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Industrially Important Fungi for Sustainable Development

Volume 2: Bioprospecting for Biomolecules

Springer

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Foreword

Natural products are the new interest of the current era worldwide over synthetic ones, as sustainability is now on everyone's mind. Various natural products have been obtained from the different sources including animals, plants, and microbes, which have great value in industries. Microbes, especially fungi, represent an incredibly rich reservoir of natural products or biomolecules. Fungi, the highly diverse clade of eukaryotes, are known to produce various biomolecules, such as enzymes, organic acids, fatty acids, pigments, secondary metabolites, and bioactive compounds. These biomolecules have been explored in various industries, including cosmetic, food, tannery, and textiles, as coloring agents, pH adjuster, and catalyst for various biochemical reactions for the production of goods. Fungal biomolecules do comprise various benefits, such as low production cost of natural products and ease to obtain. In comparison to the synthetic products, these products have no detrimental effects on the environment. This volume clearly describes the emerging industrial application of biomolecules obtained from the fungal communities.

I recommend ***Industrially Important Fungi for Sustainable Development, Volume 2: Bioprospecting for Biomolecules*** to researchers and students working in this emerging and fascinating field of mycology. The book will advance the knowledge to a greater extent in these areas with significant broader research on fungal communities. The editors of this book deserve credit for such a splendid and innovative contribution to mycological research.

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Foreword

Today, fungal communities offer important advances in global industries due to their mind-blowing potential in medical, agriculture, and pharmaceutical industries; food and feed processing; and environment for sustainable development. Fungi have been obtained from different sources including plants, soil, and water, which have great value in pharmaceutical industries and are used in several fermentative processes like production of enzymes, vitamins, pigments, lipids, glycolipids, polysaccharides, and polyhydric alcohols. The unique characteristics of fungi hold important promise for the production of various biomolecules, such as organic acid, pigments, secondary metabolites, and bioactive compounds. These biomolecules have been explored in several industries such as synthetic pigments are used as additives, antioxidants, colorants, and color intensifiers, in many aspects including the textile for the coloring agent, pharmaceutical, cosmetic, painting, food, and beverage industries, tannery and catalysts for various biochemical reactions for the goods production. Fungal secondary metabolites as structurally different compounds show a variety of biological activities like antimicrobial, antitumor, antiparasitic, antioxidant, and immunosuppressant activities, and they can also act as plant growth stimulators, pesticides, molluscicides, anthelmintics, and nematicides, leading to industrial scale production of enzyme alkaloids, acids, detergents, and bio-surfactants. Fungi are being used as high-cost food due to their high protein and low color value. This book clearly mentions the evolving industrial applications of biomolecules obtained from the fungal communities.

This volume on ***Industrially Important Fungi for Sustainable Development, Volume 2: Bioprospecting for Biomolecules*** is a very timely publication, which provides state-of-the-art information in the area of mycology, broadly involving fungi and fungus-based products for sustainable development in the industry. The book volume comprises 23 chapters. The first chapter by Nouh et al. describes the bioprospecting for biomolecules from different fungal communities. Nahas et al.

highlight fungi as a gold mine of antioxidants in Chap. 2. Chapter 3 by Abdel-Azeem et al. describes endophytic fungi as a source of new pharmaceutical biomolecules. Chapter 4 by Gezaf et al. highlights fungal communities from different habitats for tannins in industry. Nouh et al. describe recent advances in fungal antimicrobial molecules in Chap. 5. In Chap. 6, Nahas et al. have given the details of fungal laccases to where and where. Ghosh et al. highlight the current research and future challenges of fungal cellulases in Chap. 7.

In Chap. 8, Marwa Tamim A. Abdel-Wareth describes the current research, commercial aspects, and applications of fungal secondary metabolites. Balbool et al. highlight bioprospecting of thermophilic fungal enzymes and potential applications in Chap. 9. Berde et al. highlight bioactive secondary metabolites from psychrophilic fungi and their industrial importance in Chap. 10. Fungal amylases and their industrial applications have been described by Patil et al. in Chap. 11. Chapter 12 by Parsa Mahmood Dar describes current research and applications of fungal phytases in the food industry. Darwish et al. highlight insights into molecular structures and biotechnological applications of fungal lipases in the medicine and dairy industry in Chap. 13. Dar and Dar discuss fungal xylanases for different industrial applications in Chap. 14. Fungal pigments for the food industry are discussed in Chap. 15 by Soliman et al. Dikkala et al. describe the fungal production of vitamins and their food industrial applications in Chap. 16. Jagadish et al. describe the nutraceutical potential of wild edible mushroom *Hygrocybe alwisii* in Chap. 17. Current research, production, and potential applications of fungal biopharmaceuticals have been discussed in Chap. 18 by Askari et al. Chapter 19 by Ashok et al. describes natural pigments from filamentous fungi and their applications. Kour et al. describe the bioprospecting of industrially important mushrooms in Chap. 20. Bioactive attributes of *Xylaria* species from the scrub jungles of southwest India have been described by Jagadish et al. in Chap. 21. Current research and future challenges of fungicide as potential vaccine are discussed in Chap. 22 by Verma et al. Finally, the conclusion and future prospects of bioprospecting for biomolecules from industrially important fungi have been described by the editors and co-authors in the last chapter.

Overall, great efforts have been carried out by the editorial team and scientists from different countries to compile this book as a highly unique and up-to-date source on ***Industrially Important Fungi for Sustainable Development, Volume 2: Bioprospecting for Biomolecules*** for students, researchers, scientists, and academicians. I hope that the readers will find this book highly useful and interesting during their pursuit of mycology.

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Preface

Fungi are an essential, fascinating, and biotechnologically useful group of organisms with an incredible biotechnological potential for industrial exploitation. Knowledge of the world's fungal diversity and its use is still incomplete and fragmented. There are many opportunities to accelerate the process of filling knowledge gaps in these areas. The worldwide interest of the current era is to increase the tendency to use natural substances instead of synthetic ones. The increasing urge in society for natural ingredients has compelled biotechnologists to explore novel bioresources, which can be exploited in the industrial sector. Fungi, due to their unique attributes and broad range of biological activities, hold great promise for their applications in biotechnology and industry. Fungi are an efficient source of antioxidants, enzymes, pigments, and many other secondary metabolites.

Industrially Important Fungi for Sustainable Development, Volume 2: Bioprospecting for Biomolecules covers major aspects of industrially important fungi. The book focuses on fungal communities from diverse niches and habitats as potential source of industrially important compounds. The increasing use and exploration of novel bioactive compounds from fungi solve countless problems mankind faces in today's constantly changing scenario, such as emergence of life-threatening viruses and drug-resistant bacteria and increasing incidences of fungal and bacterial infections. The large-scale production of fungal pigments and their utility provide natural coloration without creating harmful effects on entering the environment, a safer alternative to synthetic colorants. Fungal enzymes can be exploited in a wide range of industries, such as food, detergent, and paper, and also for removal of toxic waste. Thus, this book will surely serve as a valuable reference to current state of knowledge and a stepping-stone for unexplored novel compounds from fungi. The book will be extremely useful for researchers, students, microbiologists, and scientists especially working in the field of mycology. Each chapter has been contributed by internationally recognized researchers and scientists with their firm viewpoints and experiences in the field of mycology. This book will serve as a valuable source of information as well as will provide new directions to researchers to conduct novel research in the field of mycology.

Industrially Important Fungi for Sustainable Development, Volume 2: Bioprospecting for Biomolecules provides a discussion of fungal communities from diverse habitats and their industrial applications for future sustainability. This volume encompasses advanced research of fungal communities and their potential biotechnological applications in industry and allied sectors. The book will be useful to scientists, researchers, and students working in microbiology, biotechnology, agriculture, molecular biology, environmental biology, and related subjects.

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Chapter 10
Bioactive Secondary Metabolites from Psychrophilic Fungi and Their Industrial Importance

Chanda Vikrant Berde, Asha Giriyan, and Vikrant Balkrishna Berde

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10.1 Introduction

Psychrophilic microorganisms are cold-adapted organisms that have an optimum growth temperature below 15 °C, and often below 5 °C. The cold biosphere includes aquatic and terrestrial environments, but many temperate habitats often have cold temperatures during autumn and winter (Margesin and Miteva 2011; Yadav et al. 2018). Cold-adapted fungi are ubiquitous in cold habitats such as the deep seas, Arctic and Antarctic areas, and glaciers. Psychrophilic fungi, including yeasts and filamentous fungi, are adapted to cold ecosystems like the Arctic and Antarctic zones. Despite the extreme conditions of glacial ice of Antarctica, such as temperatures below 0 °C, low nutrient availability (ultra-oligotrophic conditions), and low water activity, we detected a diverse fungal community, including species never before reported in the glacial ice of Arctic and Antarctica (Vincent 1988; Vishniac 1996; Del Frate and Caretta 1990; Robinson 2001; Deming 2002; Gocheva et al. 2005; Frisvad 2008; Yadav et al. 2020b).

Cold-adapted fungi have evolved special properties, for example, cold-adapted enzymes, change of membrane fluidity, and other cellular components, to enable them to grow at low temperatures at rates comparable to those of mesophiles at moderate temperatures (D'Amico et al. 2006; Ruisi et al. 2007). The terms stenopsychrophile and eurypsychrophile have therefore been proposed to modify the definitions of psychrophilic and psychrotolerant. The "steno-" and "eury-" are referred ecological terms derived from Shelford's law of tolerance that describe narrow or wide tolerance to an environmental determinant, respectively. The stenopsychrophile (equal to "psychrophile") refers to microorganisms with a restricted growth-temperature range that cannot tolerate higher temperatures. Eurypsychrophile (equal to "psychrotolerant microorganisms") describes microorganisms that "like" permanently cold environments, but can also tolerate a wide range of temperatures extending into the mesophilic range (Cavicchioli 2006).

In recent years, the diversity of filamentous fungi in cold niches has been increasingly investigated, and the number of known species has greatly expanded (Möller and Dreyfuss 1996; Robinson 2001; Blanchette et al. 2004; Arenz et al. 2006; Connell et al. 2006; Held et al. 2006; Malosso et al. 2006; Duncan et al. 2008; Onofri et al. 2008; Selbmann et al. 2008; Arenz and Blanchette 2009; Jurgens et al. 2009).

Most species in these studies, however, are psychrotolerant, and only a few were documented as psychrophiles such as *Thelebolus microsporus*, *Mucor strictus*, *Phoma herbarum*, *Humicola marvinii*, *Pseudogymnoascus destructans*, and some snow molds for example *Sclerotinia borealis*, *Microdochium nivale*, *Coprinus psychromorbidus* (Schipper 1967; Dejardin and Ward 1971; Traquair and Smith 1982; Richard et al. 1997; Hsiang et al. 1999; Tronsmo et al. 2001; Singh et al. 2006; Gargas et al. 2009; Hoshino et al. 2010; Anupama et al. 2011; Minnis, and Lindner 2013). Species in several yeast genera including *Mrakia*, *Mrakiella*, and *Rhodotorula* were usually described as psychrophilic. For example, *Mrakia frigida* grew well at 15 °C and 4 °C but poorly at 20 °C (Margaret 1966) thus proving its psychrophilic nature; *Mrakia psychrophila* from Antarctic soil had an optimal growth temperature of 10 °C (Xin and Zhou 2007); *Mrakiella cryoconiti*, *M. aquatica*, and *M. niccombsii* from alpine and Arctic habitats also exhibited psychrophilic features and failed to grow at temperatures over 20 °C (Margesin and Fell 2008; Robin et al. 2010).

During the past two decades, research on cold-adapted fungi has increased, driven by their potential value for application in biotechnology (Margesin and Schinner 1994, 1999). Cold-adapted fungi have become important sources for the discovery of novel bioactive secondary metabolites and enzymes (Flam 1994; Pietra 1997; Biabini and Laatch 1998; Gudjarnnson 1999; Höller et al. 2000; Verbist et al. 2000; Bhadury et al. 2006; Ebel 2006; Blunt et al. 2007; Rateb and Ebel 2011). This chapter highlights the production of bioactive secondary metabolites by psychrophilic fungi.

10.2 Biodiversity and Distribution of Psychrophilic Fungi

Three-quarters of the earth's surface are dominated by the cold habitats spanning from the Arctic to the Antarctic and from high-mountain regions to the deep ocean (Deming and Eicken 2007; Rodrigues and Tiedje 2008). The major fraction of this extreme environment is represented by the deep sea (90% of the ocean volume), followed by snow (35% of land surface), permafrost (24% of land surface), sea ice (13% of the earth's surface), and finally glaciers (10% of land surface). Other cold environments are cold-water lakes, cold soils, cold deserts, and caves (Lauro and Bartlett 2008; Yadav et al. 2017, 2020a). These extreme environments are colonized by enormously diverse communities of prokaryotes and eukaryotes (Cavicchioli 2006; Kalanetra et al. 2009; Margesin and Miteva 2011; Buzzini et al. 2012; Lamilla et al. 2017) are able to survive and maintain metabolic activity at subzero temperatures.

As an attempt to understand the global climate change scenario, study of the glacial ice samples for their physicochemical composition (de Menezes et al. 2019) was undertaken. During this study, the presence of fungal spores or hyphal fragments trapped in the ice matrix was observed. The probable reasons for this may also be the growth of fungi due to the occasional melting and freezing of the ice in the Arctic regions as reported by Lutz et al. (2015), DuoSaito et al. (2018), and Perini et al. (2019a, b). Paleomycological and paleoecological investigations of the North and South Poles have indicated the presence of fungi in Antarctica since at least the Permian period because diverse fossil fungi have been found from the Triassic and Jurassic Periods (Stubblefield and Taylor 1983; Taylor and Osborne 1996; Harper et al. 2012).

Despite being an extreme and ultra-oligotrophic environment, the glacial ice of Antarctica seems to harbor rich fungal diversity. Latest reports indicate the presence of Basidiomycota and Ascomycota taxa among fungal assemblages to predominant the glacial ice from the Arctic (Perini et al. 2019a, b) and Patagonia (DuoSaito et al. 2018) as well as soil from Antarctica (Connell et al. 2008; Arenz and Blanchette

2011). Zygomycetes and Chytridiomycota species have also been isolated from Antarctic lakes and ponds (Lawley et al. 2004; Paterson 1973).

Bridge and Spooner (2012) listed over 400 fungal genera and more than 1000 species that had been reported from Antarctic regions and suggested that fungi may be the most diverse biota in Antarctica. Species such as *Thelebolus*, *Glaciozyma*, *Rhodotorula*, and *Penicillium* were also found in high densities and 11 taxa were found in low densities, which had not been recorded in Antarctic glacial ice. *Thelebolus* sp. are abundant in lakes and is associated with skuas, petrels, and other birds in Antarctica (de Hoog et al. 2005; Brunati et al. 2009; Gonçalves et al. 2012a, b) and are isolated from Arctic and Antarctic regions (Kobayasi et al. 1967; Montemartini et al. 1993; Sazanova et al. 2019; Alves et al. 2019). The psychrophilic fungal diversity and incidence of fungal species in different habitats of Antarctica are given in Table 10.1.

Bovio et al. (2018) reported *Thelebolus balaustiformis* a new psychrophilic fungal species isolated from the sponge, *Dyside fragilis*, in the South, Atlantic Ocean in the glacial ice habitats. Another psychrophile *Glaciozyma antarctica* (former *Leucosporidium antarcticum*) was isolated from various locations including the Antarctic marine waters (Fell et al. 1969); the soil around Lake Fletcher, Lichen, and Taylor Valleys, and on the dead sponge (Turchetti et al. 2011). Timling et al. (2014) sampled soils along the North American Arctic Transect and was successful in isolating more than 4350 fungal species. The most frequently isolated fungal isolates were *Leotiomycetes* sp., followed by *Thelebolus*, *Penicillium*, *Cladosporium*, *Trichoderma*, *Periconia*, *Geomyces*, *Cryptococcus*, and *Pueraria.* Ascomycota dominated the communities, followed by Basidiomycota. Five families in Chytridiomycota and one family in each of Zygomycota, Glomeromycota, Blastocladiomycota, and Neocallimastigomycota were detected, while Cryptomycota were only identified at the phylum level.

Compared to the polar regions, cold-adapted fungi in the Qinghai–Tibet Plateau are less documented except for a study from wherein more than 1400 fungal strains were isolated and 150 species including 6 new species were identified and described. Among those species, *Phoma sclerotioides* and *Pseudogymnoascus pannorum* were the most dominant species. Psychrotolerant species in *Helotiales* (*Leotiomycetes*, *Ascomycota*), the most commonly found group was studied in-depth and six new species, *Psychrophila antarctica*, *P. lutea*, *P. olivacea*, *Tetracladium ellipsoideum*, *T. globosum*, and *T. psychrophilum* were described (Wang et al. 2015a, b).

Hassan (2015) isolated 77 fungal strains representing 24 fungal genera from Batura Passu and Siachen Glaciers in the Hindu Kush and Karakoram mountains in Pakistan. Most of the fungal isolates showed antimicrobial activity and production of enzymes such as cellulase, lipase, protease, DNase, phosphatase (Hassan et al. 2017).

Psychrophilic endophytic fungi (PEF) were isolated from healthy foliar tissues of *Cupressus arizonica*, *Cupressus sempervirens*, and *Thuja orientalis* (*Cupressaceae*, *Coniferales*). Most of the 110 endophytic fungal isolates belonged to ascomycetous fungi, more specifically *Phoma herbarum*, *Phoma* sp., *and Dothideomycetes* sp., with the ability to produce secondary metabolites. *Phoma*

Table 10.1 Psychrophilic fungi isolated from different habitats of Antarctica, showing antagonistic activities

Habitat	Fungi	Metabolic activities	References
Benthic mats of Antarctic lakes	160 filamentous fungi belonging to 15 fungal genera	Antimicrobial and cytotoxic activity	Brunati et al. (2009)
Algae associates from the rocky coastline of Elephant, King George, and Deception Islands, in the Antarctic Peninsula	148 fungal strains consisting of *Penicillium* (35.8%), *Geomyces* (24.3%), and the yeast *Mestchnikowia australis* (4.7%)	Antioxidants, anti-algal, antifungal, and anti-insect metabolites	Godinho et al. (2013)
Associates of endemic macroalgae *M. harioti* and *Pyropia endiviifolia*	*Pseudogymnoascus* sp., *Guehomyces pullulans*, *M. australis*	Antifungal activities	Furbino et al. (2014)
	Penicillium steckii	Inhibition of yellow fever virus	
Associates of marine sponges of Fildes Bay, King George Island	101 fungal isolates including genera *Geomyces*, *Penicillium*, *Epicoccum*, *Pseudoeurotium*, *Thelebolus*, *Cladosporium*, *Aspergillus*, *Aureobasidium*, *Phoma*, and *Trichocladium*	Antimicrobial and antitumoral compounds	Henríquez et al. (2014)
Marine sediments of Admiralty Bay	23 of the 47 fungal strains belonging to the genera *Pseudogymnoascus*, *Penicillium*, *Cadophora*, *Paraconiothyrium*, and *Toxicocladosporium*	Antibacterial activity against *Xanthomonas* species	Purić et al. (2018)
Marine and lake sediments from Deception Island	*Penicillium* sp. *Pseudogymnoascus* sp. *Schizophyllum* sp.	Antimicrobial cytotoxic and antiprotozoal	Gonçalves et al. (2015)
Terrestrial soils of Admiralty Bay, King George Island, and Deception Island	8 strains from the genera *Bauveria*, *Penicillium*, *Phanerochaete*, *Pseudoeurotium*, *Pseudogymnoascus*, *Purpureocillium*, and *Trichoderma* sp.	Antimicrobial, cytotoxic, and antiprotozoal activities	Gonçalves et al. (2015)
Union Glacier, in the southern Heritage Range	17 fungi including *A. sydowii*, *P. allii-sativi*, *P. brevicompactum*, *P. chrysogenum*, and *P. rubens*	Antibacterial, antifungal, antitumoral, antiprotozoal, and herbicidal activities	Godinho et al. (2015)
Chinese Antarctic station at Fildes Bay, King George Island	14 fungal strains	Cytotoxic, antimicrobial	Ding et al. (2016)

(continued)

Table 10.1 (continued)

Habitat	Fungi	Metabolic activities	References
Robert, Nelson, King George, and Penguin Islands at South Shetland archipelago	Filamentous fungi *Pseudogymnoascus destructans*, *Mortierella parvispora*, and *P. chrysogenum*, *P. tardochrysogenm*	Antiviral activity against dengue and Zika virus; antiparasitic activity; herbicidal activity against *L. sativa* (lettuce) and *Allium schoenoprasum* (chive)	Gomes et al. (2018)
Deception Island	6 *Pseudogymnoascus* sp. out of 33 filamentous isolates	Anti-*Xhantomonas* activity	Purić et al. (2018)
Endophytes of *D. antarctica*	21 fungal strains	Antifungal activity	Gonçalves et al. (2015)
Endophytic to moss *Schistidum antarctic* found in Admiralty Bay, King George Island	*Mortierella alpine*	Antioxidant activity and antibacterial activity	Melo et al. (2014)
Endophytic association with *D. antarctica* and *C. quitensis*	313 fungal isolates from *D. antarctica* 251 isolates from *C. quitensis*	Antiparasitic to *L. amazonensis* and *T. cruzi* Antitumor	Santiago et al. (2012)

herbarum has been reported by the number of workers as soil psychrophilic fungi that is pathogenic to plants growing in cold regions (Domsch et al. 1980; Flanagan and Scarborough 1974; Selbmann et al. 2005; Singh et al. 2006).

10.3 Associations and Cold Adaptation Mechanisms of Psychrophilic Fungi

Fungi overcome cold tolerance through several physiological mechanisms and it is likely that they employ them in combinations. Numerous adaptations and mechanisms can be observed. One of the mechanisms is the production and accumulation of intracellular solutes, also called as cryopreservants or cryoprotectants, such as glycerol, trehalose, and so on. Cryoprotectants are exopolymeric substances (e.g., sugars, alcohols, and amino acids), generated in high amounts believed to be in response to cold. These prevent cold-induced aggregation of proteins as well as maintain optimum membrane fluidity under low temperatures (Krembs et al. 2002; Mancuso Nichols et al. 2005).

Ophiocordyceps sinensis, the Chinese caterpillar fungus, is adapted to cold temperature with putative antifreeze proteins and mechanisms for increasing lipid accumulation and fatty acid unsaturation (Xiao et al. 2013). *Pseudogymnoascus pannorum* (*Geomyces pannorum*) is a soil-inhibiting fungus, isolated from Arctic and Antarctic regions, as well as glacier bank soils in some Asian countries

(Deshmukh 2002; Arenz et al. 2006; Ozerskaya et al. 2004). *P. pannorum* grows slowly at temperatures below 0 °C to as low as −20 °C. This fungus maintains cell and membrane function at low temperatures by elevating levels of unsaturated fats and compounds with cryoprotectant properties such as trehalose and various polyols at low temperatures (Finotti et al. 1996; Hayes 2012). Some of the adaptation means are discussed below:

10.3.1 Trehalose Accumulation

Trehalose is an important storage sugar in fungal vegetative cells and spores (Lewis and Smith 1967) and the most widely distributed disaccharide in fungi (Thevelein 1984). In fungal vegetative structures, trehalose is commonly found with sugar alcohols and glycogen. As per Cooke and Whipps (1993), trehalose appears to function as a general stress protectant in the cytosol and also stabilizing membranes during dehydration (Goodrich et al. 1988).

More recently, authors have demonstrated the accumulation of trehalose in fungal hyphae as a response to low temperatures. An elevation in trehalose composition was observed after the exposure of the fungi to low temperature or during growth at low temperature. Trehalose concentration in Mycorrhizal roots as well as increased accumulation in *Hebeloma* sp. is reported (Niederer et al. 1992; Tibbett et al. 1998). A shift in growth temperature, that is, lowering growth temperature further, also resulted in higher production of trehalose as seen in *Humicola marvinii*, a psychrophile, isolated from fell-field soil at Jane Col, Signy Island in Antarctica as well as *Mortierella elongata*, a psychrotrophic fungus (Weinstein et al. 2000).

10.3.2 Polyol Production

Glycerol and mannitol both polyols may increase in concentration to maintain turgor pressure against heat-mediated decreases in external water potential (Cooke and Whipps 1993). Mannitol likewise is thought to be important in protection against water stress (Lewis and Smith 1967) and maybe a cryoprotectant (Weinstein et al. 1997). Initial evidence of their potential cryoprotectant role came from a study by Weinstein et al. (1997), using an Antarctic isolate of *Humicola marvinii*.

10.3.3 Antifreeze Proteins (AFPs)

AFPs either intra- or extracellular may allow fungi to function and survive under freezing conditions by preventing the formation of ice and also preventing the freezing of cell components (Snider et al. 2000). *Glaciozyma antarctica*, a psychrophilic yeast, produces AFPs that help in its survival in glacial ice (de Menezes et al. 2019). AFP is found in the hyphae of three psychrophilic snow molds, the ascomycete *Sclerotinia Borealis*, and two basidiomycetes, *Coprinus psychromorbidus* and *Typhula incarnate* was reported back in 1994 by Newsted et al. (1994). Recently, antifreeze activity in snow-mold fungi *Typhula incarnata*, *T. ishikariensis*, and *T. phacorrhiza* has been reported by Snider et al. (2000).

10.3.4 Membrane Fluidity

Another adaptation strategy is the regulation of membrane fluidity as a response to freezing environments. The membrane is the first barrier, protecting the cells from external environments, thus acts as an interface for the fungi (Chintalapati et al. 2004). Shivaji and Prakash (2010) reported an increase in membranes rigidity at cold temperatures, which activates a membrane-associated sensor and subsequent upregulation of genes to mediate the exchange of metabolites to and from thus enhancing membrane fluidity of the cell. This process is aided by the modification of fatty acyl chains of the membrane fatty acids (Russell 2008) wherein saturated fatty acids are converted to unsaturated fatty acids by desaturase enzymes (Chintalapati et al. 2004).

It is evident from studies that membrane composition influences the survival and growth of fungi over the environmental range of temperature variations (Cooke and Whipps 1993). Such changes leading to increased fluidity of the cell membranes have been observed in *Candida*, *Leucosporidium*, *Mucor*, *Torulopsis* (Kerekes and Nagy 1980; Dexter and Cooke 1984a, b) where the degree of unsaturated fatty acids increased at low temperatures. Apart from fatty acids, changes in the membrane phospholipid saturation levels, membrane proteins, and sterols, also determine the membrane fluidity and thus help in survival in low freezing (Dexter and Cooke 1985; Hammonds and Smith 1986). Change in growth temperature of psychrophilic fungi *Geomyces pannorum*, *Mortierella elongata*, *Microdochium nivale*, showed the lipid composition to change towards unsaturation, thus modifying the membrane fluidity to adjust to the lowered temperatures and survive (Istokovics et al. 1998; Weinstein et al. 2000).

10.4 Bioactive Secondary Metabolites of Psychrophilic Fungi

Research and discovery of secondary metabolites from fungi from the tropics and temperate regions have been the focus for the last few decades. However, work on psychrophilic fungi started recently but has acquired a considerable pace, especially studies on isolation and secondary metabolite studies from different habitats of Antarctica (Table 10.2). Studies indicate dominance of *Penicillium* sp. in the glacial ice of Antarctica. Another well-studied niche for the psychrophilic fungi is the deep

Table 10.2 Secondary metabolites produced by psychrophilic fungi isolated from Antarctica

Fungi	Metabolite	Application	References
Tritirachium sp.	4-Carboxy-5,5′-dihydroxy-3,3′-dimethyl-diphenylether and macrosphelides A and J	Cell adhesion inhibitors and moderately cytotoxic agent	Ivanova et al. (2007), Hayashi et al. (1995)
Trichoderma asperellum	Asperelines A–F	Inhibitory activity against fungi and bacteria	Ren et al. (2009)
Oidiodendron truncatum	Chetracins B and C, and 5 new diketopiperazines, named chetracin D and oidioperazines A–D, melinacidin IV, T988 B, T988 C, T988 A, chetoseminudin C, and cyclo-L-Trp-L-Ser	Cytotoxic towards 5 human cancer cell lines	Li et al. (2012b)
Aspergillus sydowii SP-1	Acremolin C, and (*cyclo*-(L-Trp-L-Phe), 4-hydroxy-phenyl acetic acid, (7*S*)-(+)-hydroxyl-sydonic acid, and (7*S*,11*S*)-(+)-12-hydroxysydonic acid)	Antibacterial	Li et al. (2018), Nishanth Kumar et al. (2014), Li et al. (2015)
A. ochraceopetaliformis	Ochraceopones A–E, isoasteltoxin, asteltoxin and asteltoxin B; Ochracenes A–I, *trans* (3*R*,4*S*)-(−)-4-hydroxymellein, cis (3*R*,4*R*)-(−)-4-hydroxymellein, (3*R*,4*R*)-4,7-dihydroxymellein, 3,5-dimethylpyrone, stachyline B, and (*E*)-methyl-5-methylhexa-3,5-dienoate	Antiviral activities against the H1N1 and H3N2 influenza viruses Moderate inhibitory effects on lipopolysaccharide induced NO release in RAW 264.7 mouse macrophage cell lines	Wang et al. (2015a, 2016, 2017)
Cadophora luteo-olivacea	Spiciferone F, colomitides C and D, cadopheronenes A–D, similin C, and spicifernin B; polyketides spiciferone A, spiciferol A, dihydrospiciferone A, and dihydrospiciferol A	Phytotoxicity activity and plant growth-promoter activity	Nakajima et al. (1989), Nakajima et al. (1990), Rusman et al. (2018)
Geomyces sp.	Ethyl asterrate, n-butyl asterrate, and geomycins A–C. Asterric acid, methyl asterrate, and bisechlorogeodin	Antibacterial and antifungal activities	Li et al. (2008)
Pseudogymnoascus sp.	Pseudogymnoascins A–C and 3-nitroasterric acid, questin, pyriculamide	–	Figueroa et al. (2015)
Pseudogymnoascus pannorum	Pannomycin	Antibacterial activity	Parish et al. (2009)

(continued)

Table 10.2 (continued)

Fungi	Metabolite	Application	References
Penicillium nalgiovense	Amphotericin B	Antifungal	Svahn et al. (2015)
Penicillium sp. SCIO 05705	Penillines A and B and isopenilline A; (*E*)-3-(1*H*-imidazole-4-yimethylene)-6-(1*H*-indl-3-ylmethyl)-2,5-piperazinediol, penilloid, meleagrin, neoxaline, questiomycin A, *N*-(2-hydroxypehnyl)-acetamide, and 2-benzoxazolinone	Cytotoxicity; antituberculosis activity	Wang et al. (2015b)
Penicillium funiculosum GWT2-24	Chrodrimanins I and J Chrodrimanins A, B, E, F, and H	Inhibitory activity against influenza virus H1N1; lipid-lowering activity in HepG2 hepatocytes	Zhou et al. (2015, 2016)
Penicillium sp. S-1-18	Butanolide A, and guignarderemophilane F; penicyclone A, xylarenone A, callyspongidipeptide A, *cyclo*-(L-Phe-4*R*-hydroxyl-L--Pro), *cyclo*-(L-Pro-L-Phe), and *N*-(2-hydroxypropanoyl)-2-aminobenzoic acid amide	Tyrosine phosphatase 1B inhibition	Zhou et al. (2017)
Penicillium crustosum HDN153086	(8*E*,4*E*,6*E*,8*E*)-10-Hydroxyundeca-2,4,6,8-tetraenoic acid, fusaperazine F xylariolide D and two diketopiperazines	Cytotoxic activities	Liu et al. (2019)
Mortierella alpina	Pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-3-(2-methylpropyl) and pyrrolo[1,2-a]pyrazine-1,4-dione, hexahydro-3-(phenylmethyl)	Antibacterial activity	Melo et al. (2014)
Pseudogymnoascus strains	–	Antifungal activities	Furbino et al. (2014)
Purpureocillium lilacinum	–	Trypanocidal, antifungal, and antibacterial activities	Gonçalves et al. (2015)
218 fungal extracts including *P. destructans*, *Mortierella parvispora*, and *P. chrysogenum*	–	Antiviral activity against dengue and Zika viruses Antiparasitic activity against *Trypanosoma cruzi* and *Leishmania amazonensis*, and herbicidal activity	Gomes et al. (2018)

(continued)

Table 10.2 (continued)

Fungi	Metabolite	Application	References
Pseudogymnoasc, *Penicillium*, *Cadophora*, *Paraconiothyrium*, *Toxicocladosporium*, *Xanthomonas citri*	–	Antimicrobial inhibitory compounds against phytopathogen bacteria	Vieira et al. (2018)
Penicillium tardochrysogenum	Penicillin, secalonic acids D and F	–	Houbraken et al. (2012)
P. chrysogenum	–	Selective antimicrobial activities	Brunati et al. (2009)
P. chrysogenum	–	Antifungal and/or trypanocidal activities	Godinho et al. (2013)
Penicillium steckii	–	Antiviral activity against yellow fever virus	Furbino et al. (2014)
A. sydowii, *P. allii-sativi*, *P. brevicompactum*, *P. chrysogenum*, *P. rubens*	–	Antiviral, antimicrobial (antibacterial and antifungal), anticancer, antiprotozoal, and herbicidal activities	Godinho et al. (2015)

sea and a lot of research has been documented (Höller et al. 2000; Jensen and Fenical 2000; Verbist et al. 2000; Hentschel 2002; Bhadury et al. 2006; Ebel 2006; Konig et al. 2006; Newman and Hill 2006; Paul et al. 2006; Damare et al. 2006, 2008; Blunt et al. 2007).

Most of the species found in these cold regions have the ability to form extrolites in large amounts and have been reported to be species-specific (Larsen et al. 2005). The fungal communities found in the habitats of Antarctic regions have structures, which can be used for designing potential drugs and other products to treat tropical diseases and cancer. Rosa et al. (2019) described the extrolites produced by psychrophiles and have reported *Aspergillus*, *Cladosporium*, *Penicillium*, *Pseudogymnoascus*, *Phaeosphaeria*, *Microdochium*, *Mortierella*, and *Purpureocillium* sp. in their findings. Several such reports on the production of useful extrolites are available. Secondary metabolites produced by psychrophilic fungi are described below:

10.4.1 Antibiotics

Some unique components and products with potential bioactive properties have been isolated and characterized from psychrophilic fungi. *Penicillium* species are the best known fungal strains for their capability to produce diverse bioactive compounds, including penicillin, produced by the strain *P. chrysogenum* (Houbraken et al. 2012; Devi et al. 2020; Rastegari et al. 2019a). *Penicillium* sp. was isolated from the Antarctic soil by Antipova et al. (2018) and has been reported to produce a number of unknown metabolites with numerous bioactivities (Rosa et al. 2019). Brunati et al. (2009) reported the production of rugulosin and skyrin (*bis*-anthraquinones) by strains of *P. chrysogenum* from Antarctica which had antibacterial activity against Gram-negative and Gram-positive organisms.

Another research group reported antifungal and anti-trypanocidal activities of *P. chrysogenum* extracts, associated with Antarctic algae *Palmaria decipiens* (Godinho et al. 2013). Strains of *P. chrysogenum* isolated from Antarctica soil samples demonstrated trypanocidal and herbicidal activities (Godinho et al. 2015). The most recent report on *P. palitans*, isolated from permafrost lying undisturbed for 30,000 years, produced two metabolites namely, festuclavine and fumigaclavines A and B (Kozlovsky et al. 2020). Psychrophile fungus *Penicillium rivulum*, producing new psychrophilins, and complex alkaloids communesins was characterized by Dalsgaard et al. (2004a, b, 2005a). Thus the *Penicillium* species incident in the cold habitats of Antarctica is "mycofactories" having the ability to produce a diverse range of biometabolites with several applications.

Santiago et al. (2012) studied the capabilities of Antarctic endophytic fungi recovered from *Deschampsia antarctica* to produce bioactive secondary compounds against neglected tropical diseases and tumor cells. Li et al. (2008) worked with *Geomyces* sp. strains isolated from Antarctica, that could produce asterric acid derivatives that are known for antibacterial, antifungal, and anti-angiogenic activities (Giddings and Newman 2014; Li et al. 2008; Mahmoodian and Stickings 1964; Lee et al. 2002). Further in 2012, Li and coworkers isolated a number of compounds from psychrophilic fungus *Oidiodendron truncatum* including two new epipolythiodioxopiperazines (ETPs), chetracins, and five new diketopiperaines, chetracin D, and oidioperaines A–D (Li et al. 2012a; Jiang and Guo 2011; Giddings and Newman 2014)

10.4.2 Cytotoxic Metabolites

Several cytotoxic compounds from psychrophilic fungi have been reported by the number of workers. The secondary metabolites, some of them, new records, have weak to moderately significant activity toward cancer cells. Table 10.3 gives a summary of some of the cytotoxic secondary metabolites isolated from psychrophilic and psychrotolerant fungi.

Table 10.3 Cytotoxic secondary metabolites isolated from psychrophilic and psychrotolerant fungi

Fungal species	Secondary metabolite	Nature of metabolite	Activity	References
Penicillium algidum	Psychrophilin D, Cycloaspeptide A and B	Nitropeptide and cyclopeptides	Cytotoxic to murine leukemia cells	Dalsgaard et al. (2005b)
Aspergillus sp.	Psychrophilin E and F	Nitropeptide	Cytotoxic to murine leukemia cells; lipid-lowering activities	Ebada et al. (2014), Peng et al. (2014)
Oidiodendron truncatum GW3-13	Epipolythiodioxopiperazines chetracins B and C; diketopiperazines chetracin D; melinacidin IV, T988, and T988 A	Piperazines	Cytotoxic activity	Li et al. (2012b)
Penicillium sp. PR19 N-1	Eremophilane-type compound	Sesquiterpene compounds	Cytotoxic to HL-60 cells and A-549 cell lines	Lin et al. (2014)
	Chloro-trinoreremophilane sesquiterpene	Chloroeremophilan sesquiterpene		Wu et al. (2013)
Trichoderma velutinum	Lipovelutibols B and D	Lipopeptaibols	HL-60, MDA-MB-231, A549, and LS180 cell lines	Singh et al. (2018)

10.4.3 Diterpenes

Diterpenes having antibacterial activity toward Gram-positive and Gram-negative bacteria namely *Bacillus subtilis*, *Staphylococcus aureus*, and *Escherichia coli*, were report to be produced by *Eutypella* sp. D-1. Among the diterpenes isolated from this psychrophilic fungus, libertellenone G and libertellenone H are new while two other known pimarane diterpenes were also detected (Liu et al. 2014).

10.4.4 Cyclic Peptides

Cyclic peptides have applications in different fields, such as the pharmaceutical industry for their anti-infective, antitumor, antimalarial activity, agricultural applications as fungicides, diagnostics, and vaccines (Demmer et al. 2009; Demain and Sanchez 2009; Claro et al. 2018). Studies on secondary metabolites from psychrophilic fungi producing cyclic peptides are sparse. A new cyclic nitropeptide, Psychrophilin Dan antitumor compound, was extracted from the fungus *Penicillium algidium* a psychrophilic fungus isolated from Greenland (Ivanova et al. 2001). From the same strain, two more cyclic peptides were obtained namely, cycloaspeptide A and cycloaspeptide D. Later, Dalsgaard et al. (2004a) isolated cyclic peptides related to these, that is, psychrophilin A and cycoloaspeptide D from the extracts of the psychrophilic fungus *Penicillium reibeum*, both of which are new metabolites having antitumor and antagonistic activities (Demain and Sanchez 2009).

10.4.5 Polyketides

Polyketides (PKs) have antimicrobial activity and other clinically important applications. PKs help in nutrient assimilation resulting in lowering the capacities of competitors in the environments (Mukherjee et al. 2012). *Penicillium crustosum* PRB-2 from the deep sea of the Antarctic was found to produce Penilactones A and B, the oxygenated polyketides (Wu et al. 2012). While the same group also reported hybrid polyketides, like cladosins which were produced by *Cladosporium sphaerospermum* 2005-01-E3, a deep-sea isolates. One of the cladosins, Cladosin C showed antiviral activity influenza A H1N1 virus (Wu et al. 2014). The same workers further isolated polyketide Scequinadoline A from psychrophilic fungi *Dichotomomyces cejpii* F31-1(Wu et al. 2018) and polyketide, anthraquinone–xanthone from *Engyodontium album* LF069 (Wu et al. 2016). Scequinadoline A demonstrated antiviral activity against the dengue virus while the anthraquinone–xanthone could inhibit methicillin-resistant *Staphylococcus aureus*.

10.4.6 Exopolysaccharides (EPS)

Production of exopolysaccharide is a stress response observed in marine or aquatic organisms. Fungus EPS, apart from having good rheological properties, have numerous bioactive characteristic features such as antitumor, antioxidant, anti-inflammation, immune-stimulating, anti-anemics (Rastegari et al. 2019b). Thus it has a good potential in the health and drug industry (Li et al. 2013). It was observed that fungi with eps showed better growth under freeze-thaw conditions compared to fungi without eps (Selbmann et al. 2002; Yadav et al. 2019).

The fungal isolate from Antarctica, *Phoma herbarum* CCFEE 5080, showed the production of exopolysaccharide made up of glucan (Selbmann et al. 2002). Onofri (1999) and Selbmann et al. (2005) reported exopolysaccharide synthesis in meristematic black fungi isolated from Antarctica similar to *Friedmanniomyces endolithicus*. Exopolysaccharide has multiple applications such as in cryopreservation, for example, alginate beads containing EPS for sample preservation from freezing damage (Martínez et al. 1999). Psychrophilic fungi *Thelebolus* sp. IITKGP-BT12 isolated from Antarctica, produced EPS made up of glucan, having antiproliferative activity in cancer cells (Mukhopadhyay et al. 2014).

10.4.7 Pigment/Lipid Production

In the presence of low temperatures, fungi produce elevated concentrations of pigments and lipids. This rise in pigment or lipid content in the psychrophilic and psychrotolerant fungi is due to the synthesis of lipids like fatty acids and polyunsaturated triglycerides (Weinstein et al. 2000). These observations are supported by similar studies wherein increased amounts of carotenoid pigments and fatty acids (linoleic, stearic, linolenic, myristic, heptadecanoic, and palmitic acid) were seen in a cold-tolerant fungi *Thelebolus microspores* (Singh et al. 2014). Castrillo et al. (2018) similarly reported the synthesis of carotenoids by *Neurospora crassa*, when exposed to cold conditions. Carotenoids have application in the pharmaceutical industry as photoprotectors, incorporated in sunscreens and ointments used for protection from UV radiations. Likewise, mycosporin-derived molecules are of biotechnological interest due to their UV-absorbing properties (Volkmann et al. 2003).

Production of carotenoids and mycosporines by the number of psychrophilic yeast isolated from different sources from Antarctica, after exposure to UV radiations, has been observed by Libkind et al. (2009) and Vaz et al. (2011). The producers strain belonged to genera *Dioszegia*, *Cryptococcus*, *Exophiala*, *Microglossum*, and *Rhodotorula* genera.

10.4.8 Anti-allergic Compounds

There is a report of the production of the novel anti-allergic compounds from psychrophilic fungi. The marine isolates *Penicillium granulatum* MCCC 3A00475 from Prydz Bay, Antarctica was found to produce spirograterpene, a tetra-diterpene. This compound showed anti-IgE activity in rat mast cells (Niu et al. 2017).

10.5 Applications of Secondary Metabolites

Bioactive secondary metabolites of psychrophilic fungi have attracted a lot of attention due to their application in biotechnological and pharmaceutical fields. With new psychrophilic species being discovered and researched, bioprospecting of the fungal psychrophiles is in limelight. Some of the applications are discussed below:

10.5.1 Agriculture

The psychrophilic fungi having antibacterial, antifungal, anti-algal activities can be used against plant pathogens and pests. Some secondary metabolites having herbicidal activities as well as plant growth-promoting activities can be used to improve agriculture. *Pseudogymnoascus destructans* and *Penicillium tardochrysogenum* extracts showed strong and selective herbicidal activity against *Allium schoenoprasum* and *Lactuca sativa* (Gomes et al. 2018).

10.5.2 Medical and Pharmaceutical Applications

There is a sudden rise in the number of secondary metabolites reported from psychrophilic microorganisms in general and psychrophilic fungi in particular. Fungi are reported to produce pharmaceutical products (Schulz et al. 2002) but the recovery of such bioactive metabolites from fungi of cold regions is quite rare. The number of species of genera *Penicillium* itself is reported by the number of authors. Frisvad et al. (2006) reported the synthesis of cycloaspeptide A and griseofulvin by *Penicillium lanosum*, *P. soppii*, and *P. jamesonlandense* while *Penicillium ribium* was found to produce the metabolite, cyclic nitropeptide psychrophilin A (Dalsgaard et al. 2004a; Frisvad et al. 2006), whereas *Penicillium rivulorum* synthesized communesin G and H and psychrophilin B and C (Dalsgaard et al. 2004b, 2005a). Yet another species, *Penicillium algidum*, produced cycloaspeptide A and D and psychrophilin D (Dalsgaard et al. 2005b). All these cyclic peptides produced by the psychrophilic fungi showed bioactive properties, including antimalarial, insecticidal, and so on (Dalsgaard et al. 2005b; Lewer et al. 2006).

Some endophytic psychrophilic fungi namely were isolated *Phoma* sp., *P. herbarum*, and *Dothideomycetes* sp. having antifungal and antibacterial activity were isolated by Moghaddam and Soltani (2014). Psychrophilic fungi having antimicrobial potential were isolated from King George Island, Antarctic, and Svalbard as reported by Yogabaanu et al. (2017). Marinelli et al. (2004) and Rojas et al. (2009) have done documentation of the bioactive secondary metabolites of psychrophilic fungi of Antarctica. Table 10.4 gives a summary of the secondary metabolites produced by psychrophilic fungi along with their activity.

10.6 Conclusion and Future Prospects

With the research being focused nowadays on psychrophilic organisms, there is scope for the discovery of novel metabolites with biotechnological, medical, and industrial applications. The spectrum of bioactive compounds isolated and analyzed from psychrophilic fungi is fast broadening. Fungi from extreme environments,

Table 10.4 Secondary metabolites produced by psychrophilic fungi with their bioactivity

Psychrophilic fungi	Compound name	Application	References
Chaetomium sp.	Depsipeptide, chaetomiamide, diketopiperazines	Anticancer and cytotoxic activity	Wang et al. (2017)
Penicillium algidum	Cyclic nitropeptide, psychrophilin D; cyclic peptides, cycloaspeptide A, and cycloaspeptide D	Murine leukemia cell; anti-*Plasmodium falciparum*	Dalsgaard et al. (2005a, b)
Eutypella sp. D-1	Cytochalasins Z24, Z25, Z26; scoparasin B	Cytotoxicity toward human breast cancer MCF-7 cell line	Liu et al. (2014), Lu et al. (2014)
	Eutypenoids A–C	Immunosuppressive activities	Zhang et al. (2016)
Lindgomycetaceae strains	Lindgomycin; ascosetin	Antibiotic activities	Wu et al. (2015)
Trichoderma polysporum strain OPU1571	Novel compounds	Antifungal towards *Pythium iwayamai*	Kamo et al. (2016)
Geomyces sp.	Asterric acid; geomycins A–C	Antibacterial and antifungal	Li et al. (2008)
Trichoderma asperellum	Asperelines A–Z13	Antifungal and antibacterial	Ren et al. (2009, 2013)
Oidiodendron truncatum GW3-13	Epipolythiodioxopiperazines, diketopiperazines	Cytotoxicity to human cancer lines	Li et al. (2012b)
Penicillium sp. PR19N-1	Sesquiterpenes; eremofortine; eremophilane	Cytotoxic activity against HL-60 and A549 cancer cell lines	Wu et al. (2013), Lin et al. (2014)
Penicillium funiculosum GWT2-24	Chrodrimanins	Inhibitory activities against influenza virus A (H1N1)	Zhou et al. (2015)
Aspergillus ochraceopetaliformis SCSIO 05702	Ochraceopones A–E	Antiviral activities against the H1N1 and H3N2 influenza viruses	Wang et al. (2016)
Penicillium nalgiovense Laxa	Amphotericin B	Antifungal, antibacterial	Svahn et al. (2015)
Mrakia frigida	Toxin	Anti yeast	Hua et al. (2010), Liu et al. (2012)
Pseudogymnoascus sp.	Asterric acid derivatives	Antimicrobial activity	Henríquez et al. (2014), Figueroa et al. (2015)
Penicillium chrysogenum	*bis*-Anthraquinone (rugulosin and skyrin)	Insecticide and medicine	Parker et al. (2000), Sumarah et al. (2005)

(continued)

Table 10.4 (continued)

Psychrophilic fungi	Compound name	Application	References
Penicillium sp. PR19N-1	Chloro-trinoreremophilane sesquiterpene, eremophilane sesquiterpenes, eremofortine	Cytotoxic activity against cancer cell lines	Wu et al. (2013)
Penicillium tardochrysogenum	Penicillin, secalonic acids D and F	–	Houbraken et al. (2012)
Ophiocordyceps sinensis		Cancer, impotence, and fatigue	Chen et al. (2010), Lo et al. (2013), Stone (2008), Zhang et al. (2012)

including those living in Antarctica, may have developed specific metabolic pathways to produce singular natural products with bioactive properties. For this reason, these fungi represent potential sources of pharmaceutical molecules. Extracts obtained from fungi isolated in different Antarctic environments have shown promising antimicrobial, cytotoxic, antiparasitic, and antiviral activities. On the other hand, several pure compounds isolated from Antarctic fungal extracts show new carbon frameworks or unusual structural features, indicating that these fungi would be good sources of new chemical compounds.

This review provides a baseline or food for thought regarding the exploitation of cold-adapted fungi and their metabolites for biotechnology and industrial uses. Adaptive mechanisms of low-temperature fungi need to be investigated further, on a molecular and genetic basis. Two of the most important avenues are pharmaceuticals and replacing synthetic compounds with bio-based or biologically synthesized metabolites for use in industry and biotechnology. These fungi represent potential biological "factories" that can produce compounds with great potential for direct use in medicine and agriculture or as prototypical molecules that can be chemically modified for pharmaceutical and agrochemical applications.

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