 2015), and seed and terricolous fungi (Abdel-Azeem

IX. CHAETOMIUM *).

Char. gen.: Sporangium subglobosum, membranaceum, pilis opacis undique obsessum, demum in medio sese aperiens. Sporidia pellucida, massae gelatinosae immixta.

Ein völlig umgekehrtes Myrotheeium Tode. Es umschliefst eine häutige, mit langen, meistens steifen, undurchsichtigen Haaren besetzte Hülle von mehr oder weniger kugeliger Form eine gallertartige Masse, welcher sphärische oder spindelförmige Sporidia eingemischt sind. Bey dem Einwirken der Feuchtigkeit öffnet sich die halbdurchsichtige Umgebung im Mittelpunkte und zieht sich mehr oder weniger zurück, so dafs sie den

*) Von χάιτωμα abgeleitet.

Fig. 5.1 A part of Kunze original description of genus *Chaetomium* in 1817

Fig. 5.2 SEM of *Chaetomium* ascocarp showing peridial hairs ©Abdel-Azeem 2020

2003; Somrithipol 2004; Somrithipol et al. 2004; Abdel-Azeem 2020), and colonize living plant tissues (endophytic) (Abdel-Azeem and Salem 2012; Salem and Abdel-Azeem 2014; Abdel-Azeem et al. 2016b, 2018a; Abo Nahas 2019; Balbool and Abdel-Azeem 2020), cultural heritage wood (Abdel-Azeem et al. 2019), and compost (Abdel-Azeem 2003).

Due to their potential enzymes, *Chaetomium* species is considered a very potent cellulose and organic material degrader and acts as an antagonist against plant fungal pathogenic taxa (Soytong et al. 2001; Abdel-Azeem 2020). Several studies showed that *C. globosum* is a very strong cellulose decomposer (Umikalsom et al. 1997, 1998) with a very potent antagonist of various soil microbiota (Aggarwal et al. 2004; Dhingra et al. 2003; Soytong et al. 2001; Abdel-Azeem 2020).

In the last decades *C. globosum* and its species have drawn much attention to be used to manage several economically important diseases; for example, *Cochliobolus sativus* (Biswas et al. 2012), ascospore suspensions, and culture extracts reduced infection of apple seedlings by *Venturia inaequalis* (Cullen and Andrews 1984). Walther and Gindrat (1988) and Di Pietro et al. (1992) recorded some isolates of *C. globosum* that produced antibiotics able to suppress damping-off of sugar beet caused by *Pythium ultimum*. Other taxa, e.g., *C. cupreum* and *C. globosum*, were the target of other studies carried out by Soytong (1992a, b) and showed the potentiality to reduce leaf spot disease of corn caused by *Curvularia lunata*, rice blast disease caused by *Magnaporthe oryzae*, sheath blight disease of rice caused by *Rhizoctonia solani*, and tomato wilt disease caused by *Fusarium oxysporum* f. sp. *lycopersici.*

As a potent cellulose degrader, taxa of genus *Chaetomium* produce over 500 bioactive substances and these 500 bioactive metabolites have potential for the medicinal industry (Castagnoli et al. 2017). This chapter discusses the diversity of genus *Chaetomium* in various habitats and their potential industrial and agricultural applications.

5.2 *Chaetomium* Diversity in Different Habitats

5.2.1 Desert

A desert is defined as a region that receives extremely low rains—less than 250 mm per year—far less than the amount required to support the growth of most plants (Abdel-Azeem et al. 2016a; Abdel-Azeem 2020). Approximately one-third of Earth's land surface is a desert (Fig. 5.3) with an area more than 52,000 km^2 (Abdel-Azeem 2020).

Deserts are considered an obvious example of the harsh environment where strong solar radiation, relatively poor soil (low organic matter and very low water activity), and fungi inhabiting these areas are considered great challengers (Abdel-Azeem 2020; Kour et al. 2019b; Kumar et al. 2019; Yadav et al. 2020b, c). One of the main characteristic features of the terricolous fungi in the desert is low densities of colony-forming units (CFU) with high species diversity as recorded by several

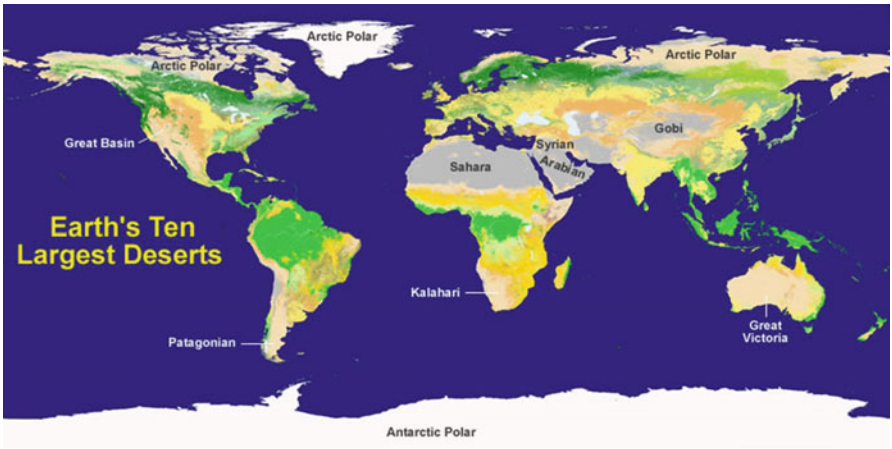


Fig. 5.3 World's desert biome

investigators, e.g., Christensen (1981), Mouchacca (1995), Abdel-Azeem (2003), Abdel-Azeem and Ibrahim (2004), and Abdel-Azeem (2020). Studies on desert terricolous fungi started with the pioneer study of Adametz (1886) when he isolated and named 4 species of yeasts and 11 species of filamentous fungi including *Aspergillus* (Watanabe 2002; Abdel-Azeem et al. 2016a; Abdel-Azeem 2020). Due to their low CFU, the desert fungi attracted less attention of various researchers worldwide in comparison with other ecosystems and they consider these extreme ecosystems as suitable in situ models to study the relationship between phylogenetic biodiversity and function (Adams et al. 2006).

Sabet (1935), the initial starter of soil mycology in Egypt, along with various brilliant mycologists like Montasir et al. (1956a, b), Mahmoud et al. (1964), Besada and Yusef (1968), Moubasher and Moustafa (1970), Moubasher and El-Dohlob (1970), Salama et al. (1971), Mouchacca (1971), Mouchacca 1973a, b, Mouchacca 1977, Mouchacca 1982), Nagiub and Mouchacca (1970–1971), Mouchacca and Nicot (1973, 1974), Mouchacca and Joly 1976), Samson and Mouchacca (1974, 1975), Moubasher et al. (1985, 1988, 1990), Nassar (1998), Abdel-Hafez et al. (1989a, b, 1990), Abdel-Sater (1990, 2000), Abdel-Hafez and El-Maghraby (1993), Abdel-Azeem and Ibrahim (2004), and Abdel-Azeem (1991, 2003, 2009), carried on his shoulders the burden of investigating and recording the native taxa in the Egyptian deserts.

In 1970, Moubasher and Moustafa recorded two species of *Chaetomium* (*C. murorum* and *C. olivaceum*) during their intensive study concerning surveying of Aspergillus and Penicillium in Egyptian soils. In his first solid study on ascomycetes in Egypt, Abdel-Azeem (2003) recorded only two species of *Chaetomium* from desert samples; they were *C. globosum* and *C. brasiliense*. In their pioneer study of Sinai terricolous fungi, Abdel-Azeem and Ibrahim (2004) recorded *C. globosum and C. brasiliense.* In 2005, Abdel-Azeem through his extensive survey of literature published a key concerning genus *Chaetomium* in Egypt with Moustafa (Moustafa

and Abdel-Azeem 2005). They recorded 53 species and one variety isolated/reported from different substrates in Egypt. Only five species of *Chaetomium* were introduced new to the science from Egyptian soil as mentioned by Abdel-Azeem (2020); they were *Chaetomium gelasinosporum* Aue and Muller (1967), *C. mareoticum* Besada and Yusef (1969a, b), *C. sinaiense* Moustafa and Ess El-Din (1989), *C. strumarium* (J.N. Rai, J.P. Tewari and Mukerji) P.F. Cannon (1986), and *C. uniporum* Aue and Muller (1967).

In Libya, soil mycobiota attracted few Egyptian mycologists like Naim (1967a, b) who studied rhizosphere and terricolous fungi of a medicinal plant, *Artemisia herba-alba*, and fungi under citrus trees in Tripoli. In 1974 Prof. Hassan Youssef (1974), the Egyptian mycologist, studied the fungal flora of Libyan soil, collected samples from 16 different localities, and recovered different species of *Chaetomium*; they were *Chaetomium bostrychodes*, *C. irregulare*, *C.* cf. *mollicellum*, *Chaetomium* sp. (new species), *C. spirale*, *C. fusisporum*, and *C. jodhpurense* with low frequency of occurrence. By available data from the checklist of Libyan fungi (El-Buni and Rattan (1981)) only ten species of *Chaetomium* were recorded.

El-Said and Saleem (2008) studied soil fungi at western region of Libya while in 2010 Mansour studied soil fungi in eastern region of Libya. The former recovered 63 species and 5 varieties belonging to 30 fungal genera out of 75 soil samples and genus *Chaetomium* was represented by only 1 species (*C. globosum*). However, Mansour (2010) recovered 59 species belonging to 23 genera out of 100 samples with only 1 taxon (*C. globosum*) and 1 unknown species.

Concerning the northern part of Israel, Volz et al. (2001) recorded 20 species of *Chaetomium* from different soil types, while Grishkan et al. (2003) recovered 11 species of *Chaetomium* by applying soil dilution plate method from soil samples gathered from western shore of the Dead Sea. They found nine species (*Alternaria alternata*, *A. raphani*, *Aspergillus niger*, *Aureobasidium pullulans*, *Chaetomium globosum*, *Ch. murorum*, *Cladosporium cladosporioides*, *Penicillium aurantiogriseum*, and *Stachybotrys chartarum*) as the indicator micromycete complex for the Dead Sea coastal habitat based on the spatial and temporal occurrence of these species.

Taxa recovered by Grishkan and Nevo (2010) from Negev Desert showed that more than 360 taxa were identified. *Chaetomium* came in 25 recorded species. In 2018, Grishkan (2018) studied the thermotolerant communities in Israeli desert and north territories and she recovered 165 species from 82 genera isolated at 37 °C using the soil dilution plate method. Aspergilli (*Aspergillus fumigatus* and *A. niger*) and teleomorphic ascomycetes (*Canariomyces notabilis*, *Chaetomium nigricolor*, and *Ch. strumarium*) comprised the basic part of the thermotolerant communities. In Tunisia 16 fungal strains were isolated from arid Tunisian soils by Mtibaà et al. (2017). The most interesting strain was identified based on the analysis of the amplified nucleotide sequences of the nuclear ribosomal ITS1-5.8-ITS4 region (600 bp) as *Chaetomium*.

Egyptian mycologists studied desert fungi in Saudi Arabia, e.g., Ali (1977) and Abdel-Hafez (1981, 1982a, b) who identified 24 genera and 47 species and 34 genera and 80 species, respectively. Abdel-Hafez (1982a) isolated and identified only one

species of *Chaetomium* (*C. globosum*) out of 34 genera and 80 species in addition to 1 variety out of 40 soil samples collected from different places in the desert of Saudi Arabia.

In his extensive study, Abdel-Hafez (1982b) isolated and identified 75 species in addition to 5 cellulose-decomposing varieties which belong to 27 genera. *Chaetomium* recorded 7 species (*C. spirale, C. globosum, C. bostrychodes, C. cochliodes, C. olivaceum, C. jodphurence,* and *C. subglobosum*). In their study on cellulose-degrading fungi, Bahkali and Khiyami (1996) isolated 30 fungal species belonging to 15 genera from 30 soil samples where genus *Chaetomium* was represented by only 1 unknown species in this study in Saudi Arabia. Saadabi (2006) studied the fungal biota (flora) of Saudi Arabian soils in 16 different localities in southern area of the kingdom. He identified only seven species of *Chaetomium* in this study.

Another group of researchers in 2018 studied the fungal community of six sand samples from Saudi Arabia and Jordan deserts and they characterized taxa by culture-independent analysis via next-generation sequencing of the 18S rRNA genes and by culture-dependent methods followed by sequencing of internal transcribed spacer (ITS) region (Murgia et al. 2018). They isolated 11 colonies of filamentous fungi from six samples under investigation where *Chaetomium* (*C. madrasense*) was recorded. In Sudan, Nour (1956) made a preliminary survey of fungi from various soil types. He isolated 18 genera and 35 species without any *Chaetomium* at all. One hundred and twenty sites, from six localities from the Sudan Gezira, were examined for soil mycoflora by Amin and Abdalla (1980). Only one species of *Chaetomium* as *C. globosum* was isolated from the six localities.

The desert fungi of Kuwait were investigated by Halwagy and his colleagues in Halwagy et al. (1982); they identified a total of 52 genera and 130 species. Six species of *Chaetomium* were recovered during this study; they were *Chaetomium elatum*, *C. virginicum, C. olivaceum*, *C. rectopilium, C. globosum*, and *C. spirale.* Recently, Suleiman et al. (2019) examined the general soil fungi and AM fungal communities associated with a Lonely Tree species (*Vachellia pachyceras*) existing in the Sabah Al-Ahmad Natural Reserve located at the Kuwait desert. Their results recorded only one species of *Chaetomium* and their work thus provides a baseline of the fungal and mycorrhizal community associated with rhizosphere in the Kuwaiti desert. *Chaetomium atrobrunneum, Chaetomium bostrychodes*, *Chaetomium globosum, Chaetomium murorum,* and *Chaetomium spirale* were recorded by Maharachchikumbura et al. (2016) in Oman. In 2017, *C. homopilatum* and *Chaetomium* sp. were recorded by Al-Sadi et al. (2017) in dam reservoir soils of arid climates in Oman.

The study carried out by Moubasher and Al-Subai (1987) is considered the real start of soil mycology in Qatar and they isolated three species of *Chaetomium*. *Chaetomium thermophilum* was recorded by Mandeel (2002) during his study of microfungal community associated with rhizosphere soil of *Zygophyllum qatarense* in arid habitats of Bahrain.

5.2.2 Salterns and Mangrove

When evaporation of seawater is accompanied with high concentration of halite (NaCl) greater than 10% (m/w), thalassohaline (hypersaline) environments originate (Oren 2002) and provide some of the most extreme harsh habitats in the world. These habitats are common all around the globe, and include marine ponds, salt marshes, salt or soda lakes, and sea-salt and man-made salterns (Trüper and Galinski 1986; Gaba et al. 2017; Yadav et al. 2020a; Yadav et al. 2020e; Yadav et al. 2015). In Kuwait, Moustafa and Abdel-Azeem (2011) studied the fungi of salt marshes where they isolated 82 species and 44 genera from 40 composite soil samples. In their study genus *Chaetomium* was represented by three species (*Chaetomium globosum, C. spirals,* and *C. olivaceum*). As the author of a pioneer study on ascospore-producing fungi in Egypt, Abdel-Azeem (2003) mentioned that different species of genus *Chaetomium* are among the filamentous fungi that appear with moderate frequencies in salterns (Abdel-Azeem 2003). *Chaetomium* is one of the filamentous fungi that have been isolated from different salterns around the world (Cantrell et al. 2006).

Abdel-Azeem (2003) recorded a list of *Chaetomium* taxa isolated from salt marshes and salty soil in Egypt, namely *C. circinatum* Chivers, *C. hamadae* (Udagawa) Arx, *C. hexagonosporum* A. Carter & Malloch, *C. homopilatum* Omvik, *C. piluliferum* J. Daniels, *C. rectopilium* Fergus & Amelung, and *C. subspirilliferum* Sergejeva. For the first time in 2011 Moustafa and Abdel-Azeem published an updated checklist of Ascomycota reported from soil and other terricolous substrates in Egypt. They recorded that at the generic level *Chaetomium* came first among all reported genera represented by 51 taxa. The pan-global stable taxa of genus *Chaetomium* that occurred in hypersaline habitats were C. *globosum, C. spirale, C. olivaceum, C. circinatum*, *C. hamadae, C. hexagonosporum*, *C. homopilatum*, *C. piluliferum*, *C. rectopilium,* and *C. subspirilliferum* (Abdel-Azeem 2003). Sridhar (2009) studied fungi in Pichavaram mangroves of the south-east coast of India and he recorded two species of *Chaetomium* (*C. globosum* and *C. olivaceum*).

5.2.3 Indoor Air

In 2013 a study of airborne fungus spores by viable and nonviable methods in Havana, Cuba, was carried out by Almaguer et al. (2013). Their study on the Havana aeromycobiota diversity was extended from November 2010 to October 2011 using two complementary volumetric methods. A total of 35 fungal genera were characterized; 26 of them were recognized only by nonviable methods, 6 with viable methodology, and the other 3 with both sampling methods. Furthermore, 47 species were identified by cultivation and the spores collected with the nonviable methodology. These could not be included in a specific genus, and thus were categorized

into five fungal types. In general, the main, spread worldwide, mitosporic fungi also predominated the Havana atmosphere. The predominant species were *Cladosporium cladosporioides*, *Aspergillus flavus*, and *Penicillium citrinum*. Moreover, several Zygomycetes (*Syncephalastrum racemosum, Rhizopus stolonifer,* and *Rhizopus oryzae*), Ascomycetes (*Chaetomium globosum*), and Basidiomycetes such as *Coprinus* or *Ganoderma* were isolated.

In their extensive study Wang et al. (2016) recovered 145 isolates belonging to Chaetomiaceae that were cultured from air, swab, and dust samples from 19 countries. Countries included Algeria, Australia, Canada, China, Cuba, Denmark, Germany, India, Indonesia, Mexico, The Netherlands, New Guinea, Solomon Islands, South Africa, Spain, Switzerland, Thailand, Uruguay, and the USA. Based on the phylogenetic analyses of DNA-directed RNA polymerase II second largest subunit (rpb2), β-tubulin (tub2), ITS, and 28S large subunit (LSU) nrDNA sequences, together with morphological comparisons with related genera and species, 30 indoor taxa are recognized, of which 22 represent known species, 7 are described as new, and 1 remains to be identified to species level. In our collection, 69% of the indoor isolates with six species cluster are members of the *Chaetomium globosum* species complex, representing *Chaetomium* sensu stricto. The other indoor species fall into nine lineages that are separated from each other with several known chaetomiaceous genera occurring among them. No generic names are available for five of these lineages, and the following new genera are introduced here: *Amesia* with three indoor species, *Arcopilus* with one indoor species, *Collariella* with four indoor species, Dichotomopilus with seven indoor species, and Ovatospora with two indoor species. The generic concept of Botryotrichum is expanded to include Emilmuelleria and the Chaetomium-like species *B. murorum* (= *Ch. murorum*) in which two indoor species are included. The generic concept of Subramaniula is expanded to include several *Chaetomium*-like taxa as well as one indoor species. Humicola is recognized as a distinct genus including two indoor taxa. According to this study, *Ch. globosum* is the most abundant Chaetomiaceae indoor species (74/145), followed by *Ch. cochliodes* (17/145), *Ch. elatum* (6/145), and *B. piluliferum* (5/145). The morphological diversity of indoor Chaetomiaceae as well as the morphological characteristics of the new genera were described and illustrated in their study. This taxonomic study redefines the generic concept of *Chaetomium* and provides new insight into the phylogenetic relationships among different genera within Chaetomiaceae.

Fourteen toxigenic indoor *Chaetomium*-like isolates from buildings in Finland were investigated by Castagnoli et al. (2017). Six *C. globosum*-like strains from indoor dusts were toxic with boar sperm assay and cytotoxic to porcine kidney cells (PK-15), emitted green fluorescence, and produced chaetoglobosin-inhibiting cellular glucose transporter. OT7 and OT7b strains from indoor dust were cytotoxic with PK-15 cells and were nonfluorescent and produced the extremely cytotoxic protein synthesis inhibitor, chaetomin. The six *C. globosum*-like strains were resistant to borax and very sensitive to the wetting agent Genapol used in cleaning chemicals. This may indicate that indoor *Chaetomium*-like fungi occupy their own ecological niche in buildings.

Abdel-Rahim et al. (2018) evaluated the correlation between fungi causing paint deterioration and air contamination in Assiut University Hospitals to give a complete picture of the fungal quantity and spectrum. Seventeen fungal species were isolated from 15 samples of deteriorated water-based paint collected from the hospitals. *Chaetomium globosum* was the most common paint-deteriorating fungal species, followed by *Alternaria alternata*, *Aspergillus parasiticus, Penicillium oxalicum*, and *Setosphaeria rostrata*. Direct examination confirmed the ability of these fungi to colonize the paint samples producing mycelia, conidia, and fruiting bodies. In vitro, these fungi exhibited high potential to utilize the thin layer of polyacrylic paint and significant enzymatic activities of cellulase, lipase, and urease that may play a main role in paint degradation and as virulence factor of human diseases. Moreover, 27 fungal species were isolated as air-contaminating mycobiota. *Aspergillus* spp., *Cladosporium cladosporioides*, *P. oxalicum*, *A. alternata*, and *C. globosum* caused a considerable amount of indoor air contamination. The results indicated that there is a clear correlation between fungi causing paint deterioration and air contamination, whereas certain fungi were responsible for wall paint deterioration and frequent indoor air contamination. The current study suggests that improvement of antimicrobial additives of paints may be a promising approach to reduce paint biodeterioration and subsequently air contamination of indoor environments.

5.2.4 FreshWater

Chaetomium globosum besides actinomycetes and cyanobacteria was identified as a producer of the volatile metabolites geosmin and 2-phenylethanol (Kikuchi et al. 1981), which contribute to earthy–musty odor and taste of public water supplies. However, *Chaetomium* (Nasser 2004; Gonçalves et al. 2006; Hageskal et al. 2006; Gashgari et al. 2013) and anamorphic Humicola (Göttlich et al. 2002a; Göttlich et al. 2002b; Nasser 2004) and Botryotrichum (Nasser 2004) were repeatedly isolated from drinking water samples, and further investigations are needed to clarify the origin of odor metabolites and the significance of the fungal contribution to production in water systems. Similarly, the potential mycotoxin production by *Chaetomium* spp. in water and their concentration have not been evaluated. *C. globosum* was isolated in some studies from relatively high number of drinking water samples (Nasser 2004) and such contamination may tend to increase in stored water. Some *Chaetomium* species have the potential to cause life-threatening infections in immunocompromised individuals, but these species have not been reported from drinking water, and other sources in the indoor environment are more likely the source of infection.

5.2.5 Foods

As a food contaminant, *Chaetomium* taxa are frequently isolated from different food products whereas only in a limited number of cases do they act as spoilage fungi. With regard to ascomycetous fungus-contaminated food, *Chaetomium* was the only one that produced brown to black ascocarp which was easily identified (Pitt and Hocking 2009).

Only a few *Chaetomium* species were recorded in foods, e.g., *C. globosum*, as the most frequently encountered species; some other taxa, e.g., *C. brasiliense* and *C. funicola*, are common species in tropical commodities (Saito et al. 1976; Pitt and Hocking 2009). High contamination rate by those species was recorded in soybeans, mung beans, black beans, rice, maize, barley, nuts overall, copra, and sorghum (Pitt et al. 1993, 1994, 1998; Freire et al. 1999; Pitt and Hocking 2009; Sumalan et al. 2011).

C. globosum has been isolated from a variety of commodities, particularly wheat, barley, maize (also as *C. cochliodes*), oat grains (as *C. ochraceum* and *C. cochliodes*), rice (also as *C. olivaceum*), sorghum, millet, beans (also as *C. cochliodes*), soybeans (also as *C. olivaceum* and *C. cochliodes*), mung beans, copra, peanuts, kemiri nuts, cashew nuts, walnuts, hazelnuts, pea seeds (also as *C. cochliodes*), tomato (as *C. cochliodes*), margarine, green tea, black tea, sugarcane (as *C. fibripilium*), and spices such as black pepper, white pepper, chili and hot pepper seeds (as *C. cochliodes*), ginger, cinnamon, cumin, fennel, and Bishop's weed (Abdel-Azeem 2003; Hubka 2015). High level of infection by *C. globosum* was observed particularly in rice, copra, soybean, mung beans, maize, barley, cashew nuts, candlenuts, and nuts overall (Hubka 2015). This species has also been implicated in causing disease in pears in Egypt (Ismail and Abdalla 2005).

C. funicola has been recorded at relatively high frequencies from soybean samples, beans overall, and cashew nuts (Hubka 2015). The species was further isolated from rice, maize, peanuts, cashew nuts, copra, beans, mung beans, soybeans, pea seeds (also as *C. dolichotrichum*), sorghum, radish, eggplant, and spices (as *C. dolichotrichum*). *C. indicum* is phylogenetically close to *C. funicola*, but distinct. This species also resembles *C. funicola* in morphology and is distinguished solely by the absence of stiff, unbranched ascomatal hairs. *C. indicum* has been isolated from beans, soybeans, pea seeds, rice, and spices, and it is possible that it is commonly misidentified with *C. funicola*. Another species clearly distinct from *C. funicola* based on ITS and LSU rDNA data, but morphologically similar, is *C. reflexum* that has been reported from pepper[158] and pea seeds.[158] *C. brasiliense* was isolated from a similar spectrum of tropical commodities as *C. funicola* including soybeans, mung beans, black beans, rice, maize, cashew nuts, peanuts, sorghum, and black pepper (Hubka 2015).

Other species are isolated rarely from food products, viz: *C. aureum*, *C. atrobrunneum*, and *C. murorum* were reported from rice; *C. nigricolor*, *C. raii*, and *C. subaffine* from cereals; *C. bostrychodes*, *C. elatum*, *C. murorum*, and *C. succineum* from pea seeds; *C. aureum* and *C. bostrychodes* from oat grains;

and *C. aureum* from snap beans and butter (Hubka 2015). *C. convolutum* (as *C. biapiculatum*) was reported from spices; *C. carinthiacum* from thyme; *Achaetomium globosum* from cumin; *C. bostrychodes*, *C. robustum*, and *C. aureum* from pepper; and *Chaetomium* cf. *fusiforme* and *C. aureum* from tea (Hubka 2015). Webb and Mundt (1978) isolated *C. fimeti* (usually classified in the genus *Chaetomidium*) at relatively high frequencies from vegetables; *C. crispatum* was isolated from rotting potatoes, *C. elatum* from rotting onion, and *C. murorum* from Latundan banana (Hubka 2015).

Chaetomium spp. were reported from various seeds, some of which may be used as food or for oil extraction. *C. funicola* (as *C. dolichotrichum*), *C. globosum* (also as *C. cochliodes*), *C. indicum*, *C. madrasense*, and *C. murorum* were isolated from linseed (*Linum usitatissimum*); *C. bostrychodes* and *C. globosum* from okra (*Hibiscus esculentus*); *C. aureum*, *C. globosum*, *C. funicola*, and *C. murorum* from cucumber seeds (*Cucumis sativus*); *C. elatum*, *C. globosum*, and *C. murorum* from pumpkin seeds (*Cucurbita maxima*); *C. carinthiacum* from poppy seeds (*Papaver somniferum*); *C. funicola* from sesame (*Sesamum indicum*); and *C. globosum* from safflower (*Carthamus tinctorius*) and vegetable marrow (*Cucurbita pepo*, also as *C. cochliodes*) (Hubka 2015). Unidentified *Chaetomium* spp. were found on meat products, dried milk, rice, maize, wheat, sorghum, soybeans, beans, mung beans, copra, tapioca, black pepper, peanuts, cashew nuts, sorghum, sesame seeds, Bishop's weed, cumin, lotus seeds (Pitt et al. 1994), pumpkin seeds (Weidenbörner 2001), and herbal drugs (Chourasia 1995; Hubka 2015).

5.2.6 Polar

Around 2.3% of the world's fungal biota exists in the Arctic and fungi in this region have been isolated from various substrates and habitats (Ivarson 1965; Reeve et al. 2002; Säwström et al. 2002; Callaghan et al. 2004; Ozerskaya et al. 2009; Pathan et al. 2009). More than 1000 species and over 400 genera of non-lichenized fungi have been reported from Antarctic regions (including the sub-Antarctic) (Bridge and Spooner 2012; Arenz et al. 2014) including genus *Chaetomium*. Selbmann et al. (2015) published distributional records of Antarctic fungi based on strains preserved in the Culture Collection of Fungi from Extreme Environments (CCFEE) Mycological Section associated with the Italian National Antarctic Museum (MNA) with only one record of *Chaetomium* spp.

Fungal diversity in the Arctic and Antarctic permafrost has been studied intensively over the last decade, and it has been shown to have considerable taxonomic diversity, with significant numbers of new taxa (Ruisi et al. 2007; Yadav et al. 2018, 2019b, d). In some permafrost regions, yeasts represented an important, or even the major (up to 100%), part of all of the fungi isolated, and 20–25% of the total aerobic heterotrophs (Vorobyova et al. 1997; Steven et al. 2006).

In the cold deserts in Antarctica, like in the McMurdo Dry Valleys and the Ross Desert in southern Victoria Land, which is considered one of the harshest

environments known on Earth (Nienow and Friedmann 1993), primarily xerophilic, basidiomycetous yeasts have been isolated (Vishniac and Onofri 2003; Onofri et al. 2004; Takano et al. 2004). These were found at the highest frequencies in the youngest layers, which were less than 10,000 years old, although they have also been detected in three-million-year-old Pliocene samples (Dmitriev et al. 1997a, b; Rivkina et al. 2000).

In both the active layer and the perennially frozen Arctic sediments, a large variety of filamentous fungi have been detected, belonging to Ascomycota, Basidiomycota, Zygomycota, Chytridiomycota, and Glomeromycota (Wallenstein et al. 2007). *Chaetomium* is one of the most frequently occurring genera of the filamentous fungi recorded by several researchers: Vishniac (1993), Azmi and Seppelt (1998), Ivanushkina et al. (2005), Kurek et al. (2007), Ozerskaya et al. (2008, 2009), and Stakhov et al. (2008).

5.2.7 *On Herbivore Dung*

Although *Chaetomium* is not a strictly coprophilous fungus genus, the diversity of representatives of the genus *Chaetomium* on dung is continuously represented in studies of dung fungi diversity worldwide (Simões Calaça et al. 2020). One of the most representative and recent researches on the occurrence of this genus on dung, and that was a precursor of others, was developed by Doveri (2004, 2008, 2011, 2013, 2016)). In arid Sinai, Egypt, Abdel-Azeem and Salem (2015) studied the coprophilous fungi and they recorded seven species of *Chaetomium* on camel, donkey, and goat dung. Doveri (2018) provided an updated key to sexual genera of Chaetomiaceae, where a new species of the related genus *Chaetomidium* (*C. vicugnae* Doveri) is described from a sample of vicuña dung (*Vicugna vicugna*). In 2020, Abdel-Azeem published an updated dichotomous key of all taxa of *Chaetomium* worldwide.

5.2.8 *Living Plants, Lichens, and Animals*

Endophytes colonize without any apparent symptoms in the living internal tissues of plants (Petrini 1991; Suman et al. 2016). There are 1.3 million species of endophytic fungi alone, the majority of which are likely found in tropical ecosystems (Verma et al. 2014; Rana et al. 2019b). There has been great interest in endophytic fungi as potential producers of novel biologically active products (Schutz et al., 2002; Wildman 2003; Strobel and Daisy 2003; Tomita 2003; Urairuj et al. 2003; Spiering et al. 2006; Manoharachary et al. 2013; Abdel-Azeem et al. 2016a, b, c, 2018a; Kour et al. 2019c; Rana et al. 2019a).

In the last 5 years, there has been evidence of the use of endophytes for producing various bioactive metabolites, e.g., anticancer, antimicrobial, antirheumatoid, liver

protection, and antioxidant compounds, and for biotransformation process (Strobel et al. 2008; Vega et al. 2008; Pimentel et al. 2011; Salem and Abdel-Azeem 2014; Abdel-Azeem et al. 2016a; Abdel-Azeem et al. 2018a; Darwish et al. 2020; Devi et al. 2020).

Species of *Chaetomium* as a member of non-clavicipitaceous endophytes attracted the attention of researchers as effective producers of bioactive metabolites (Abdel-Azeem 2020). Such studies may lead to the description of new *Chaetomium* species; for example, Sharma et al. (2013) described *C. jatrophae* recovered from *Jatropha podagrica* in India. Also Blanchette et al. (2017) and Abdel-Azeem et al. (2018b) recovered new Egyptian and African records of *Chaetomium*, namely *C. iranianum* and *C. grande*, respectively. In 2008, Abdel-Lateff (2008) produced Chaetominedione as a new tyrosine kinase inhibitor isolated from the algicolous marine fungus *Chaetomium* sp. recovered from seaweed *Valonia utricularis*, collected from the waters around the Azores (Atlantic Ocean). Abdel-Azeem and Salem (2012) studied the laccase-producing fungi in Egypt by screening nine sources under investigation. They recovered endophytic ones, namely *Chaetomium globosum*, *Phoma exigua*, *Thanatephorus cucumeris*, and *Sordaria fimicola*. pH 7, incubation temperature 30 °C, 1% maltose, and 0.3% peptone supported the highest biomass and laccase production for *Chaetomium.*

Mustafa et al. (2013) studied the ability of some endophytic taxa for green synthesis of AgNPs. They found that the most abundant species were *Alternaria alternata*, *Nigrospora oryzae*, and *Chaetomium globosum*.

In Egypt, Salem and Abdel-Azeem (2014) recovered 15 species of endophytic taxa, namely *Chaetomium atrobrunneum, C. bostrychodes*, *C. brasiliense, C. globosum, C. gracile, C. hamadae, C. iranianum, C. mareoticum, C. murorum, C. nigricolor, C. perlucidum, C. piluliferum, C. senegalense, C. strumarium,* and *C. subspirilliferum* that hosted eight vascular higher medicinal plants in Saint Katherine Protectorate, South Sinai, Egypt. Jin et al. (2014) recovered *C. globosum* during their study on fungal communities of South China Sea sponges *Theonella swinhoei* and *Xestospongia testudinaria*. Endolichenic fungi associated with lichens of Champawat district, Uttarakhand, northern India, were studied by Suryanarayanan and Thirunavukkarasu in Suryanarayanan and Thirunavukkarasu (2017). They recovered *Acremonium, Chaetomium,* and *Xylaria*.

5.2.9 Human

Infections caused by *Chaetomium* species are rarely implicated in human disease; their spectrum of mycoses includes keratitis, onychomycosis, and sinusitis in immunocompetent individuals and empyema, pneumonia, and fatal disseminated cerebral disease in immunocompromised hosts and intravenous drug users. Despite being saprobic ascomycetes with only occasional involvement in human disease processes, *Chaetomium* species are capable of inducing a broad spectrum of mycoses including

light diseases up to fatal disseminated cerebral disease (Hoppin et al. 1983; Anandi et al. 1989; Yeghen et al. 1996; Aru et al. 1997; Thomas et al. 1999).

Chaetomium atrobrunneum is a notably invasive, neurotropic species, and its ability to grow at elevated temperatures may contribute to its neurotropism (Stiller et al. 1992; Guarro et al. 1995; Friedman 1998; Guppy et al. 1998; Rock 1998; Lesire et al. 1999) and causes serious diseases in a bone marrow transplant patient (Thomas et al. 1999). *Chaetomium strumarium* is another invasive, neurotropic species which causes fatal cerebral mycosis (Abbott et al. 1995). *C. strumarium* was detected through sectioning and histopathology and recovered from infected tissue of the brain. Recently, *Chaetomium perlucidum* is confirmed as a neurotropic species and Barron et al. (2003) documented the first two cases of invasive human mycoses caused by this taxon.

5.2.10 Decaying Wood

Chaetomium is one of the most potent soft rotter fungi. These fungi typically attack higher-moisture and lower-lignin-content wood and can create unique cavities in the wood cell wall. Less is known about the soft-rot degradative enzyme systems, but their degradative mechanisms are reviewed along with the degradative enzymatic and nonenzymatic systems known to exist in the brown-rot and white-rot fungi.

Degradation of ancient Egyptian papyrus papers by microbiota has been the target of intensive study carried out by Kowalik and Sadurska (1973) in Cairo museums. They recovered different fungi imperfecti (anamorphic ascomycetes), teleomorphic Ascomycetes, and Actinomycetes too. Some species of the genus *Chaetomium* and some actinobacteria related to the genus Streptomyces seemed to be specific for papyrus and/or for Egyptian climatic conditions. They recovered 12 species of *Chaetomium*; they were *Ch. angustum, Ch. atrobrunneum, Ch. bostrychodes, Ch. cochliodes, Ch. elatum, Ch. fusiforme, Ch. globosum, Ch. indicum, Ch. ochraceum, Ch. olivaceum, Ch. trilaterale,* and *Ch. turgidopilosum.*

Among the fungi commonly found in environmental studies performed in archives and museums, some display cellulolytic properties such as species from the genera *Trichoderma, Penicillium, Botrytis, Trichothecium, Phoma, Chaetomium, Aspergillus, Cladosporium, Stemphylium, Alternaria, Hormodendrum,* and *Aureobasidium*. Among the proteolytic genera, one can find *Aureobasidium, Chaetomium, Cladosporium, Botrytis, Trichoderma, Verticillium, Mucor, Epicoccum,* and *Gymnoascus* (da Pinheiro 2014). *Aureobasidium, Botrytis, Chaetomium, Cladosporium, Epicoccum,* and *Mucor* genera were identified in the present study, in both air and surface samples (de Paiva Carvalho et al. 2018). Regarding the wooden sculptures, *Chaetomium globosum* Kunze and *P. copticola* were the most frequent fungal species in the study carried out by de Paiva Carvalho et al. (2018) on fungal contamination of paintings and wooden sculptures inside the storage room of a museum. Moreover, *Aspergillus sclerotiorum* G.A. Huber and

Penicillium oxalicum Currie and Thom were exclusively found on wooden sculpture samples, and not in any of the air samples.

In 2019 Abdel-Azeem et al. studied the assessment of biodegradation in ancient archaeological wood from the Middle Cemetery at Abydos, Egypt. Identification of the recovered taxa was done by examining morphological characteristics and extracting rDNA from pure cultures and sequencing the ITS region. Wooden objects, made from *Cedrus*, *Juniperus*, and *Acacia* as well as several unidentified hardwoods, were found with extensive degradation and were exceedingly fragile. Recovered taxa were *Chaetomium*, *Cladosporium*, *Fusarium*, *Penicillium*, *Stemphylium, Talaromyces*, and *Trichoderma*. Results provide important information on the current condition of the wood and give insights into the identity of the fungi in wood and soils at the site.

5.3 Enzymes

The interest in *Chaetomium* enzymes almost has begun as one of the early researchers have developed a method for testing the effectiveness of mildew proofing agents on cotton fabrics in which the fungus, *Chaetomium globosum*, is used as the test organism (Darwish and Abdel-Azeem 2020). This particular fungus was selected because it was found on nearly all outdoor fabrics as one of the most important organisms responsible for the loss of breaking strength of fabrics (Thom et al. 1934).

In the 1940s, researchers (Rogers et al. 1940) determined the action of *Chaetomium globosum* on bleached cotton duck by measuring the changes in breaking strength, weight per square yard, thickness, staple length, fluidity, methylene blue absorption, moisture content, ash content, and rate of evolution of carbon dioxide as an indication of the rate of growth of the organisms on the fabric.

After three decades, the interest switched to studying of the cellulolytic system in more detail, such as the effect of temperature on growth and cellulase production in the thermophilic compost fungus *Chaetomium thermophile* var. *dissitum* (Eriksen and Goksoyr 1977) and the isolation, taxonomy, and growth rate of the genus *Chaetomium Kunze* ex Fr. as a wheat straw decomposer for mushroom growth (Chahal and Hawksworth 1976).

Later, stored useful books and important documents which were noticed to have moldy appearances were analyzed for isolation of cellulolytic fungi. Several fungi were isolated in pure form and identified, and the genus *Chaetomium* was the most dominant fungus. Thirteen different *Chaetomium* species were undertaken for screening of their cellulase-producing capability by the filter paper degradation ability (Yadav and Bagool 2015).

Recent investigations were more specific in studying new *Chaetomium* cellulolytic fungal species, enzyme profiles and genotypes of *Chaetomium* isolates, and isolation and screening of other *Chaetomium* enzymes such as L-methioninase, laccase, polysaccharide monooxygenase (PMO), β-1,3-glucanase, dextranase, and

pectinolytic, lipolytic, amylolytic, proteolytic, and chitinolytic and new classes of cellulose-degrading enzymes and synergistic enzyme systems (Abdel-Azeem et al. 2016c; Benhassine et al. 2016; Chen et al. 2018; Coronado-Ruiz et al. 2018; Hamed et al. 2016; Wanmolee et al. 2016).

Based on the abovementioned data that emphasize the enduring interest and importance of fungal enzymes for sustainability, this chapter is focused on presenting various enzymes produced by *Chaetomium* species and their miscellaneous applications.

5.3.1 Cellulase

Lignocellulosic materials consist mainly of three different types of biopolymers organized into a complex structure: (i) cellulose, a linear homopolymer of D-glucose organized into highly crystalline microfibers which are intimately associated with an intricate network of (ii) hemicellulose, an amorphous branched polymer comprising various pentoses, hexoses, and sugar acids, and (iii) lignin, a heteropolymer of phenolic alcohols which shields the polysaccharide microstructure from external physical, chemical, and biological attacks (Feldman 1985).

Cellulose is one of the most abundant renewable carbohydrates on the Earth (Sahay et al. 2017; Singh et al. 2016; Yadav et al. 2016). Enzymatic degradation of cellulose to glucose has great potential for economic biofuel production (Kaur et al. 2020; Prasad et al. 2020; Yadav et al. 2020f). Cellulases comprise three major groups of enzymes: (1) endoglucanases (EC 3.2.1.4), which attack regions of low crystallinity in cellulose fibers, creating free chain ends; (2) exoglucanases or cellobiohydrolases (EC 3.2.1.91), which further degrade the molecule by cleaving cellobiose from the free chain ends; and (3) β-glucosidases (EC 3.2.1.21), which hydrolyze cellobiose to produce glucose. In addition to the three major groups of cellulases, there are a number of endo- and exo-acting enzymes that attack the heterogeneous hemicelluloses, such as *endo*-β-1,4-xylanase, β-xylosidase, galactomannanase, glucomannanase, and acetylesterase A (Zhang et al. 2013). The applications of cellulases in various industries are exhibited in Table 5.1 (Kuhad et al. 2011).

Chaetomium is a *saprobic* fungus belonging to Ascomycota with high capability of degrading plant materials; it grows well and decomposes cellulose very rapidly, producing thermostable cellulases (Sajith et al. 2016). Studies have been conducted on various *Chaetomium* species such as *Chaetomium cellulolyticum, C. erraticum, C. fusisporale, C. globosum,* and *C. thermophile* to investigate their cellulolytic ability, localization, multiplicity, and characteristics of cellulase components.

Soni and Soni (2010) discussed a possible mechanism of regulation of cellulases and their existing polymorphism in *Chaetomium erraticum*. They concluded that *C. erraticum* appears to have the potential for the production of a complete cellulose enzyme complex and therefore can be exploited for hydrolysis of cellulosic waste. The regulation mechanism including catabolite repression and presence of multiple

Table 5.1 Summary of bioactive Chaetoglobosin (Chen et al. 2020)

Compounds	Activities	References
Chaetoglobosin A	Antitumor	Huang et al. (2016), Ashrafi et al. (2017)
	Antifungus	Huang et al. (2016)
	Antibacterial	Dissanayake et al. (2016)
	Phytotoxicity	Li et al. (2014), Ichihara et al. (1996)
	Nematicidal	Ashrafi et al. (2017)
	Fibrinolytic activity	Shinohara et al. (2000)
19-*O*-Acetylchaetoglobosin	Antitumor	Ashrafi et al. (2017)
	Nematicidal	Ashrafi et al. (2017)
20-Dihydrochaetoglobosin	Antitumor	Li et al. (2014)
Chaetoglobosin B	Antitumor	Jiao et al. (2004)
	Antifungus	Zhou et al. (2017)
	Antibacterial	Zhou et al. (2017)
19-*O*-Acetylchaetoglobosin	–	Probst and Tamm (1981)
Chaetoglobosin C	Antitumor	Thohinung et al. (2010), Huang et al. (2016)
	Antifungal	Huang et al. (2016), Zhou et al. (2017)
	Antibacterial	Gao et al. (2019)
	Phytotoxicity	Ichihara et al. (1996), Li et al. (2014)
Chaetoglobosin D	Antitumor	Thohinung et al. (2010)
	Antifungal	Jiao et al. (2004), Zhou et al. (2017)
	Antibacterial	Mourão et al. (2006)
19-*O*-Acetylchaetoglobosin D	–	Probst and Tamm (1981)
Chaetoglobosin E	Antitumor	Mourão et al. (2006), Huang et al. (2016)
	Antifungal	Huang et al. (2016)
	Phytotoxicity	Li et al. (2014)
Chaetoglobosin F	Antitumor	Thohinung et al. (2010), Li et al. (2014), Huang et al. (2016)
	Phytotoxicity	Li et al. (2014), Huang et al. (2016)
Chaetoglobosin fa	Immunosuppressive property	Hua et al. (2013)
	Antitumor	Li et al. (2014)
	Phytotoxicity	Li et al. (2014)
Chaetoglobosin F (ex)	Antitumor	Shen et al. 2015
	Phytotoxicity	Li et al. (2014)
Chaetoglobosin G	Anti-inflammatory property	Dou et al. (2011)
	Antitumor	Thohinung et al. (2010), Huang et al. (2016)
	Antifungal	Xue et al. (2012), Huang et al. (2016)
	Antibacterial	Xue et al. (2012)
Chaetoglobosin J	Antitumor	Jiao et al. (2004)

(continued)

Table 5.1 (continued)

Compounds	Activities	References
Chaetoglobosin K	Antitumor	Matesic et al. (2006)
	Antifungal	Rogers et al. (2014)
Chaetoglobosin M	Antifungal	Rogers et al. (2014)
Chaetoglobosin N	–	Burlot et al. (2003)
Chaetoglobosin O	Antitumor	Iwamoto et al. (2001)
Chaetoglobosin P	–	Donoso et al. (1997)
Chaetoglobosin Q	Antitumor	Jiao et al. (2004)
Chaetoglobosin R	Antifungal	Yan et al. (2018)
Chaetoglobosin S	–	Xue et al. (2012)
Chaetoglobosin T	Antitumor	Jiao et al. (2004)
	Antifungal	Yan et al. (2018)
	Antibacterial	Yan et al. (2018)
Chaetoglobosin U	Antitumor	Mourão et al. (2006)
Chaetoglobosins V	Antitumor	Thohinung et al. (2010), Li et al. (2014)
	Antifungal	Xue et al. (2012)
	Antibacterial	Gao et al. (2019)
	Phytotoxicity	Li et al. (2014)
Chaetoglobosin V (b)	Antifungal	Li et al. (2014)
	Antibacterial	Xue et al. (2012)
	Phytotoxicity	Xue et al. (2012)
Chaetoglobosin W	Antitumor	Li et al. (2014)
Chaetoglobosin X	Antitumor	Zhang et al. 2010
	Antifungal	Wang et al. (2012)
Chaetoglobosin Y	Antitumor	Zheng et al. (2014)
Chaetoglobosin Z	Antitumor	Jiang et al. 2016
Chaetoglobosin-510	Antitumor	Christian et al. (2005)
Chaetoglobosin-540	Antitumor	Christian et al. (2005)
Chaetoglobosin-542	Antitumor	Christian et al. (2005)
Isochaetoglobosin D	Antitumor	Thohinung et al. (2010)
Isochaetoglobosin J	–	Oikawa et al. (1992)
Yamchaetoglobosin A	Antitumor	Ruan et al. (2018)
	Anticoagulant activity	Ruan et al. (2018)
Penochalasin A	Antitumor	Mourão et al. (2006)
Penochalasin B	Antitumor	Numata et al. (1996)
Penochalasin C	Antitumor	Numata et al. (1996)
Penochalasin D	Antitumor	Iwamoto et al. (2001)
Penochalasin E	Antitumor	Iwamoto et al. (2001)
Penochalasin F	Antitumor	Iwamoto et al. (2001)
Penochalasin G	Antitumor	Iwamoto et al. (2001)
Penochalasin H	Antitumor	Iwamoto et al. (2001)
Penochalasin I	Antitumor	Huang et al. (2016)
	Antifungal	Huang et al. (2016)

(continued)

Table 5.1 (continued)

Compounds	Activities	References
	Antibacterial	Gao et al. (2019)
Penochalasin J	Antitumor	Huang et al. (2016)
	Antifungal	Huang et al. (2016)
Penochalasin K	Antitumor	Zhu et al. (2017)
	Antifungal	Zhu et al. (2017)
Prochaetoglobosin I	Antitumor	Jiao et al. (2004)
	Antibacterial	Gao et al. (2019)
Isprochaetoglobosin I	—	Christian et al. (2005)
Prochaetoglobosin II	Antitumor	Jiao et al. (2004)
Prochaetoglobosin III	Antitumor	Thohinung et al. (2010)
	Antiamebic	Mori et al. 2018
Prochaetoglobosin IIIed	Antitumor	Thohinung et al. (2010)
Prochaetoglobosin IV	–	Oikawa et al. (1992)
Trimethylated chaetoglobosin	–	Burlot et al. (2003)
Armochaetoglasin A	Antitumor	Chen et al. (2016)
	Antibacterial	Gao et al. (2019)
Armochaetoglasin B	Antitumor	Chen et al. (2015a)
	Antibacterial	Gao et al. (2019)
Armochaetoglasin C	Antitumor	Chen et al. (2015b)
	Antibacterial	Gao et al. (2019)
Armochaetoglasin D	Antitumor	Chen et al. (2015b)
Armochaetoglasin E	Antitumor	Chen et al. (2015b)
Armochaetoglasin F	–	Chen et al. (2015b)
Armochaetoglasin G	Antitumor	Chen et al. (2015b)
Armochaetoglasin H	Antitumor	Chen et al. (2015b)
Armochaetoglasin I	Antitumor	Chen et al. (2015b), Huang et al. (2016)
	Antifungal	Huang et al. (2016)
Armochaetoglasin J	Antitumor	Chen et al. (2015b)
Armochaetoglasin K	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin L	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin M	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin N	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin O	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin P	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin Q	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin R	Anti-HIV I	Chen et al. (2015a)
Armochaetoglasin S	Antitumor	Chen et al. (2016)
7-*O*-Acetylarmochaetoglobin S	Antitumor	Chen et al. (2016)
Armochaetoglasin T	Antitumor	Chen et al. (2016)
Armochaetoglasin U	Antitumor	Chen et al. (2016)

(continued)

Table 5.1 (continued)

Compounds	Activities	References
Armochaetoglasin V	Antitumor	Chen et al. (2016)
Armochaetoglasin W	Antitumor	Chen et al. (2016)
Armochaetoglasin X	Antitumor	Chen et al. (2016)
Armochaetoglasin Y	Antitumor	Chen et al. (2016)
	Antibacterial	Gao et al. (2019)
Armochaetoglasin Z		
Aureochaeglobosin A	Antitumor	Chen et al. (2016)
Aureochaeglobosin B	Antitumor	Yang et al. (2018)
Aureochaeglobosin C	Antitumor	Yang et al. (2018)
Oxichaetoglobosin A	Antitumor	Yang et al. (2018)
	Immunomodulatory activity	Wang et al. (2018)
Oxichaetoglobosin B	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	
Oxichaetoglobosin C	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	
Oxichaetoglobosin D	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	
Oxichaetoglobosin E	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	
Oxichaetoglobosin F	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	
Oxichaetoglobosin G	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	
Oxichaetoglobosin H	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	
Oxichaetoglobosin I	Antitumor	Wang et al. (2018)
	Immunomodulatory activity	Wang et al. (2018)

molecular forms of endoglucanase and β-glucosidase suggests a level of complexity for the synthesis of cellulases in this fungus and cellulases are probably regulated by separate genes.

Alvarez et al. (2013) reported a novel cellulase belonging to GH5 family, named as CelE1, retrieved from a sugarcane soil metagenomic library, which is a promising biocatalyst in biofuel production. They provided details about the three-dimensional structure, catalytic properties, and stability of CelE1 that might encourage the use of

sugarcane biomass as substrate. This enzyme was shown to be an endo-acting glucanase with high catalytic activity at a broad temperature range and under alkaline conditions that usually cause enzyme inactivation of classical acidic cellulases. Moreover, its crystal structure might confer higher conformational stability in comparison with its psychrophilic orthologs.

Five *Chaetomium* species were reported as potentially able to secrete high exoglucanase and endoglucanase cellulases, *Chaetomium dolichotrichum*, *C. funiculosum*, *C. globosum*, *C. anguistispirale*, and *Chaetomium* sp. which were found to perform as very good producers of total cellulase and endoglucanase (Yadav and Bagool 2015). Wanmolee and coauthors (Wanmolee et al. 2016) provided an approach for developing an active synergistic enzyme system of the soft-rot fungus *C. globosum* (BCC5776) applied for hydrolysis of alkaline-pretreated rice straw for lignocellulose saccharification and modification in feasible bio-industries. Moreover, the crude enzyme was characterized for its catalytic activities and its components identified by proteomics.

Recently, rampant biodeterioration by fungi was marked in the archive of the Universidad de Costa Rica which maintained a nineteenth-century French collection of drawing sand lithographs especially in the nutritional conditions that encouraged their growth. Given the interest in the developing methods for protecting and preserving ancient documents from microbial degraders and the importance of obtaining microorganisms or enzymes with the capacity to degrade lignocellulosic wastes (Yadav et al. 2020d), Coronado-Ruiz and coauthors (Coronado-Ruiz et al. 2018) isolated and identified cellulose degrader fungi belonging to 19 fungal genera from this archive including *Chaetomium*, in addition to two new species, namely, *Periconia epilithographicola* sp. *nov*. and *Coniochaeta cipronana* sp. *nov*., that showed important cellulolytic activity.

5.3.2 Polysaccharide Monooxygenase (PMO)

Recently, a new class of cellulose-degrading enzymes, called Cu^{2+}-dependent lytic polysaccharide monooxygenases (PMOs), has been discovered and is attracting increasing interest because their oxidative degradation of cellulose dramatically boosts cellulase activity in cellulose hydrolysis. Based on their amino acid sequence similarities, PMO enzymes are classified into four families: auxiliary activity 9 (AA9), auxiliary activity 10 (AA10), auxiliary activity 11 (AA11), and auxiliary activity 13 (AA13). Additionally, genome analysis and transcriptomic studies revealed that cellobiose dehydrogenase (CDH) is a biological redox partner that is almost always co-expressed with PMOs in filamentous fungi (Corrêa et al. 2016; Vu and Ngo 2018).

Chaetomium thermophilum is a thermophilic fungus and can grow in temperatures up to 60 °C. Chen and coauthors isolated and characterized polysaccharide monooxygenase (PMO) from *C. thermophilum* isolated from China. *C. thermophilum* genome analysis revealed 19 genes encoding putative AA9PMOs

(http://www.fungalgenomics.cn). In addition they amplified a gene (KC441882) encoding a special putative AA9PMO protein, CtPMO1. The CtPMO1 protein was predicted to be a secreted enzyme with a 17-amino acid potential signal peptide. The mature CtPMO1 protein is composed of 229 amino acids with a calculated molecular weight of 24.63 kDa (Chen et al. 2018).

5.3.3 β-1,3-Glucanase

β-1,3-glucanases belong to enzymes hydrolyzing the *O*-glycosidic linkages of 1,3-*b*-D glucan which are widely distributed in nature and isolated from many kinds of organisms. Increasing interest in enzymes from thermophilic fungi was expected to produce thermostable enzymes. Li and coauthors' success in purification and partial characterization of thermostable extracellular *exo*-β-1,3-glucanase from *Chaetomium thermophilum* may represent an important progression industrial wise (Li et al. 2007).

In the feed industry, thermostable β-1,3-glucanases are used for more complete utilization of feed components originating from plants reducing the anti-nutritional effect of non-starch polysaccharides (NSP) (Mourão et al. 2006). The utilization of thermostable β-1,3-glucanases in malting and brewing processes replacing native barley β-glucanase is susceptible to irreversible inactivation at temperatures above 55 °C. During malting, β-glucans in barley are hydrolyzed by β-glucanase which leads to clarification of beer improvement. Genetic transformation of barley with thermostable β-glucanase genes has been attempted in order to ensure sufficient β-glucanase activity during mashing (Nuutila et al. 1999). Thermostable β-1,3-glucanases can also be utilized in production processes of yeast extract and soluble 1,3-glucan, which is a potential immune activator, in addition to its applications in biological control of plant pathogens and medical fields (Li et al. 2007).

5.3.4 Dextranase

Dextranase is an important industrial enzyme which has many applications, in the sugar industry in rendering the technical processing of alternated sugar beet, in the preparation of clinical low-molecular-weight dextran, and in the coupling of dextranase to tumor cell-specific antibodies followed by administration of cytotoxic dextran conjugate (Erhardt and Jördening 2007). Dextranase is currently commercially produced from *Chaetomium erraticum* by Sigma-Aldrich®; its synonym is 1,6-α-D-glucan 6-glucanohydrolase, Dextranase Plus L.

For successful enzymatic synthesis of sucrose conversion, two enzymes must be present, dextran sucrase for the conversion of sucrose to dextran and dextranase for dextran breakdown as the dextran hydrolysis generates about 20% of unwanted branched isomaltooligosaccharides (IMOs). Erhardt and Jördening (2007) applied

dextranase from a submerged culture of *Chaetomium erraticum* strain in co-immobilization of dextran sucrase and dextranase. The immobilization of technical operation ought to be performed by entrapped dextranase immobilized in alginate, so the particle size of dextranase must fall far below the size of alginate beads in order to be trapped within the alginate beads, which was achieved by *Chaetomium* dextranase.

5.3.5 *Laccase*

Laccase (benzenediol:oxygen oxidoreductase, EC 1.10.3.2) is a part of a broad group of enzymes called polyphenol oxidases containing copper atoms in the catalytic center; they are usually called multi-copper oxidases, which are able to oxidize a variety of organic and inorganic compounds, including mono-, di-, and polyphenols; aromatic amines; carboxylic acids; and non-phenolic substrates (Khushal et al. 2010).

Fungal laccases play an important role in plant pathogenesis, pigment production, and degradation of lignocellulosic materials (Shraddha et al. 2011). Fungal laccases were isolated and characterized from *Chaetomium* species (Ref051A) isolated from Chettaba Forest, Constantine, Algeria. Isolated laccase proved to be suitable for industrial production (Benhassine et al. 2016). In Egypt, Abdel-Azeem and Salem (2012) studied laccases from *Chaetomium globosum*.

5.3.6 *L-Methioninase*

L-Methioninase (EC 4.4.1.11) is a pyridoxal phosphate-dependent enzyme; it fulfills several functions of an enzyme system because it stimulates the γ-, α-, and β-removal reactions of methionine and its derivatives. Physiologically, normal cells have the capability to grow on homocysteine, instead of methionine, due to their efficient methionine synthase. Unlike normal cells, tumor cells freed from efficient methionine synthase thus rely on external methionine supplementation from diet. Hence, there is reasonable scope of using L-methioninase as a therapeutic agent against different kinds of methionine-dependent tumors. Methionine reduction has a broad spectrum of antitumor activities (Sharma et al. 2014; Suganya et al. 2017).

A few studies were concentrated on the enzymes from eukaryotes especially fungi, due to the recurrent classification of L-methioninase as an extracellular enzyme in the fungal extract; fungi can be considered as robust resources of this enzyme. Hamed and coauthors (Hamed et al. 2016) identified and produced L-methioninase from *Chaetomium globosum* isolated from Egyptian soil (GenBank under accession number KXO24450). The predicted specific activity of the produced L-methioninase was ≈2225 U/mg; it has been suggested as a good source for clinical therapeutic applications.

5.3.7 *Other* Chaetomium *Enzymes*

Abdel-Azeem and coauthors (2016) recovered ten *Chaetomium globosum* isolates, designated from TUCg 1 to TUCg 10 in the GenBank. All *Chaetomium globosum* isolates showed amylolytic, cellulolytic, and proteolytic activities; six isolates were chitinolytic and laccase producers, five were pectinolytic, and three showed lipolytic activities with different arrays. Applied molecular techniques such as internal transcribed spacer (ITS) region sequencing and specific gene random primer polymerase chain reaction (SGRP-PCR) have shown high DNA polymorphism of *Chaetomium globosum*, so the authors suggested these techniques for identification of different fungal isolates.

Studies revealed that Chaetomium enzymes such as cellulases, L-methioninase, laccase, polysaccharide monooxygenase (PMO), β-1,3-glucanase, dextranase, pectinolytic, lipolytic, amylolytic, proteolytic, and chitinolytic represent a significant factor in sustainability in various fields. Future research in this era is crucial for a more thorough understanding of the mechanisms, structure, function, and substrate characteristics targeting efficient enzyme production to contribute to the development of a feasible biorefinery industry.

5.3.8 *Thermophiles and Thermostable Enzymes of Chaetomium*

The thermophilic biocatalysts are important not only due to their thermostabilities but also because they are more resistant to denaturing agents and tolerant to higher solute (reactant) concentrations. A higher degree of thermophilicity of an organism does not necessarily imply that pure enzymes derived from such organisms will always be very thermostable. The fact remains, however, that one has a better chance of finding more thermostable or more chemoresistant enzymes in thermophiles than in mesophiles (Abdel-Azeem and Sheir 2020; Hesham et al. 2021; Kour et al. 2019a; Yadav et al. 2020g). High productivity is also expected from thermophiles. According to Arrhenius law, an increase in temperature speeds up chemical and enzymatic reactions, and therefore microbial growth and product formation. Productivity is unfortunately given in terms of yield coefficients only, and not specific product formation rates, a parameter that allows easy and direct comparison between organisms (Sonnleitner and Fiechter 1983).

The benefits of using enzymes as catalysts in industrial processes lie in their specificity and efficiency leading to the production of by-products, less toxic wastes, and reduced handling problems. The main disadvantages of using enzyme reside in stability problems and high cost. The latter partially depends on the former, since the frequency of replacement of enzyme in a bioreactor (and therefore total production costs) is stability dependent. Production cost itself is generally high due to low yields of enzyme per unit biomass, expense of extraction and concentration and/or

purification, losses of activity during purification and storage, and handling stability of the enzyme again being a factor (Kristjansson 1989; Coolbear et al. 1992).

The use of thermostable enzymes reduces stability problems and in doing so alleviates some of the expense of production and replacement in a bioreactor. The stability of enzymes from thermophiles should lead to higher recoveries at ambient temperatures than is possible for mesophiles. The low activity of extremely thermophilic enzymes at ambient temperatures eases handling and storage problems, and the comparative molecular inflexibility that results in this activity at lower temperature has been suggested to lower the immune response to such proteins, thus reducing potential health risks (Coolbear et al. 1992). Besides higher thermostability, the other expected advantages of thermophilic enzymes are increased chemoresistance, a longer useful shelf life, and less contamination problems (Sonnleitner and Fiechter 1983).

Many of the enzymes presently used in industrial processes are quite thermostable even though they originate from mesophilic bacteria or fungi (Kour et al. 2019a; Suman et al. 2015; Yadav et al. 2019c). Thermostability in enzymes from mesophiles is, however, the exception, not the rule. Since industrially useful enzymes must usually be thermostable, this characteristic is of primary importance in screening programs for enzymes. This is also important because the intrinsic basis underlying the thermostability of thermophilic enzymes is yet to be revealed and so engineering this characteristic into less thermophilic enzymes is not possible at this time. Successful cloning and expression of genes encoding hyperthermophilic enzymes in mesophilic hosts have improved the availability of high-temperature biocatalysts (Adams and Kelly 1998).

On the industrial front, the use of thermophilic strains can be an effective solution to the maintenance of optimal temperature in industrial fermentation for the entire cultivation period. It is well known that thermophilic activities of microbes are generally associated with protein and enzyme thermostability. The advantages of the use of thermostable proteins and enzymes for conducting biotechnological processes at high temperature include a reduced risk of contamination with mesophilic microbes, a decrease in the viscosity of the culture medium, an increase in the bioavailability and solubility of organic compounds, and an increase in the diffusion coefficient of substrates and products, resulting in a higher rate of reactions. Further, their involvement in genetic manipulations is a much more recent development. Nevertheless, because of these and many more advantages, thermophilic fungi appear to be suitable candidates in biotechnological applications. Additionally, with the paradigm shift in industry as it moves from fossil fuels toward renewable resource utilization, the need for microbial biocatalysts is envisaged to increase, and undoubtedly there will be an unrelenting and increased need for thermostable selective biocatalysts in the near future. Thus, future perspectives relating to their diversity, taxonomy, phylogeny, genome-wide study, and biotechnology, entailing research on thermophilic fungi, are warranted.

The biotechnological potential of thermophilic fungi has been known to microbiologists for a considerable period because composting as a means of providing nutrient-enriched plant material has been in vogue for degradation of agro-residues,

mushroom production, solid waste management, and understanding the role of fungi in plant litter ecosystem (Prasad et al. 2021; Sharma et al. 2021; Yadav 2020). The early history of the descriptions of thermophilic fungi from hay and retting gauyule is too well known to be narrated but this infused interest in unraveling the enzymatic potential especially in the realm of polysaccharases, proteases, and lipases (Rastegari et al. 2019a, b; Yadav et al. 2019a).

The major commercial application of glucoamylase is to catalyze starch and to yield glucose for use in the food and fermentation industries. Glucose production from starch, along with glucoamylase, requires the synergistic action of a series of amylases. In the first step, ~30–35% dry solid starch slurry is gelatinized (~60–90 °C) and subsequently liquefied at 95–105 °C (pH 6.5) by α-amylase to short-chain dextrins. These dextrins in the next step are saccharified by glucoamylase to release glucose. The fungal glucoamylase being optimally active at around pH 4.0–4.5, the saccharification is essentially carried out under acidic conditions at 60 °C for 3–4 days to achieve a final yield of ~96% glucose (Crabb and Mitchinson 1997; Reilly 1999).

Additionally, debranching enzymes (pullulanase or isoamylase) are used to hasten starch processing by cleaving α-1,6 glycosidic bonds, which allows to attain an early peak in glucose yield with less by-product formation (Uma Maheswar Rao et al. 2011). Glucose has ~75% of the sweetness of sucrose, while its isomer fructose is twice sweeter than sucrose. Consequently, fructose is preferred especially in so-called low-calorie health/diet foods, where it provides double the sweetness of sucrose at half the weight and can be metabolized without insulin (Uma Maheswar Rao et al. 2011). Commercially fructose is produced by the isomerization of glucose using fungal glucose/xylose isomerase (EC 5.3.1.5, D-xylose-ketol isomerase) at 50–60 °C and pH 7–8. Glucose isomerase is the most expensive of all the enzymes involved in starch processing, and thus is reused until it loses most of its activity. The concentrated glucose syrup is passed through the immobilized glucose isomerase column or sometimes through the glucose isomerase-producing cells (Uma Maheswar Rao et al. 2011). The process yields around 40–42% of fructose and the concentration of fructose in the final product is raised to ~55% by chromatographic enrichment of glucose–fructose mixture (Uma Maheswar Rao et al. 2011).

Obtaining new biotechnological products from uncultivable microfungi is quite interesting and a current topic of debate. Both basic research and biotechnological developments require routinely applicable tools for the functional analysis, expression, and manipulation of genes. These techniques include procedures for genetic transformation and selection of the transformants, well-characterized molecular markers, and expression signals. As thermophilic fungi colonize, multiply, and survive in habitats having elevated temperatures, they represent a formidable pool of bioactive compounds and are a strategic source for new and successful commercial products. Recent technological advances made in genomics, proteomics, and combinatorial chemistry show that nature continues to preserve compounds in its metagenome having the essence of bioactivity or function within the host and the environment. Bioprospecting of fungal genomes, such as thermophilic fungi, offers several advantages over their biocatalysts, besides being thermostable. However,

studies on fungal distribution and mapping are challenging due to the lack of sufficient knowledge about their taxonomy and the lack of expert mycologists around the world. Nevertheless, the fungal world provides a fascinating and almost continual source of biological diversity, which is a rich source to exploit for human welfare.

5.3.8.1 Glucoamylases

The application of glucoamylases (EC 3.2.1.3, glucan 1,4-α-glucosidase) in starch saccharification lies in the sugar industry due to its ability to release glucose as the major end product, which is used in food, beverage, ethanol, amino acids, and organic acids (Kumar et al. 2009). Glucoamylase is one of the enzymes of world-wide interest in starch saccharification to yield glucose for use in the food and fermentation industries. Glucoamylase is one of the high-demand commercial biocatalysts in the food industry, which is required in higher tonnage than almost any other enzyme (Reilly 1999; Ford 1999).

Chen et al. (2005) purified a thermostable extracellular glucoamylase (exo-1,4-a-D-glucanohydrolase, EC 3.2.1.3) from the culture supernatant of a thermophilic fungus *Chaetomium thermophilum* to sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) homogeneity by using ammonium sulfate fraction, DEAE-Sepharose Fast Flow chromatography, and Phenyl-Sepharose Fast Flow chromatography. SDS-PAGE of the purified enzyme showed a single protein band of molecular weight of 64 kDa. The glucoamylase exhibited optimum catalytic activity at pH 4.0 and at 65 °C. It was thermostable at 50 °C and 60 °C, and retained 50% activity after 60 min at 65 °C. The half-life of the enzyme at 70 °C was 20 min. N-terminal amino acid sequencing (15 residues) was AVDSYIERETPIAWN. Different metal ions showed different effects on the glucoamylase activity of *C. thermophilum*. Ca^{2+}, Mg^{2+}, Na^{+}, and K^{+} enhanced the enzyme activity, whereas Fe^{2+}, Ag^{+}, and Hg^{2+} caused obvious inhibition. These properties make it applicable to other biotechnological purposes.

5.3.8.2 Cellulases

The thermophilic ascomycete *C. thermophilum* also awakes interests for biotechnological applications. In order to determine the enzymatic properties, these fungus glycosyl hydrolase-encoding genes have been cloned and expressed in *P. pastoris* and *T. reesei*. Cellobiohydrolase II (CBHII)-encoding gene was subject to in vitro-directed evolution (Wang et al. 2012) aiming the thermostability increase. In addition to an enhanced thermal stability, the two CBHII mutant versions produced in *P. pastoris* also presented higher optima temperature and pH values (60 °C, pH 5–6) in comparison to the wild-type enzyme (50 °C and pH 4). Not only thermostability accounts for *C. thermophilum* enzymes' advantages but also Voutilainen et al. (2008) reported that the acidic cellobiohydrolase Cel7A produced in *P. pastoris*

was more thermostable (by 10 °C) and more active (by fourfold) in the hydrolysis of microcrystalline cellulose when compared to *T. reesei* Cel7A, thus representing a competitive choice for industrial purposes. Another interesting example of such a versatility is xylanase Xyn11A which is produced by *T. reesei* (Mäntylä et al. 2007). Experiments showed that at pH 7.0 and at 70 °C this enzyme could be commercially feasible for industrial-scale bleaching of kraft pulp at high temperatures in comparison with other enzymes produced by other taxa.

5.3.8.3 Xylanases

Next to cellulose, xylan is the most abundant structural polysaccharide in nature. Its complete degradation requires the cooperative action of a variety of hydrolytic enzymes: the endoxylanases (EC 3.2.1.8), which randomly cleave 13-1,4-linked xylose (the xylan backbone); the 13-xylosidases (EC 3.2.1.37), which hydrolyze xylooligomers; and the different side-branch-splitting enzymes, for example, α-glucuronidase and α-arabinosidase, acetylxylan esterase, and acetyl esterase, which liberate other sugars (glucuronic acid arabinose) that are attached as branches to the backbone (Biely 1985).

In 2003, Hakulinen et al. found the crystal structures of thermophilic xylanases isolated from *Chaetomium thermophilum* determined at 1.75 Å and compared with other 12 xylanases. The enzymes have the overall fold typical to family 11 xylanases with two highly twisted β-sheets forming a large cleft. The comparison of 12 crystal structures of family 11 xylanases from both mesophilic and thermophilic organisms showed that the structures of different xylanases are very similar. The sequence identity differences correlated well with the structural differences. Several minor modifications appeared to be responsible for the increased thermal stability of family 11 xylanases: (a) higher Thr:Ser ratio; (b) increased number of charged residues, especially Arg, resulting in enhanced polar interactions; and (c) improved stabilization of secondary structures involving a higher number of residues in the β-strands and stabilization of the α-helix region. Some members of family 11 xylanases have a unique strategy to improve their stability, such as a higher number of ion pairs or aromatic residues on protein surface, a more compact structure, a tighter packing, and insertions at some regions resulting in enhanced interactions (Rastegari et al. 2020a, b).

The xylanases from *Chaetomium thermophilum* possess optimum temperatures between 60 and 80 °C and are very stable in this range. These enzymes are usually glycoproteins and most show highest activity at an acid pH (4.5–6.5). They exist in a multiplicity of forms and the majority exhibit variable MWs in the range of 6–38 kDa. Many endoxylanases from thermophiles have some degree of structural homology with those from mesophiles. A number of authors have tried to explain the thermostability observed in enzymes from thermophiles in terms of extra disulfide bridges, an N-terminal proline residue causing a reduction in conformational freedom, salt bridges, and presence of hydrophobic side chains (Turunen et al. 2001). Hakulinen et al. (2003) describe also some minor modifications responsible for the

increased thermal stability of xylanases: (1) higher Thr/Ser ratio; (2) increased number of charged residues, especially Arg, resulting in enhanced polar interactions; and (3) improved stabilization of secondary structures involving a higher number of residues in the β-strands and stabilization of the α-helix region to the backbone (Biely 1985). Xylanases of thermophilic Chaetomium are receiving considerable attention because of their application in biobleaching of pulp in the paper industry, wherein the enzymatic removal of xylan from lignin-carbohydrate complexes facilitates the leaching of lignin from the fiber cell wall, obviating the need for chlorine for pulp bleaching in the brightening process. They also have applications in the pretreatment of animal feed to improve its digestibility.

5.3.8.4 Cellobiohydrolase

Thermoactive and thermostable cellulases, in general, have favorable effects on the resistance of adverse conditions, including high salt concentrations and extreme pHs. In particular, enzymes with such excellent properties are desired to effectively enhance hydrolysis efficiency at elevated temperatures while simultaneously reducing microbial contamination in industrial processes (Alponti et al. 2016). Therefore, it is essential to explore thermoactive enzymes with considerable thermostability. *Chaetomium thermophilum* produces multiple thermostable cellulases with high efficiencies (Bock et al. 2014), such as a β-1,4-endoglucanase CTendo45 (Chen et al. 2018) and two cellobiohydrolases CtCel6 (Zhou et al. 2017) and CtCBH1 (Lee et al. 2017). According to the classification of the Carbohydrate-Active Enzyme (CAZy) database (Cantrell et al. 2006), cellobiohydrolases are mainly assigned into two glycoside hydrolase families (GH6 and GH7). Besides, the GH6 cellobiohydrolase is extensively considered to act processively from the nonreducing terminal of cellulose chains to release disaccharide cellobioses with an atypical single-displacement mechanism (Thompson et al. 2012). However, although GH6 cellobiohydrolases possess excellent activity and high thermostability, there is certainly room for characteristic improvement (Baramee et al. 2017).

Han et al. (2018) studied a thermostable cellobiohydrolase CtCel6 from *Chaetomium thermophilum* with high hydrolytic activity that was employed to construct mutants to further enhance catalytic activity and thermostability. Based on structural analysis of the corresponding homologous model, four conserved and noncatalytic residues around the substrate-binding site in buried cleft were selected for site-directed mutagenesis. These recombinant enzymes were successfully expressed using the yeast *Pichia pastoris* and purified to determine the biochemical properties. The wild-type and mutant cellobiohydrolases shared a similar pattern of the optimum reaction condition at pH 5 and 70 °C, which could be attributed to the inapparent conformational rearrangement caused by residue substitutions (Xie et al. 2014).

5.3.8.5 Superoxide Dismutase

A thermostable superoxide dismutase (SOD) from the culture supernatant of a thermophilic fungus *Chaetomium thermophilum* strain CT2 was purified to homogeneity by fractional ammonium sulfate precipitation, ion-exchange chromatography on DEAE-Sepharose, and phenyl-Sepharose hydrophobic interaction chromatography (Guo et al. 2008). The pure SOD had a specific activity of 115.77 U/mg of protein and was purified 7.49-fold, with a yield of 14.4%.

In industry, a major requirement for commercial SOD is thermal stability because thermal denaturation is a common cause of enzyme inactivation. Thermostable SOD potentially is useful due to its high stability. In recent years, there has been an increasing interest in SOD of thermophiles, which were expected to produce thermostable SOD. In the 1990s, an antioxidant enzyme—superoxide dismutase (SOD)—was introduced into the market. Although the enzyme initially showed great promise in therapeutic applications, it did not perform up to expectations. Consequently, its use was limited to nondrug applications in humans and drug applications in animals.

5.4 Bioconversion of Lignocellulosic Residues into Single-Cell Protein (SCP)

The term single-cell protein (SCP) refers to dead, dry cells of microorganisms such as yeast, bacteria, fungi, and algae which serve as food and/or feed supplements (Abdel-Azeem and Sheir 2020). SCP will be an alternative to conventional proteins like casein, soybean meal, egg protein, or meat protein in animal feed. SCP is one of the alternatives that cannot be affected by climate change. SCP has a high protein content containing all the essential amino acids (Abdel-Azeem and Sheir 2020). Microorganisms are an excellent source of SCP because of their rapid growth rate, their ability to use very inexpensive raw materials as carbon sources, and their uniquely high efficiency, expressed as grams of protein produced per kilogram of raw material, with which they transform these carbon sources to protein. SCP has many benefits. It is a very fast way of producing protein compared to the production of protein through cultivation of agricultural crops or animal farming. The amino acid profile of many SCP is favorable and very similar to that of fishmeal. SCP can be produced from residual streams from different industries giving the possibility of a cheap production. In addition, SCP production can be performed in bioreactors and does not require agricultural land. Production of SCP may very well fit into the request of a sustainable high-quality alternative to fishmeal since the production can be performed using renewable and sustainable feedstocks such as residual streams from second-generation bioethanol production. The second-generation bioethanol production is predicted to increase in the future, resulting in large volumes of residual and waste streams. These residual streams are commonly used as substrates

for biogas production. SCP production is an interesting alternative to biogas production, possibly with a higher economic value. SCP has been found to meet all the requirements for its inclusion as diet supplement for livestock. SCP can replace up to 20–30% of the protein supply by soybean meal without any deleterious effects on growing broiler chicks.

Lignocellulosic biomass presents a readily available feedstock for microbial bioconversion which does not compete with feedstocks used for human food. Lignocellulose is the major structural component of woody plants and nonwoody plants and represents a major source of renewable organic matter—a substrate of enormous biotechnological importance. Microorganisms are involved in bioconversion of low-cost carbon feedstocks such as lignocellulose to produce biomass rich in proteins and amino acids. Production of SCP from lignocelluloses is gaining much attention, with the recovery of valuable by-products and simultaneous reduction of the organic load as the chief economic advantages of such processes.

Chahal et al. (1981) examined the effects of different pretreatment methods on aspen wood for SCP production with *Chaetomium cellulolyticum* and found that high-pressure steam was superior to atmospheric pressure steam, because high-pressure steam could make wood break to smaller pieces. More complete delignification of wood using sodium chlorite increased the protein composition in the final product to 37.9%, at a specific growth rate of 0.19 h^{-1}, and the cellulose utilization was highest, reaching 90%. The hemicellulose fraction of eucalyptus wood can be easily removed by acid treatment and the hydrolysate is rich in fermentable sugars, mainly xylose, which has been used as a substrate for different bioconversion products.

5.5 Secondary Metabolites and Chaetoglobosins

In 1981 Sekita et al. screened mycotoxin production by *Chaetomium* spp. and related fungi on rice culture. Their study was conducted by a combination of cytotoxicity tests using HeLa cells and thin-layer chromatography. Producers of sterigmatocystin, O-methylsterigmatocystin, chaetochromin, chaetocin, chaetomin, cochliodinols, and mollicellin G were found and the taxonomic significance of these findings is discussed in their study.

In a previous paper (Udagawa et al. 1979) 57 isolates of Chaetomium and its allied genera were screened for their ability, on rice culture, to produce chaetoglobosins, a novel class of cytochalasins (Natori 1977), and other metabolites. Five species, *C. cochliodes* Palliser, *C. globosum* Kunze ex Fr., *C. mollipilium* Ames, *C. rectum* Serg., and *C. subaflne* Serg., all belonging to the *C. globosum*-Gruppe sensu Dreyfuss (1975), were found to be producers of the cytochalasins. Unexpectedly, strains identified as *C. thielavioideum* Chen (Chen 1973) (vide infra) were found to produce sterigmatocystin (I), its O-methyl ether (II), and a new phenolic compound, as well as a known antibiotic substance, chaetocin (111). The details of the separation of the metabolites and the structural elucidation of the new

phenolic compound, designated chaetochromin (IV), were recently published (Sekita et al. 1980). Since sterigmatocystin is a well-known hepatocarcinogen, further surveys for mycotoxin production employing the same methods have been conducted on about 60 other isolates of Chaetomium and its allied genera.

Chaetomium and related fungi have been isolated from various agricultural commodities such as foods, feeds, and raw materials of pharmaceutical preparations on numerous occasions, but only recently have these fungi received comprehensive attention with regard to the production of mycotoxins (Sekita et al. 1981). Udagawa et al. (1979) reviewed the literature up to the middle of 1978 concerning the production of *Chaetomium* mycotoxins and presented data on the cytotoxicity and mycotoxigenic screening of 57 cultures of *Chaetomium* and related fungi. In that screening the production of chaetoglobosins was limited to species belonging to the *C. globosum*-Gruppe sensu Dreyfuss (1975). This conclusion has been confirmed by the present screen, since there is no producer of chaetoglobosins among the 26 species of *Chaetomium* and 4 species of related genera tested.

A type strain of *A. virescens* v. Arx, ATCC 32393; an additional isolate, AC-274; and another isolate of *C. thielavioideum* produced a set of mycotoxins, i.e., sterigmatocystin (I), O-methylsterigmatocystin (11), chaetocin (III), and chaetochromin (IV) (Udagawa et al. 1979). Reexamination of the morphology of *A. virescens* led to the conclusion that *C. thielavioideum* is identical with *A. virescens* in all macroscopic and microscopic characteristics. The genus *Achaetomiella* was erected by Von Arx (1970) with *A. virescens* as the type species. The genus is characterized by very reduced terminal hairs in the perithecium, ascospores with two germ pores, and thermotolerance in growth. With the exception of the number of germ pores on the ascospores, there are only minor differences in the characteristics of the perithecia, asci, and ascospores between *Achaetomiella* and *Chaetomium* and Udagawa (1980) has relegated *Achaetomiella* to synonymy with *Chaetomium. Chaetomium cellulolyticum* Chahal and Hawksworth (Chahal and Hawksworth 1976) is also considered to be identical to *C. thielavioideum* because of the identical pattern of its metabolites as well as its very close morphological similarities to the type strain (DAOM).

The taxonomy of *C. udagawae* Serg. ex Udagawa, another producer of sterigmatocystin (I) found in the present screening, has already been discussed (Udagawa et al. 1979). A toxic pigment, chaetochromin (IV), was originally isolated from *C. thielavioideum* cultures (Sekita et al. 1980). This pigment is of particular interest, since it has now been proven to be widely associated with the *Chaetomium* spp.: *C. caprinum* Bain. in the *C. bostrychodes*-Gruppe, *C. gracile* Udagawa in the *C. spirale*-Gruppe, and *C. tetrasporum* Hughes in the *C. crispatum*-Gruppe. The occurrence of chaetochromin in species in four different groups indicates that the toxin may be quite common and that the latter three fungi, although not closely related in their morphology, may have identical hazardous characteristics. Since oral and intraperitoneal administration of the pigment of mice results in noticeable toxicity such as selective inhibition of hematopoiesis (Sekita et al. 1981), precise examination of the toxicity of the pigment and the moldy rice is now in progress.

Chetomin (V), an antibiotic first reported from *C. cochliodes* Palliser, was subsequently discovered in a culture of *C. globosum* Kunze ex Fr., and *C. globosum* has been reported as a toxic agent of moldy corn for rats (Udagawa et al. 1979).

The production and toxicological data of chetomin from both these species have been furnished by Brewer et al. (1972). Furthermore, in the mycotoxin survey of *Chaetomium* isolates in Canada (Brewer and Taylor 1978), the same toxin was isolated from *C. funicola* Cooke and *C. umbonatum* Brewer. A fifth chetomin-producing species, *C. subglobosum* Serg., which is taxonomically related to *C. globosum*, appeared in the present screening.

A purple pigment, cochliodinol (VI), was previously isolated from liquid shake cultures of *C. cochliodes* and *C. globosum* (Brewer et al. 1968) and the antibiotic effect was reported (Brewer et al. 1970). *Chaetomium globosum* is the principal cochliodinol-producing fungus, but both species are in the *C. globosum*-Gruppe of Dreyfuss and are widely distributed in nature. In this screening, *C. elatum* Kunze ex Fr., another common species belonging to the *C. globosum*-Gruppe, also produced the compound. Two new isomers of cochliodinol, isocochliodinol and neocochliodinol, were isolated from rice cultures of *C. murorum* Corda and a new species, *C. amygdalisporum* Udagawa and Muroi (NHL 2874), respectively. The compounds were not identical with asterriquinones from *Aspergillus terreus* Thom (Yamamoto et al. 1976, 1980) and the structural elucidation will be reported in a separate paper (Sekita et al. 1981). *Chaetomium murorum*, which is assigned to a separate group (viz. the *C. murorum*-Gruppe), is also widely distributed but it is not particularly abundant. Taxonomic consideration of *C. amygdalisporum* is also reported elsewhere (Udagawa and Muroi 1981).

Mollicellins, a series of fungal depsidones showing mutagenicity, were recently discovered in a culture of *C. mollicellum* Ames (Stark et al. 1978). The presence of mollicellin G (VII) in the *C. amygdalisporum* culture is of interest, considering the morphological resemblance between *C. mollicellum* and this fungus.

Whether mycotoxins produced by *Chaetomium* spp. are significant in outbreaks of foodborne diseases of humans and animals is still uncertain but, because of their ubiquity in deteriorated plant materials including foods and feeds, and their ability to produce a number of potentially significant mycotoxins, they should be included in the hazardous group of mycotoxigenic fungi.

Chaetoglobosins as an example represent a large class of fungal secondary metabolites and belong to cytochalasan alkaloids, which contain a 10-(indol-3-yl) group, a macrocyclic ring, and a perhydroisoindolone moiety (Hamed et al. 2020). According to the chemical structure characteristics, they are divided into the sub-families chaetoglobosin, penochalasin, prochaetoglobosin, armochaetoglasin, aureochaeglobosin, and oxichaetoglobosin (Fig. 5.4). To date, around 100 chaetoglobosins and their analogues have been isolated and identified over the years from a variety of fungi, including *Chaetomium elatum*, *Chaetomium globosum*, Phomopsis sp., *Botryosphaeria dothidea*, and *Chaetomium subaffine*,

mainly from the fungus *Chaetomium globosum* (Chen et al. 2020). Increasing evidence has indicated that chaetoglobosins possess a broad range of biological activities, including antitumor, antifungal, phytotoxic, fibrinolytic, antibacterial, nematicidal, anti-inflammatory, and anti-HIV activities (Table 5.1).

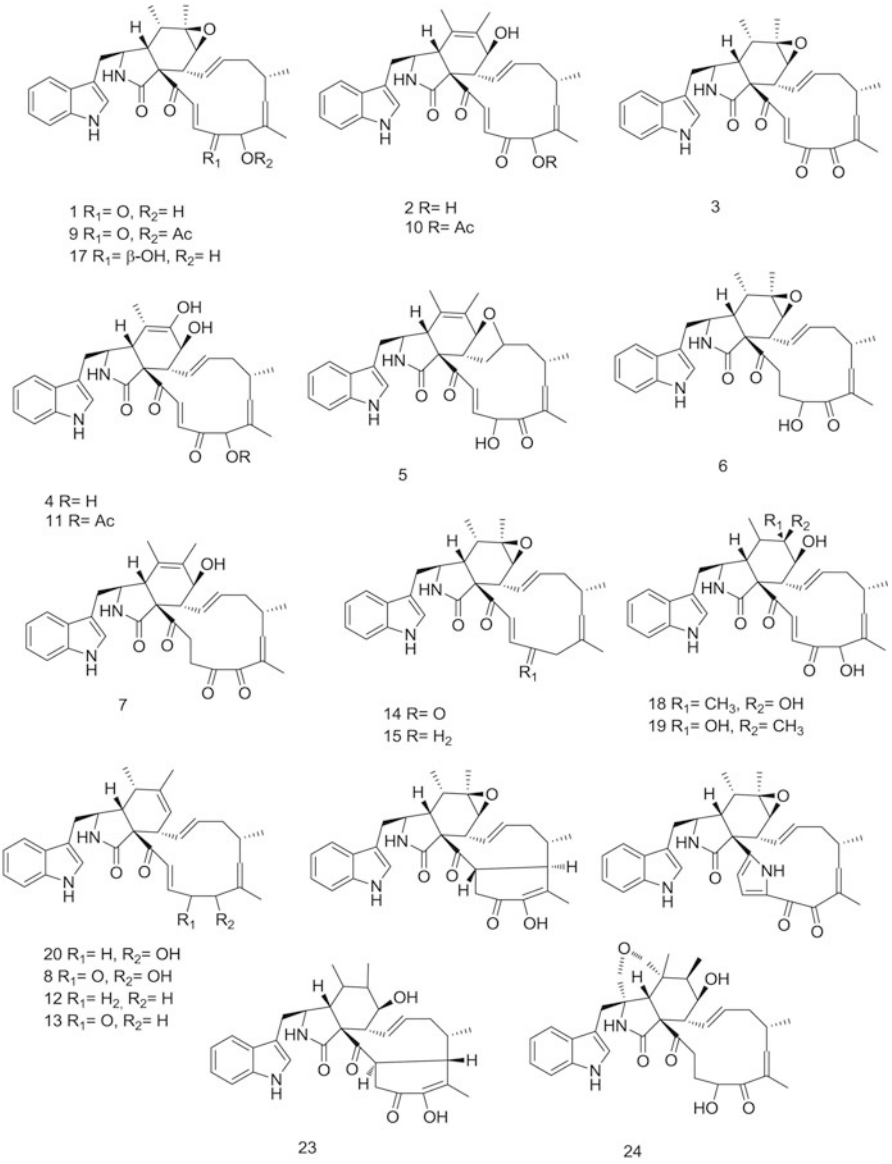
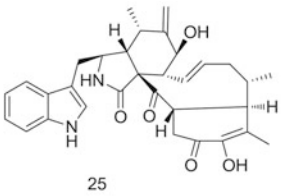


Fig. 5.4 Chemical structures of chaetoglobosins (Chen et al. 2020)



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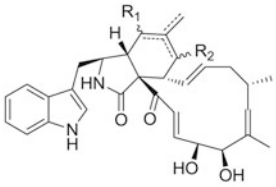
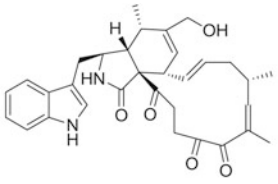


26 R_1= OMe, R_2= βOH
27 R_1=Me, R_2= βOH
28 R_1= αMe, R_2= H



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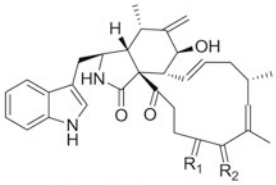
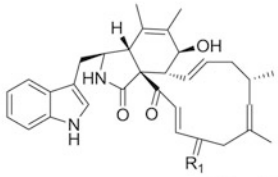
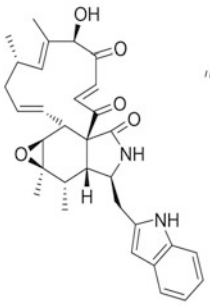


30 R_1= O, R_2= H, βOH
31 R_1= R_2= βOH
32 R_1= R_2= O
16 R_1= H, βOH, R_2= O



33 R_1= H_2
34 R_1= O



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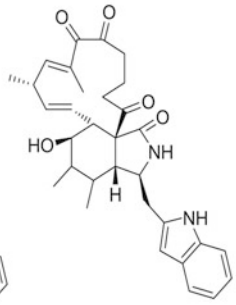

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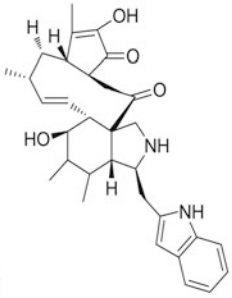

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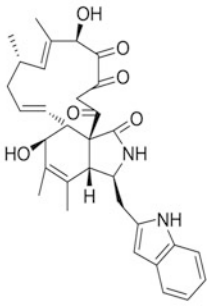

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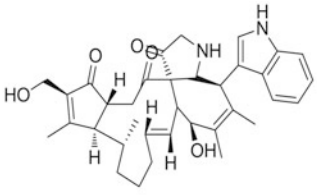

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Fig. 5.4 (continued)

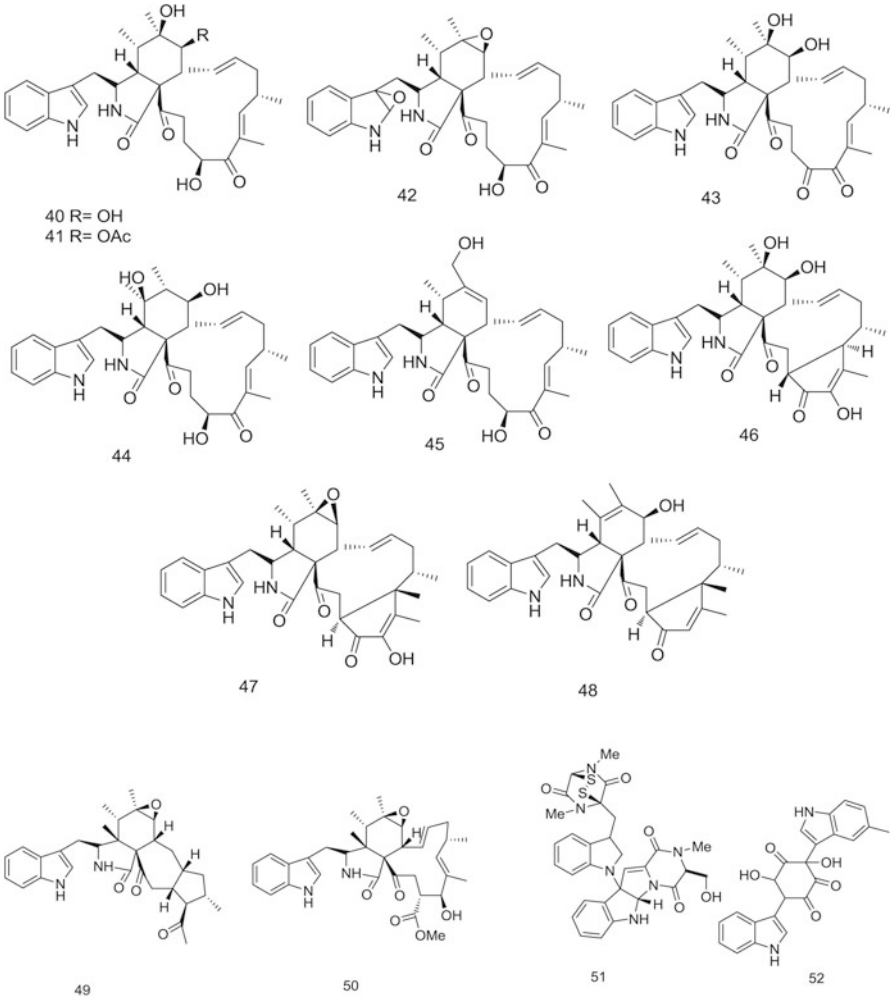

Fig. 5.4 (continued)

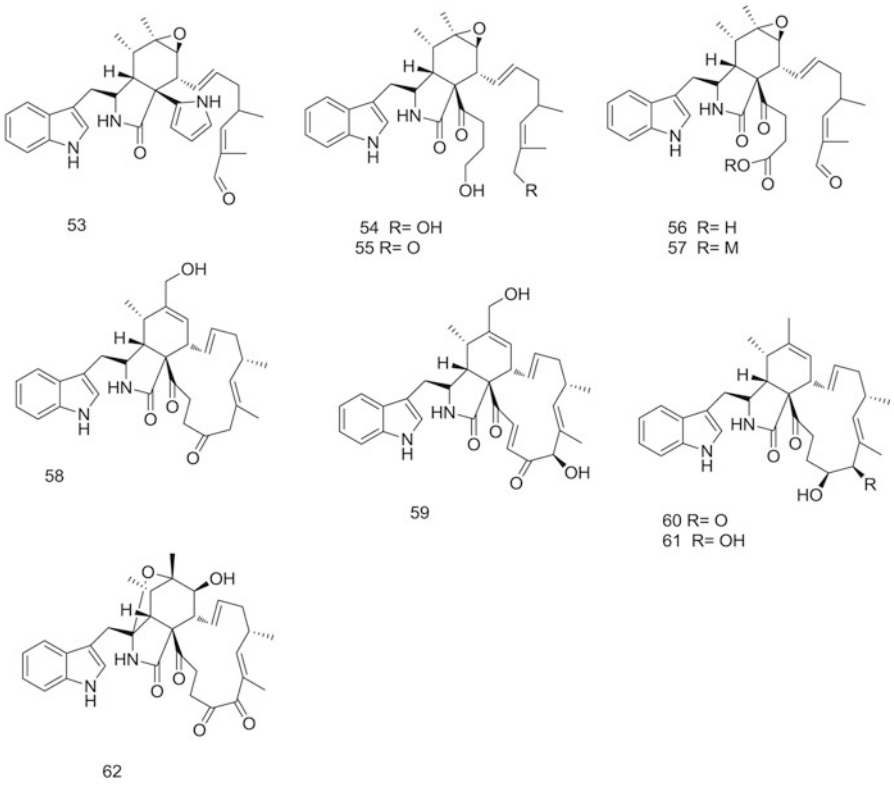

Fig. 5.4 (continued)

5.6 Antioxidant Compounds Associated with Different Endophytic *Chaetomium*

Recently, the genus *Chaetomium* has received attention as a rich source producing more than 200 small secondary metabolite compounds with diverse bioactivities, such as antitumor, phytotoxicity (on numerous plants), immunomodulatory, antifungal, nematicidal, antimalarial, enzyme inhibitory, antibiotic, and other activities which have significance for drug development (Hu et al. 2018; Soytong et al. 2001).

Chaetomium species can be antagonistic against various soil microorganisms and plant pathogens. Chaetoglobosins are well known for their robust cytotoxic bioactivity and potential pharmaceutical significance. Chaetoglobosins are grouped in the cytochalasin family of natural products and are actually polyketide derivatives found in fungi. They have unique biochemical property of binding eukaryotic actin proteins, disturbing the normal actin network in the cell. To date, more than 80 chaetoglobosins have been reported from different genera of filamentous fungi, including species of the genus *Chaetomium* (Wang et al. 2017).

Chaetomium globosum CDW7, an endophyte from *Ginkgo biloba*, exhibited strong inhibitory antifungal activity against phytopathogens such as *Fusarium graminearum*, *Rhizoctonia solani*, *Magnaporthe grisea*, *Pythium ultimum*, and *Sclerotinia sclerotiorum* both in vitro and in vivo. Attia et al. (2020) studied the production of antimicrobial, extracellular enzymes and antioxidants by endophytic teleomorphic Ascomycota associated with medicinal plants. A total of 11 teleomorphic species were isolated from 4 medicinal plant species in Saint Katherine Protectorate in Egypt. *Chaetomium grande* and *Sordaria fimicola* were the most frequently isolated species and were represented by 12 (Chg1–Chg12) and 7 (Sf1–Sf7) isolates, respectively. In vitro, the antioxidant activity of the extracts was investigated using DPPH radical scavenging assay, and was equal to 0.06% and 0.39%, respectively, in the extract of both taxa.

5.6.1 Flavipin

Flavipin is a well-known natural product that is isolated from endophytes belonging to *Chaetomium* sp. associated with leaves of *Ginkgo biloba* (Ye et al. 2013). Yan et al. (2018)) succeeded in isolating bioactive metabolites with antifungal activities from this fungus; the metabolites are flavipin, chaetoglobosins A and D, chaetoglobosins R (4) and T (5), new isocoumarin derivative prochaetoviridin A (1), new indole alkaloid, and chaetoindolin A (2) and chaetoviridin A (3). Flavipin is considered the major antioxidant component of CDW7's metabolites; it reacts by donating its electrons to the free radicals, leading to SOD and GSH-Px activity improvement and suppression of MDA content. This metabolite possesses three phenolic hydroxyl and two aldehyde groups, which are characteristic functional groups with antioxidant activity. When cultured under the optimal condition (25 °C, 100/250 mL flask, 12 discs/flask, 150 rpm, pH 6.5) for 14 days, *Chaetomium globosum* CDW7 was a highly yielded bio-source of antioxidant flavipin synthesizing a remarkable production of 315.5 mg/L (Ye et al. 2013).

Another endophytic fungus from *Ginkgo biloba*, *Chaetomium* sp. NJZTP21 (GenBank accession number: JN588553), isolated from the healthy leaf of the plant was able to produce flavipin, which significantly inhibited the growth of several plant pathogenic fungi, especially *Fusarium graminearum*. But the extract from *C. globosum* CDW7, which had been deposited in the China General Microbiological Culture Collection Center (CGMCC) with an accession number 6658, has the strongest antioxidant activity among the studied endophytic fungi from *G. biloba* comparable to those of vitamin C and Trolox, the well-known antioxidants (Ye et al. 2013).

Chaetomium globosum and *C. cochlioides* are antagonistic to species of *Fusarium* and *Helminthosporium*. They exhibited good control over many plant pathogens; seed coating treatments with viable spores of *Chaetomium globosum* were found to exert antagonistic effects: controlled *Fusarium roseum* f. sp. *cerealis "graminearum"* in corn; reduced disease incidence of apple scab caused by *Venturia*

inaequalis; suppressed damping-off of sugar beet caused by *Pythium ultimum*; had an antagonistic effect against *Macrophomina phaseolina*, *Pythium ultimum*, *Bipolaris sorokiniana*, *Rhizoctonia solani*, and *Alternaria brassicicola*; and reduced the quantity of sporulation of *Botrytis cinerea* on dead lily leaves exposed in the field (Biswas et al. 2012; Shternshis et al. 2005).

5.6.2 Chaetopyranin

The basic structure of chaetopyranin (I) is chromenol (I) (chromene carrying one or more hydroxyl substituents). It is chemically known as 3,4-dihydro-2H-chromene substituted by a hydroxyl group at position 6, a 3-hydroxybut-1-en-1-yl at position 2, a formyl group at position 5, and a prenyl group at position 7 (Fig. 5.5) (Wang et al. 2006). These two compounds have been isolated from an endophytic fungus *Chaetomium globosum*, associated with *Polysiphonia urceolata*, and are found to possess antioxidant activity. The former compound also exhibits anticancer activity (Wang et al. 2006). Chaetopyranin also showed antioxidant activity.

5.6.3 Azaphilone

The most remarkable and valuable properties of azaphilones include their natural origin, yellow-red spectra, thermostability (in comparison with other natural red pigments), and water solubility. The azaphilone (Fig. 5.6) compounds produced by different *Chaetomium* species display various biological activities such as antioxidant, nematicidal, antimicrobial, antifungal, anticancer, and inflammatory activities (Borges et al. 2011).

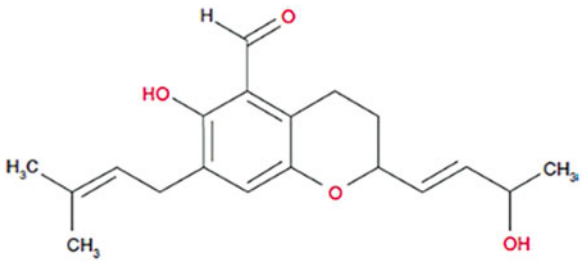

Fig. 5.5 Chaetopyranin (I) (Wang et al. 2006)

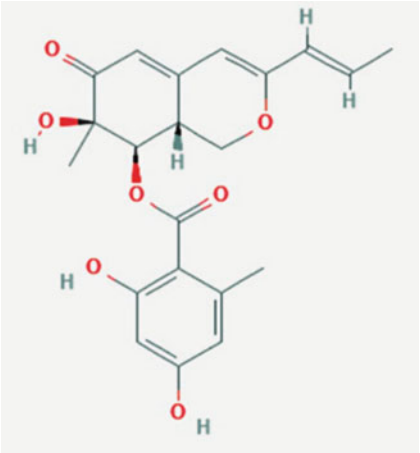

Fig. 5.6 Azaphilone (Darwish et al. 2020)

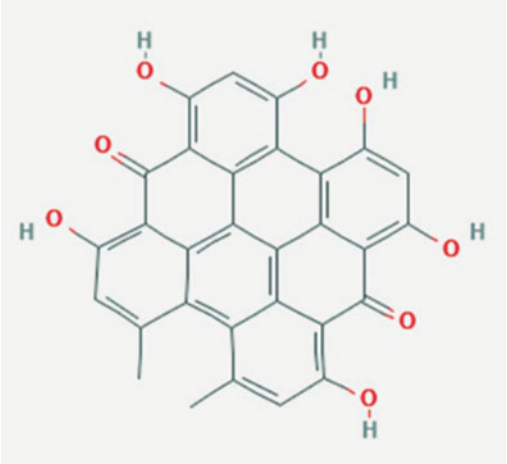

Fig. 5.7 Hypericin (Darwish et al. 2020)

5.6.4 Hypericin and Emodin

Endophytic fungus *Chaetomium globosum* INFU/Hp/KF/34B isolated from *Hypericum perforatum* has been shown to produce hypericin (Fig. 5.7) and emodin of high medicinal value as antioxidants. This endophytic fungus has significant scientific and industrial potential to meet the pharmaceutical demands in a cost-effective, easily accessible, and reproducible way (Kusari et al. 2008; Zhao et al. 2011).

5.6.5 *Mollicellins*

Mollicellins O (1) isolated from the endophytic fungus *Chaetomium* sp., Eef-10, which was isolated from *Eucalyptus exserta* by Ouyang et al. (2018), showed antioxidant activity based on DPPH radical scavenging.

5.7 Light, Electromagnetic Radiations, and Photostimulation

Electromagnetic radiations (EMR) can enhance production of bioactive secondary metabolites of actinomycetes; these include microwaves, ultraviolet light, visible light, and lasers. For example, actinomycete strains isolated from a volcanic cave in western Canada could produce novel antimicrobial compounds against six multidrug-resistant pathogens when exposed to UV light (Rule and Cheeptham 2013). There are four main ways in which EMR can be essential for life including thermal effects, photosynthesis, photomorphogenesis, and mutagenesis. EMR has properties of both waves (where it has a wavelength) and particles (where energy is transferred as quanta or photons).

For example, our data indicate the importance of photosensitizer in the enhancement of laser radiation to stimulate cholesterol decomposition of *Streptomyces fradiae* (Yew et al. 1982). In a photostimulation study on endophytic fungi from medicinal plants, 13 species out of 22 entophytic fungi were screened for production of AgNPs, and photostimulation was carried out by red polarized laser and ultraviolet radiations. Reaction conditions such as silver nitrate concentration, pH, temperature, and efficiency of photostimulation using monochromatic red polarized light and UV radiations were optimized and assessed for high production of AgNPs (Abu-Elsaoud et al. 2015). High concentrations of AgNPs were produced by *Chaetomium globosum* and *Trichoderma viride* recovered from *Tanacetum sinaicum* and *Chiliadenus montanus*, respectively. Both *C. globosum* and *T. viride* showed significantly different response to photostimulation by either red polarized or red LED light. *T. viride* showed promising results and significant increase in AgNP production after photostimulation by monochromatic red polarized light and red light-emitting diodes (rLEDs) (Abu-Elsaoud et al. 2015). For more details about how photostimulation can increase production of active biomolecules please consult Abu-Elsaoud and Abdel-Azeem (2020).

5.8 Conclusion

Recently, new practices in the agricultural systems lead to looking for new management alternatives in different fields like biocontrol. The uncontrolled use of chemical products already has negative effects on the humans, animals, plants, and ecosystem.

Thus, urgent needs for ecogreen and sustainable alternatives for crop production are requested worldwide. Ascomycete genera as Chaetomium, used for disease management, do not generate the negative effects produced by chemical synthesis products such as fungal resistance to fungicides. In the last decades, various studies were carried out by several investigators on different species of Chaetomium recovered from different ecological habitats that have been applied for agriculture as biocontrol agent, plant growth promoter, and secondary metabolite producer. Besides, it was studied as enzyme source for agricultural and industrial application. At present, there are commercial formulations for the mentioned uses, oriented principally to diseases caused by soil fungi. For this reason, it would be necessary to develop new research to expand the spectrum toward other pathologies. Chaetomium and its metabolites combined with new technologies as nanotechnology and biostimulant production are giving good results leading to a potential new avenue of research and exploration. The results of this chapter let readers know the actual update state of Chaetomium knowledge for agricultural and industrial uses. They considered a start point for new researchers and future biotechnology developments in a sustainable approach.

Acknowledgments We would like to express our deep thanks and appreciation to the authors of the literatures used in this chapter.

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