



RESEARCH ARTICLE

HIGHLIGHTS ON AQUATIC FUNGI AND MUSHROOMS ECOLOGY AND BIOTECHNOLOGY, WITH DESCRIPTION OF THE RARELY ISOLATED AQUATIC MUSHROOM *PSATHYRELLA AQUATIC* AS A NOVEL TAXON

Waill Elkhateeb^{1*}, Paul Thomas^{2,3}, Abdel-Nasser Zohri⁴, Ghoson Daba¹, Xiu-Hong Xu⁷ and Ting-Chi Wen^{5,6,7}

¹Chemistry of Natural and Microbial Products Department, Pharmaceutical Industries Division, National Research Centre, Dokki, Giza, 12622, Egypt

²University of Stirling, Stirling, UK; ³Mycorrhizal Systems Ltd, Lancashire, UK

⁴Department of Botany and Microbiology, Faculty of Science, Assiut University, Assiut, Egypt

⁵State Key Laboratory Breeding Base of Green Pesticide and Agricultural Bioengineering, Key Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China

⁶The Engineering Research Center of Southwest Bio-Pharmaceutical Resources Ministry of Education, Guizhou University, Guiyang 550025, Guizhou Province, China

⁷The Mushroom Research Centre, Guizhou University, Guiyang 550025, China

ARTICLE INFO

Article History:

Received 19th February, 2021

Received in revised form

17th March, 2021

Accepted 29th April, 2021

Published online 20th May, 2021

Keywords:

Agaricales, Aquatic Fungi, Biotechnology, Secondary Metabolites, Psathyrellaceae, *Psathyrella Aquatic*.

ABSTRACT

Mushrooms are macrofungi that exist everywhere around us. They have significant roles in human life as source of nutrition and bioactive compounds. Many aquatic isolated fungi and mushrooms have been reported as promising biotechnological tools for production of secondary metabolites of various biologically activities. Recently, *Psathyrella aquatica* has been discovered in Rogue River, Oregon, United States. *Psathyrella aquatica* represents a novel taxon within the family Psathyrellaceae in the large polyphyletic genus *Psathyrella*, and is considered as the only reported aquatic gilled mushroom till now. Aquatic gilled mushrooms are especially interesting due to the rareness of Basidiomycetes that can grow underwater. In this review, the ecology, occurrence, of unique aquatic gilled mushrooms are described, and available information about the novel mushroom *P. aquatica* was highlighted.

INTRODUCTION

Fungi have a truly global distribution and can be found across the whole terrestrial biosphere, from both polar and hot deserts, to tropical rainforests and estuarine environments. The majority of described fungi inhabit the land (terrestrial) environments, but several fungal species live only in aquatic habitats. The majority of fungi have a saprobic lifestyle and live in either soil or dead organic matter, but many are symbionts of plants, animals, or other fungi, and all fungi have a key role in ecosystem functioning (Elkhateeb and Daba, 2018). Fungi, along with bacteria that are found in soil, are the primary decomposers of organic matter in terrestrial ecosystems.

*Corresponding author: Waill Elkhateeb,

Chemistry of Natural and Microbial Products Department, Pharmaceutical Industries Division, National Research Centre, Dokki, Giza, 12622, Egypt.

The decomposition of dead organisms is a crucial component of ecosystem functioning, returning nutrients to the soil and to the environment (Elkhateeb and Daba, 2018; Elkhateeb, 2005; Shearer *et al.*, 2007; Zohri *et al.* 2014; Elkhateeb *et al.*, 2016). However, fungi may have aquatic origins and indeed the earliest evidence for any fungi have been found in Canada, in strata representing estuarine environments and dated to 1–0.9-billion years old. These earliest microfossils have been assigned to the species *Ourasphaira giraldae* and suggest an occurrence in estuarine settings although the fungus may also have been transported from land or deeper marine environments (Loron *et al.* 2019). Today, marine fungi appear ubiquitous and have been found in almost every habitat that has been checked: from hydrothermal vents to deep sea sediments and arctic sea ice (Gladfelter *et al.* 2019). Marine fungi even infect primary producers, such as diatoms, and may be an important component of the global carbon cycle. Perhaps as little of 1% of marine fungi have been identified but of these (aside from yeasts), many marine fungal species belong to

Ascomycotina, Basidiomycotina, Mastigomycotina (zoosporic fungi), Deuteromycotina, and some Zygomycotina (Kohlmeyer, 1984; Richards *et al.* 2012; Kohlmeyer and Kohlmeyer, 2013; Gladfelter *et al.* 2019). Whether many marine fungi are truly amphibious is an unanswered question and indeed, many fungi can be found in habitats both above and below the high tide line. However there is evidence for, and an expectation that, some species may exist in water for their whole life-cycle, during a single stage of their life-cycle, or as a truly amphibious (Amend *et al.* 2019; Grossart *et al.* 2019). Indeed some fungi, identified as marine through detection of DNA, may actually be terrestrial and have arrived in an aquatic environment by wind or by flood water (Dix and Webster, 1995). In this review, an overview about mushrooms, aquatic fungi in general, and aquatic mushrooms in particular are detailed, and the ecology and occurrence of the unique rarely isolated aquatic gilled mushrooms are highlighted.

Mushrooms: Mushrooms are the epigeous fruiting bodies of terrestrial fungi and as they lack cellulose and chlorophyll, they have a different lifestyle to other nonmotile life, such as plants. The inability to produce sugars through photosynthesis, creates a dependency on other plants or animals, either live or deceased, for the acquisition of nutrition. We usually only see a the above-ground parts of mushrooms –often likened to the shape of a tree or umbrella, although fruiting structures come in a whole plethora of shapes, colours and sizes. The most famous mushroom shape is an umbrella-like structure appearing as a stem (stipe), carrying above it a cap (pileus), which carry the mushroom spores (Sridhar, 2020). The bulk of the fungi that gives rise to the mushroom is often dispersed over a relatively large area. Mushroom producing fungi belong to Basidiomycetes and Ascomycetes, including edible and non-edible species, and some mushroom fruiting body produces basidiospores at the tip of club like structures called basidia, which are arranged along the gills of the mushroom (Elkhateeb *et al.* 2019a; Elkhateeb, 2020; Elkhateeb and Daba, 2020; Kamalakannan *et al.* 2020). Mushrooms have been documented for centuries as use as food and medicine as they are generous sources of nutrients and biologically-active compounds that have various applications in agriculture, food, pharmaceuticals, cosmetics, and food-related industries, amongst others (Cheung, 2010; Ali El-Hagrassi *et al.* 2020; Daba *et al.* 2020). Mushrooms obtain their nutrition through being saprotrophs, parasites, or symbionts such as mycorrhiza. Mushrooms are the reproductive phase (fruiting bodies) but they there is also a vegetative phase to these fungi (mycelia). Edible mushrooms are often low in calories and can be healthy sources of proteins, flavonoids, metals, amino acids, minerals, volatile oils, carotenoids fats, phenolic compounds, and different vitamins and ergosterol that can be used as a source for vitamin D2 (Hobbs, 2002; Rathee *et al.* 2012; Ma *et al.* 2013; Xu and Beelman, 2015). Moreover, mushrooms have a long history of safe use in traditional Asian medicine for the treatment of different diseases (Halpern, 2007; Rahi and Malik, 2016; Elkhateeb *et al.* 2019b; Elkhateeb *et al.* 2020). Mushroom production is often observed as land-efficient and does not require high-value agricultural land and can be done on waste and unproductive land. Utilizing indoor cultivation methods, one can exploit vertical space for higher productivity. Agricultural/forest waste can be used as a substrate to produce quality food through mushroom production. Their legendary effects on promoting good health and vitality and increasing our body's adaptive abilities have been supported by recent studies.

The diversity of compounds extracted from mushrooms has attracted attention as a mine for novel compounds. Some compounds they contain have been classified as Host Defence Potentiators (HDP) which can have immune system enhancement properties (De Silva *et al.* 2013; Kamalakannan *et al.* 2020). Various compounds are responsible for different therapeutic activities of many mushrooms genera. Various biological activities have been reported such as anticancer, anti-inflammatory, hypoglycemic, antimicrobial, antioxidant, immunomodulatory, antiviral, hepatoprotective, anti-neurodegenerative, antiangiogenic, and hypocholesterolemic activities (Choi *et al.* 2010; Patel and Goyal, 2012; Sánchez, 2017; Elkhateeb *et al.* 2018).

Aquatic fungi: Freshwater fungi are commonly represented in genera belonging to Oomycota and Chytridiomycota, in addition to the anamorphic forms of some Ascomycota and Basidiomycota (aquatic hyphomycetes) (Shearer *et al.* 2007; Shearer *et al.* 2004). Aquatic fungi are microscopic organisms with mostly mycelial growth and hyphae developing on or within the, typically submerged, organic substrates of plant or animal origin. Aquatic fungi are able to complete their whole life cycle in freshwater and often have special adaptations for growth, sporulation, and dispersal in aquatic environments (Manoharachary *et al.* 2005). Hyde *et al.*, (2007) have estimated that there are approximately 1.5 million fungal species on earth. Of these, only around 3000 species are known to be associated with aquatic habitats and only 465 species occur in marine waters. However, perhaps less than 1% of aquatic fungi have yet been discovered. Aquatic fungi are usually microscopic organisms, which usually do not produce visible fruiting bodies but grow asexually (anamorphic fungi) (Ali and Abdel-Raheem, 2003; Gulis *et al.* 2009).

Aquatic fungi play key roles in aquatic ecosystems and in transition zones these may be similar to terrestrial fungi, such as nutrient cycling and the degradation of organic compounds alongside symbiotic associations with semi-aquatic plants. Elsewhere, from coral reefs to deep sea sediments, the function is less well understood but certainly fungi in these habitats have numerous and complex roles from the degradation of organic compounds to pathological associations with a range of organisms from mammals to algae. In the latter example, this pathogenesis may be a critical component of nutrient cycling within marine habitats (Gladfelter *et al.* 2019). Of topical interest is the fact that marine fungi may also represent a source for novel secondary metabolites of specific medical, industrial, or agricultural interest. Although most interest is focused around the identification of novel antibiotic or anticancer compounds, these fungi also appear to have the potential to contribute to bioremediation of different forms of pollutants in wastewaters and potentially even in the degradation of plastics which has the potential to address some of the greatest issues in the earth's oceans (Zhang *et al.* 2015; Kan *et al.* 2015). Definitely fungi represent an important component of aquatic microbiota. Microbial ecologists are just starting to understand the contributions of aquatic fungi to biodiversity, ecosystem functions and services but there is much that remains unexplored (Baerlocher and Boddy, 2016). Marine fungi can exist on sand grains, plankton, algae, sediments, plastisphere, and as mentioned before on estuarine plants and submerged wood (Kohlmeyer and Kohlmeyer, 1979; Jones, 2011; Overy *et al.* 2019). The submerged wood is usually a favourable environment for the growth of genera belonging to the family Halosphaeriaceae, and orders

Torpedosporales, and Lulworthiales exclusively in open oceans areas (Jones, 1995). Generally, marine fungi have developed several adaptation mechanisms to protect and succeed in dispersing their spores in such environment. One of the strategies is the absence of the central long necks in the ascospores of arenicolous marine fungi. Also, the ascospores are usually found trapped in sea foam. On the other hand, ascospores growing on submerged wood are found partly or completely immersed within the substrata (Kohlmeyer and Kohlmeyer, 1979). Furthermore, many ascomycotal fungi release their spores during low tide periods, which rest on the ascospores and become washed off into the water at the period of high tide. The produced ascospores are often with gelatinous sheaths (Dothideomycetes), appendages (Sordariomycetes), or, in some species, both to assist in attaching the spores to substrata (Jones, 2011). Similarly, ways of adaptation applied on some conidia (asexual spores) include being branched, ornamented, or extremely long in size in order to help in floatation and dispersal (Overy *et al.* 2014a). It should be noted that aquatic fungi represent a generous source for natural products existing mostly in their secondary metabolites. Genome mining was used to reveal the biosynthetic potentials of many marine members of ascomycetes, basidiomycetes, and Zoopagomycetes, and as a result they were nominated as rich sources of secondary metabolite (Arvas *et al.* 2007; Lackner *et al.* 2012).

Aquatic fungi as biotechnological tools for production of bioactive compounds: Till 2002, about 272 compounds originated from marine fungi were discovered, and characterized (Bugni and Ireland 2004; Overy *et al.* 2014b). After that, a dramatic increase in the number of discovered natural compounds took place to record over 1000 novel secondary metabolites, thanks to the development of extraction and identification techniques (Rateb and Ebel, 2011). Some of the natural compounds originated from marine ascomycetous fungi are aigialomycins A–G, aigialospirol and associated derivatives, and aigialone produced by an isolate of *Aigialus parvus* (Kohlmeyer *et al.* 1985; Alias *et al.* 1995; Tan *et al.* 1995; Isaka *et al.* 2002; Vongvilai *et al.* 2004; Isaka *et al.* 2009). Similarly, three new lipodepsipeptides, five new macrocyclic polyethers, and five new linear polyesters were produced by the marine ascomycete, *Halorosellinia oceanica* (syn. *Hypoxylon oceanicum*) (Abbanat *et al.* 1998). *Alternaria alternata* isolated from the soft coral *Litophyton arboreum* tissues was the source of 5 novel secondary metabolites (alternariol9methyl ether 3O sulphate, alternariol9methyl ether, alternariol, maculosin and maculosin5). Moreover, such compounds showed promising natural antimicrobial and anticancer activities besides a potent inhibitory effect against HCV NS3NS4A protease (Hawas *et al.* 2015; Hawas *et al.* 2016).

Zofimarin, the potent antifungal sordarin derivative was produced by an isolate of the marine fungus *Zopfiella marina* (Ogita *et al.* 1987; Konda *et al.* 1987). Recently, analogs and sordarin-inspired scaffolds are under in vivo investigations for their effectiveness against wide spectrum of susceptible pathogens (Chakraborty *et al.* 2016; Wu and Dockendorff, 2018). On the other hand, *Aspergillus versicolor* XZ-4 isolated from a Taiwan hydrothermal vent crab was the source of different metabolites as versicomides A–D, and the cyclopenin derivatives: 7-methoxycyclopeptin, 7-methoxydehydrocyclopeptin, 7-methoxycyclopenin, and 9-hydroxy-3-methoxyviridicatin (Pan *et al.* 2017).

The marine fungus, *Phaeosphaeria spartinae* isolated from the inner tissues of the marine alga, *Ceramium* sp., produced eight novel natural products including spartinolide and spartinol C, which showed inhibition action on the human leukocyte elastase, and cystic fibrosis (Elsebai *et al.* 2009; Elsebai *et al.* 2010). Marine *Aspergilli* were reported as promising sources of biologically active metabolites. Preussins C–K produced by *Aspergillus flocculosus* 16D-1 showed antiinflammatory activity against Interleukin 16 (IL-16) (Gu *et al.* 2018). *Aspergillus versicolor* exhibited activity against Inducible nitric oxide synthase (Li *et al.* 2018). Luteoride E; Lovastatin; Versicolactone G; Territrem A; Brasilanone A; Brasilanone E; and Methyl 3,4,5-trimethoxy-2-(2-(nicotinamido)benzamido)benzoate produced individually by two different *A. terreus* marine isolate exerted activity against NO (Liu *et al.* 2018; Wu *et al.* 2018). Moreover, several antiinflammatory compounds were identified from different *Aspergillus* Sp. such as Dihydrobipolaroxins B–D; Dihydrobipolaroxin; Aspertetranones A–D; Diorcinol; Cordyol C; and 3,7-dihydroxy-1,9-Dimethyldibenzofuran (Wang *et al.* 2015; Tian *et al.* 2015; Wang *et al.* 2016). Similarly, many marine originated species belonging to the genus *Penicillium* showed produced various compounds having promising biological activities such as methylpenicillinolone; Citrinin H1; Penicillinolide A; Penstyrylpyrone; Chrysamide C; Viridicaol; Brevicompanines E and F (Lee *et al.* 2013a; Lee *et al.* 2013b; Chen *et al.*, 2016; Ngan *et al.*, 2017). Different other marine fungi were reported as producers of bioactive compounds including for example *Eurotium* Sp.; *Graphostroma* Sp.; *Chondrostereum* Sp.; *Hypocreales* Sp.; *Phoma* Sp.; *Acremonium* Sp.; and *Alternaria* Sp. (Belofsky *et al.* 2000; Kyoung-Su *et al.* 2013; Hong *et al.* 2013; Chen *et al.* 2015; Ko *et al.* 2016; Hsiao *et al.* 2017; Niu *et al.* 2018).

Aquatic gilled mushrooms as example of adaptation to the aquatic environment: Previously it has been observed that some aquatic ascomycetous fungi can form fruiting bodies on submerged wood and this has been noted in freshwater systems in Japan, Thailand and Costa Rica (Minoura and Muroi 1978, Pinruan *et al.* 2004, Ferrer *et al.* 2008). However, a recently discovered species of aquatic gilled mushrooms known as *Psathyrella aquatica* (Fig. 1), was described in the mid-2000s and one of only a few known aquatic gilled fungi. The discovery is traced back to 2005, when researchers from Southern Oregon University, stumbled upon the mushrooms in the Rogue River, by chance. The appearance of a submerged and gilled basidiomycetes, was unexpected and it appears that this structure in an aquatic environment is quite rare. The majority of underwater fungal species are members of Ascomycetes or Hypomycetes. The fruiting bodies of *P. aquatica* were found underwater and are usually growing on wood as a substrate, existing submerged in the water rather than the substrate of the water bed (Frank *et al.* 2010). The aquatic gilled mushrooms from southern Oregon appear to represent a novel taxon within the Psathyrellaceae in the large polyphyletic genus *Psathyrella* (Padamsee *et al.* 2008). Other Ascomycota fruit on submerged wood in lakes in Japan, Thailand and Costa Rica (Pinruan *et al.* 2004; Ferrer *et al.* 2008). However, *P. aquatica* is not the only species to form mushroom-like fruiting structures underwater. Another basidiomycete, this time with a smooth hymenium, *Gloiocephala aquatica* Desjardin, Martinez-Peck & Rajchenberg, that forms submerged basidiocarps has been reported from lakes and ponds in southern Argentina

(Desjardin *et al.* 1995). Basidiocarps of 11 species of homobasidiomycetes occur in marine ecosystems (Hibbett and Binder, 2001; Larsson and Örstadius, 2008; Jones, 2000).

***Psathyrella aquatica* (Frank *et al.* 2010) as a novel aquatic gilled mushroom taxon:** The precise description of that *Psathyrella aquatica* was having basidiomata 4.5–10 cm alta, immersa. Pileus 0.8–1.5 cm latus, brunneolus vel brunneigriseus. Basidiopora ellipsoideae, leves, brunneae, 10–14 × 6–8 μm, poro germinali. Cystidia hymeniales: cheilocystidia pleurocystidiaque similia, ventricosa, 25–45 × 10–18 μm. Lamellae adnatae. Stipes textura porrecta.

***Psathyrella aquatica* macromorphology:** Basidiomata immersed, 4.5–10 cm tall; pileus 0.8–1.5 cm diam, broadly parabolic to campanulate, light brown to brownish gray, sometimes with central orange-brown disk, sometimes mottled or striate, smooth, hygrophanous; pileus context thin above gills, light tan to orange-brown; odor not distinctive; lamellae adnate, thin, light tan, densely speckled with dark brown spores, extending to pileus margin, lamellulae in two ranks and extending from one-half to one-fourth of the radius; stipe 4.0–9.5 cm long, diameter expanding from 1.0–2.2 mm at apex to 1.8–3.2 mm at base, white to pale yellow, hollow, lacking annulus, fibrous, surface fibrillose covered with wefty white to gray-white mycelium, and with cottony rhizomorphs and mycelial tomentum emanating from base.



Fig. 1. *Psathyrella aquatica* taken by Jonathan Frank, Locality, Jackson, upper Rogue river, Oregon, United States, hosted by <http://mycoportal.org>

***Psathyrella aquatica* micromorphology:** Basidiospores 10–14 × 6–8 μm, ave. 12.3 × 6.9 μm, elliptical with a germ pore, smooth, dark reddish brown in water and in Melzer's, fading to gray-brown in KOH and to lilac in H₂SO₄, spore print purple-black; basidia 4-spored, clavate, 32–40 × 10–13 μm, hyaline; cheilocystidia 25–45 × 10–18 μm ventricose, apex subacute to elongate, thin walled, colourless, hyaline; pleurocystidia 25–40 × 10–13 μm, ventricose, apex subacute, scattered, thin-walled, colourless, hyaline; caulocystidia 32–40 × 10–13 μm, cylindrical to ventricose, in fascicles, apex obtuse; pileipellis

cellular, suprapellis a single layer of spherical to isodiametric, inflated cells, 25–35 μm diam, on 30–50 × 3–5 μm peduncles that extend into the pileus trama, clamp connections absent; pileus trama thin-walled hyphae 8–15 μm diam, interwoven; stipe hyphae 35–70 × 8–14 μm, parallel; clamp connections present in mycelium at stipe base, absent elsewhere. Because the mycelium of *Psathyrella aquatica* inhabits river substrates, the fruiting body of the mushroom is fully submerged under the water. This leads scientists to speculate about how the spores of this underwater mushroom are dispersed.

Conclusion

Fungi are found everywhere on earth where there exists a carbon and water source. From ancient caves, to polar deserts, tropical rainforests, and also in saline and freshwater aquatic environments. Discovering rare mushrooms in unusual environments such as saline habitats can change our ideas about the capabilities of fungi to withstand and exist in different systems and under different pressure. Moreover, such rarely isolated mushrooms can represent unique sources for novel metabolites that may contribute in treatment of currently untreated diseases or have other promising applications that help in serving humanity.

ACKNOWLEDGEMENTS

This work was supported by the Science and Technology Foundations of Guizhou Province (No. (2019)2451-3, No. (2018)2323 & No. (2019)2451-4).

Conflict of Interest: Authors declare there is no conflict of interest.

REFERENCES

- Abbanat D, Leighton M, Maiese W, Jones E, Pearce C, Greenstein M. 1998. Cell wall active antifungal compounds produced by the marine fungus *Hypoxylon oceanicum* LL-15G256. *J. Antibiot.*, 51: 296–302.
- Ali EH, Abdel-Raheem A. 2003. Distribution of zoosporic fungi in the mud of major Egyptian lakes. *J Basic Microbiol.*, 43(3): 175–184.
- Ali El-Hagrassi A, Daba G, Elkhateeb W, Ahmed E, Negm El-Dein A, Fayad W, Shaheen M, Shehata R, El-Manaway M, Wen T-C. 2020. In vitro bioactive potential and chemical analysis of the n-hexane extract of the medicinal mushroom, *Cordyceps militaris*. *Malaysian J Microbiol.*, 16(1): 40–48.
- Alias SA, Kuthubutheen AJ, Jones EB. 1995. Frequency of occurrence of fungi on wood in Malaysian mangroves. In *Asia-Pacific Symposium on Mangrove Ecosystems* (pp. 97–106). Springer, Dordrecht.
- Amend A, Burgaud G, Cunliffe M, Edgcomb VP, Ettinger CL, Gutiérrez MH, Heitman J, Hom EF, Ianiri G, Jones AC, Kagami M. 2019. Fungi in the marine environment: Open questions and unsolved problems. *MBio.*, 10(2): 1–15.
- Arvas M, Kivioja T, Mitchell A, Saloheimo M, Ussery D, Penttila M, Oliver S. 2007. Comparison of protein coding gene contents of the fungal phyla Pezizomycotina and Saccharomycotina. *BMC genomics*, 8(1): 325.
- Ba'rlocher F, Boddy L. 2016. Aquatic fungal ecology — How does it differ from terrestrial? *Fungal Ecol*; 19: 5–13.
- Belofsky GN, Anguera M, Jensen PR, Fenical W, Kock M. 2000. Oxepinamides A-C and Fumiquinazolines H-I: Bioactive metabolites from a marine isolate of a fungus of the genus *Acremonium*. *Chem. A Eur. J.*, 6: 1355–1360.
- Bugni T, Ireland C. 2004. Marine-derived fungi: a chemically and biologically diverse group of microorganisms. *Nat Prod Rep.*, 21: 143–163.
- Chakraborty B, Sejal NV, Payghan PV, Ghoshal N, Sengupta J. 2016. Structure-based designing of sordarin derivative as potential fungicide with pan-fungal activity. *J Mol Graph Model.*, 66: 133–142.

- Chen C, Zhou Y, Liu X, Zhang W, Hu S, Lin LP, Huo G, Jiao R, Tan R, Ge H. 2015. Antimicrobial and anti-inflammatory compounds from a marine fungus *Pleosporales* sp. *Tetrahedron Lett.* 56: 6183–6189.
- Chen S, Wang J, Lin X, Zhao B, Wei X, Li G, Kaliaperumal K, Liao S, Yang B, Zhou X. 2016. Chrysamides A-C, three dimeric nitrophenyl trans-epoxyamides produced by the deep-sea-derived fungus *Penicillium chrysogenum* SCSIO41001. *Cheminform*, 18: 3650–3653.
- Cheung PC. 2010. The nutritional and health benefits of mushrooms. *Nut Bull.*, 35(4): 292-299.
- Choi SY, Hur SJ, An CS, Jeon YH, Jeoung YJ, Bak JP, Lim BO. 2010. Anti-inflammatory effects of *Inonotus obliquus* in colitis induced by dextran sodium sulfate. *BioMed Res Inter.*, Article ID 943516, 1-5.
- Daba G, Elkhateeb W, EL-Dien AN, Fadl E, Elhagrasi A, Fayad W, Wen TC. 2020. Therapeutic potentials of n-hexane extracts of the three medicinal mushrooms regarding their anti-colon cancer, antioxidant, and hypocholesterolemic capabilities. *Biodiversitas J Biol Divers.*, 21(6): 2437-2445.
- De Silva D, Rapior S, Sudarman E, Stadler M, Jianchu XU, Aisyah A, Kevin D. 2013. Bioactive metabolites from macrofungi: ethnopharmacology, biological activities and chemistry. *Fungal Div.*, 62: 1–40.
- Desjardin DE, Martinez Peck L, Rajchenberg M. 1995. An unusual psychrophilic aquatic agaric from Argentina. *Mycol.*, 87: 547–550.
- Dix NJ, Webster J. 1995. Aquatic Fungi. *Fungal Ecol.*, 225–283.
- Dong-Cheol K, Hee-Suk L, Wonmin K, Dong-Sung L, Jae S, Joung Y, Youn-Chul K, Hyuncheol O. 2014. Anti-Inflammatory effect of methylpenicillinolone from a marine isolate of *Penicillium* sp. (SF-5995): inhibition of NF- B and MAPK pathways in lipopolysaccharide-induced RAW264.7 macrophages and BV2 microglia. *Molecul.*, 19: 18073.
- Elkhateeb WA, Daba GM, Elnahas MO, Thomas PW. 2019b. *Fomitopsis officinalis* mushroom: ancient gold mine of functional components and biological activities for modern medicine. *Egyptian Pharma J.*, 18(4): 285-289.
- Elkhateeb WA, Daba GM, Wen TC, Thomas PW. 2019a. Medicinal mushrooms as a new source of natural therapeutic bioactive compounds. *Egyptian pharma J.*, 18(2): 88-101.
- Elkhateeb WA, Daba GM. 2018. Where to Find? A Report for Some Terrestrial Fungal Isolates, and Selected Applications Using Fungal Secondary Metabolites. *Biomed J Sci Technol Res.*, 4(4): 1-4.
- Elkhateeb WA, Daba GM. 2020. Termitomyces Marvel Medicinal Mushroom Having a Unique Life Cycle. *Open Acc J Pharma Res.*, 4(1): 1-4.
- Elkhateeb WA, Elnahas MO, Thomas PW, Daba GM. 2020. *Trametes Versicolor* and *Dictyophora Indusiata* Champions of Medicinal Mushrooms. *Open Acc J Pharma Res.*, 4(1): 1-7.
- Elkhateeb WA, Zaghlol GM, El-Garawani IM, Ahmed EF, Rateb ME, Moneim AE. 2018. *Ganoderma applanatum* secondary metabolites induced apoptosis through different pathways: in vivo and in vitro anticancer studies. *Biomed Pharmacol.*, 101: 264–277.
- Elkhateeb WA, Zohri AA, Mazen M, Hashem M, Daba GM. 2016. Investigation of diversity of endophytic, phylloplane and phyllosphere mycobiota isolated from different cultivated plants in new reclaimed soil, Upper Egypt with potential biological applications. *Inter J MediPharm Res.*, 2(1): 23-31.
- Elkhateeb WA. 2005. Some mycological, phytopathological and physiological studies on mycobiota of selected newly reclaimed soils in Assiut governorate, Egypt (master thesis). Assiut, Egypt: Faculty of Science, Assiut University (Doctoral dissertation) 2005.
- Elkhateeb WA. 2020. What Medicinal Mushroom Can Do? *Chem Res J.*, 5(1): 106-118.
- Elsebai M, Kehraus S, Gütschow M, Koenig GM. 2010. Spartinoxide, a new enantiomer of A82775C with inhibitory activity toward HLE from the marine-derived fungus *Phaeosphaeria spartinae*. *Nat. Prod. Commun.*, 5: 1071–1076.
- Elsebai MF, Kehraus S, Gütschow M, Koenig GM. 2009. New polyketides from the marine-derived fungus *Phaeosphaeria spartinae*. *Nat. Prod. Commun.*, 4: 1463–1468.
- Ferrer A, Huzefa AR, Shearer CA. 2008. *Lucidascocharpa pulchella*, a new ascomycete genus and species from freshwater habitats in the American tropics. *Mycol.*, 100(4): 642–646.
- Frank JL, Coffan RA, Southworth D. 2010. Aquatic gilled mushrooms: *Psathyrella* fruiting in the Rogue River in southern Oregon. *Mycol.*, 102(1): 93-107.
- Gladfelter AS, James TY, Amend AS. 2019. Marine fungi. *Curr Biol.*, 29(6): R191-R195.
- Grossart HP, Van den Wyngaert S, Kagami M, Wurzbacher C, Cunliffe M, Rojas-Jimenez, K. 2019. Fungi in aquatic ecosystems. *Nat Rev Microbiol.*, 17(6): 339-354.
- Gu B, Jiao F, Wu W, Jiao W, Li L, Sun F, Wang S, Yang F, Lin H. 2018. Preussins with inhibition of IL-6 expression from *Aspergillus flocculosus* 16D-1, a fungus isolated from the marine sponge *Phakellia fusca*. *J. Nat. Prod.*, 81: 2275–2281.
- Gulis V, Kuehn K, Suberkropp K. 2009. Fungi. *Encyclopedia of Inland Waters*, (Pages 233-243).
- Halpern G. 2007. Healing mushrooms. Garden City Park, New York, USA: Square One Publishers Inc., (pp. 1-194).
- Hawas U, El-Desouky S, Abou El-Kassem L, Elkhateeb W. 2015. Alternariol Derivatives from *Alternaria alternata*, an Endophytic Fungus Residing in Red Sea Soft Coral, Inhibit HCV NS3/4A Protease. *Appl Biochem and Microbiol.*, 51(5): 579–584.
- Hibbett DS, Binder M. 2001. Evolution of marine mushrooms. *Biol Bull.*, 201: 319–322.
- Hobbs C. 2002. Medicinal mushrooms: an exploration of tradition, healing, and culture. Book Publishing Company (pp. 1-402).
- Hong Z, Hua X, Gong T, Jie P, Qi H, Ping Z. 2013. Hypocreaterpenes A and B, cadinane-type sesquiterpenes from a marine-derived fungus, *Hypocreales* sp. *Phytochem Lett.*, 6: 392–396.
- Hsiao G, Chi W, Pang K, Chen J, Kuo Y, Wang Y, Cha H, Chou S, Lee TH. 2017. Hirsutane-type sesquiterpenes with Inhibitory Activity of Microglial Nitric Oxide Production from the Red Alga-Derived Fungus *Chondrostereum* sp. NTOU4196. *J. Nat. Prod.*, 8: 1615–1622.
- Hyde KD, Bussaban B, Paulus B, Crous PW, Lee S, Mckenzie EH, Lumyong S. 2007. Diversity of saprobic microfungi. *Biodiv and Conserv.*, 16(1): 7-35.
- Isaka M, Suyarnsestakorn C, Tanticharoen M, Kongsaree P, Thebtaranonth Y. 2002. Aigialomycins A-E, new resorcylic macrolides from the marine mangrove fungus *Aigialus parvus*. *J. Org. Chem.*, 67: 1561–1566.

- Isaka M, Yangchum A, Intamas S, Kocharin K, Jones E, Kongsaree P, Prabpai S. 2009. Aigialomycins and related polyketide metabolites from the mangrove fungus *Aigialus parvus* BCC 5311. *Tetrahedron*, 65: 4396–4403.
- Jones E. 1995. Ultrastructure and taxonomy of the aquatic ascomycetous order Halosphaeriales. *Canadian J Bot*, 73(S1): 790-801.
- Jones EG. 2000. Marine fungi: some factors influencing biodiversity. *Fungal Divers.*, 4(193): 53-73.
- Jones EG. 2011. Fifty years of marine mycology. *Fungal div.*, 50(1): 73–112.
- Kamalakkannan A, Syamala M, Sankar PM, Shreedeevasena MS, Ajay MB. 2020. *Mushrooms—A Hidden Treasure*. JPS Scientific Publications, Tamil Nadu, India. (pp. 1-136).
- Kan SH, Sun BY, Xu F, Song QX, Zhang SF. 2015. Biosorption of aquatic copper (II) by mushroom biomass *Pleurotus eryngii*: kinetic and isotherm studies. *Water Science and Technol.*, 71(2): 283-288.
- Ko W, Sohn JH, Jang JH, Ahn JS, Kang DG, Lee HS, Kim JS, Kim YC, Oh H. 2016. Inhibitory effects of alternanamide on inflammatory mediator expression through TLR4-MyD88-mediated inhibition of NF- B and MAPK pathway signaling in lipopolysaccharide-stimulated RAW264.7 and BV2 cells. *Chem Biol Interact.*, 244: 16–26.
- Kohlmeyer J, Kohlmeyer E. 1979. *Marine Mycology: The Higher Fungi*; Academic Press: New York, NY, USA.
- Kohlmeyer J, Kohlmeyer E. 2013. *Marine mycology: the higher fungi*. Elsevier academic press, 1-704.
- Kohlmeyer J, Schatz S. 1985. *Aigialus* gen. nov. (Ascomycetes) with two marine species from mangroves. *Trans. Br. Mycol. Soc.*, 85: 699–707.
- Kohlmeyer J. 1984. Tropical marine fungi. *Marine Ecol.*, 5(4): 329-378.
- Kondo M, Takayama T, Furuya K, Okudaira M, Hayashi T, Kinoshita M. 1987. A nuclear magnetic resonance study of Zopfinol isolated from *Zopfiella marina*. *Annu. Rep. Sankyo Res. Lab.*, 39: 45–53.
- Kyoung-Su K, Xiang C, Dong-Sung L, Jae S, Joung Y, Youn-Chul K, Hyuncheol O. 2013. Anti-inflammatory effect of neoechinulin A from the marine fungus *Eurotium* sp. SF-5989 through the suppression of NF- B and p38 MAPK pathways in lipopolysaccharide-stimulated RAW264.7 macrophages. *Molecul.*, 18: 13245–13259.
- Lackner G, Misiek M, Braesel J, Hoffmeister D. 2012. Genome mining reveals the evolutionary origin and biosynthetic potential of basidiomycete polyketide synthases. *Fungal Gen and Biol.*, 49(12): 996-1003.
- Larsson E, Örstadius L. 2008. Fourteen coprophilous species of *Psathyrella* identified in the Nordic countries using morphology and nuclear rDNA sequence data. *Mycol res.*, 112(10): 1165-1185.
- Lee D, Jang J, Ko W, Kim K, Sohn J, Kang M, Ahn J, Kim Y, Oh H. 2013a. PTP1B inhibitory and anti-inflammatory effects of secondary metabolites isolated from the marine-derived fungus *Penicillium* sp. JF-55. *Mar Drugs*, 11: 1409–1426.
- Lee D, Ko W, Quang T, Kim K, Sohn J, Jang J, Ahn J, Kim Y, Oh H. 2013b. Penicillinolide A: a new anti-inflammatory metabolite from the marine fungus *Penicillium* sp. SF-5292. *Mar. Drugs*, 11: 4510–4526.
- Li H, Sun W, Deng M, Zhou Q, Wang J, Liu J, Chen C, Qi C, Luo Z, Xue Y. 2018. Aspersiamides, linearly fused prenylated indole alkaloids from the marine-derived fungus *Aspergillus versicolor*. *J. Org. Chem.*, 83: 8483–8492.
- Liu M, Sun W, Wang J, He Y, Zhang J, Li F, Qi C, Zhu H, Xue Y, Hu Z. 2018. Bioactive secondary metabolites from the marine-associated fungus *Aspergillus terreus*. *Bioorg Chem.*, 80: 525–530.
- Loron CC, François C, Rainbird RH, Turner EC, Borensztajn S, Javaux E. 2019. Early fungi from the Proterozoic era in Arctic Canada. *Nat.*, 570(7760): 232-235.
- Ma L, Chen H, Dong P, Lu X. 2013. Anti-inflammatory and anticancer activities of extracts and compounds from the mushroom *Inonotus obliquus*. *Food Chem.*, 139: 503–508.
- Manoharachary C, Sridhar K, Singh R, Adholeya A, Suryanarayanan TS, Rawat S, Johri B. 2005. Fungal biodiversity: distribution, conservation and prospecting of fungi from India. *Curr Sci.*, 58-71.
- Minoura K, Muroi T. 1978. Some freshwater Ascomycetes from Japan. *Trans Mycol Soc Japan*, 19: 129–134.
- Ngan NT, Quang T, Kim K, Kim H, Sohn J, Kang DG, Lee H, Kim Y, Oh H. 2017. Anti-inflammatory effects of secondary metabolites isolated from the marine-derived fungal strain *Penicillium* sp. SF-5629. *Arch Pharm Res.*, 40: 328–337.
- Niu S, Xie C, Xia J, Luo Z, Shao Z, Yang X. 2018. New anti-inflammatory guaianes from the Atlantic hydrotherm-derived fungus *Graphostroma* sp. MCCC 3A00421. *Sci Rep.*, 8: 520-530.
- Ogita J, Hayashi A, Sato S, Furutani W. 1987. Antibiotic Zopfimarín. *Japan Patent* 62-40292, 1987.
- Overy DP, Bayman P, Kerr RG, Bills GF. 2014a. An assessment of natural product discovery from marine (sensu strictu) and marine-derived fungi. *Mycol.*, 5(3): 145-167.
- Overy DP, Berrue F, Correa H, Hanif N, Hay K, Lanteigne M, Carr GS. 2014b. Sea foam as a source of fungal inoculum for the isolation of biologically active natural products. *Mycol.*, 5(3): 130-144.
- Overy DP, Rämä T, Oosterhuis R, Walker AK, Pang KL. 2019. The neglected marine fungi, sensu stricto, and their isolation for natural products' discovery. *Marine Drugs*, 17(1): 42-61.
- Padamsee M, Matheny PB, Dentinger BT, McLaughlin DJ. 2008. The mushroom family Psathyrellaceae: evidence for large-scale polyphyly of the genus *Psathyrella*. *Mol Phylogenet Evol.*, 46: 415–429.
- Pan C, Shi Y, Chen X, Chen AC-T, Tao X, Wu B. 2017. New compounds from a hydrothermal vent crab-associated fungus *Aspergillus versicolor* XZ-4. *Org Biomol Chem* 15: 1155–1163.
- Patel S, Goyal A. 2012. Recent developments in mushrooms as anti-cancer therapeutics: a review. *Biotech.*, 2: 1–15.
- Pinruan U, Sakayaroj J, Gareth Jones EB, Hyde KD. 2004. Aquatic fungi from peat swamp palms: *Phruensis brunneispora* gen. et sp. nov. and its hyphomycete anamorph. *Mycol.*, (400)96: 1163–1170.
- Rahi D, Malik D. 2016. Diversity of mushrooms and their metabolites of nutraceutical and therapeutic significance. *J Mycol.*, ID 7654123, 1-19.
- Rateb ME, Ebel R. 2011. Secondary metabolites of fungi from marine habitats. *Nat Prod Rep.*, 28: 290–344.
- Rathee S, Rathee D, Rathee D, Kumar V, Rathee P. 2012. Mushrooms as therapeutic agents. *Braz J Pharmacog* 22: 459–474.
- Richards TA, Jones MD, Leonard G, Bass D. 2012. Marine fungi: their ecology and molecular diversity. *Ann rev marine sci.*, 4: 495-522.

- Sánchez C. 2017. Bioactives from mushroom and their application. In Munish Puri. Food bioactives. Cham: Springer, 23–57.
- Shearer CA, Descals E, Kohlmeyer B, Kohlmeyer J, Marvanová L, Padgett D, Porter D, Raja HA, Schmit JP, Thorton HA, Voglymayr H. 2007. Fungal biodiversity in aquatic habitats. *Biodivers Conserv*, 16: 49–67.
- Shearer CA, Langsam DM, Longcore JE. 2004. Fungi in freshwater habitats. In: Mueller GM, Bills GF, Foster MS, eds. Biodiversity of fungi. London: Elsevier Academic Press, (pp. 513–531).
- Sridhar KR. 2020. The fascinating world of mushrooms. *Green Horizon*, 1: 15–17.
- Tan, T.K.; Teng, C.L.; Jones, E.B.G. Substrate type and microbial interactions as factors affecting ascocarp formation by mangrove fungi. *Hydrobiologia* 1995, 295, 127–134.
- Tian Y, Qin X, Lin X, Kaliyaperumal K, Zhou X, Liu J, Ju Z, Tu Z, Liu Y. 2015. Sydoxanthone C and acemolin B produced by deep-sea-derived fungus *Aspergillus* sp. SCSIO Ind09F01. *J. Antibiot.*, 68: 703–706.
- Usama W. Hawas, Eman F. Ahmed, Ali Halwany, Ahmed Atif, Elkhateeb W, Abou El-Kassem L. 2016. Bioactive metabolites from the Egyptian red sea fungi with potential anti-hcv protease effect. *Chem Nat Comp.*, 52(1): 104-110.
- Vongvilai P, Isaka M, Kittakoop P, Srikitikulchai P, Kongsaree P, Thebtaranonth Y. 2004. Ketene acetal and spiroacetal constituents of the marine fungus *Aigialus parvus* BCC 5311. *J. Nat. Prod.*, 67: 457–460.
- Wang L, Li M, Tang J, Li X. 2016. Eremophilane sesquiterpenes from a deep marine-derived fungus, *Aspergillus* sp. SCSIO2, cultivated in the presence of epigenetic modifying agents. *Molecules*, 21: 473.
- Wang Y, Qi S, Zhan Y, Zhang N, Wu A, Gui F, Guo K, Yang Y, Cao S, Hu Z. 2015. Aspertetranones A-D, putative meroterpenoids from the marine algal-associated fungus *Aspergillus* sp. ZL0-1b14. *J. Nat. Prod.*, 78: 2405–2410.
- Wu Y, Dockendorff C. 2018. Synthesis of a novel bicyclic scaffold inspired by the antifungal natural product sordarin. *Tetrahedron Lett*, 59: 3373–3376.
- Wu Z, Li D, Zeng F, Tong Q, Zheng Y, Liu J, Zhou Q, Li X, Chen C, Lai Y. 2018. Brasilane sesquiterpenoids and dihydrobenzofuran derivatives from *Aspergillus terreus* (CFCC 81836). *Phytochem.*, 156: 159–166.
- Xu T, Beelman RB. 2015. The bioactive compounds in medicinal mushrooms have potential protective effects against neurodegenerative diseases. *Adv Food Technol Nut Sci.*, 1: 62–66.
- Zhang T, Wang N-F, Zhang Y-Q, Liu H-Y, Yu L-Y: 2015. Diversity and distribution of aquatic fungal communities in the Ny-A° lesund Region, Svalbard (High Arctic). *Microb Ecol.*, 1-12.
- Zohri AA, Elkhateeb WA, Mazen M, Hashem M, Daba GM. 2014. Study of soil mycobiota diversity in some new reclaimed areas. *Egypt. Egyptian Pharmaceu J.*, 13(1): 58-63.
