

Myrothecium as Promising Model for Biotechnological Applications, Potentials and Challenges

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ABSTRACT

Myrothecium is a fungal genus that belongs to family Stachybotryaceae and has been involved as promising tool in many important mycotechnological applications such as potent bioherbicides with strong virulence against wide range of weeds and harmful plants from different plant families. Furthermore, *Myrothecium* exhibited strong insecticidal activities especially against mosquitoes and nematodes among other insects, promising antimicrobial activities, *Myrothecium* species are involved in many biotechnological applications due to secondary metabolites produced by them, and this review discuss challenges and potentials concerning using this genus as a tool in some medicinal and biotechnological applications.

Keywords: *Myrothecium*; Biological Control; Biotechnology; Secondary Metabolites

Introduction

Myrothecium species have a worldwide distribution as endophytic fungi that colonize various hosts [1], as saprophytic fungi in the soil and decaying tissues of plants [2-4], or as pathogens on various hosts [5-9]. *Myrothecium* species belong to the fungal family Stachybotryaceae, and over 30 species have been reported till 2011 [10], while the Index Fungorum database listed 90 records for *Myrothecium* in March 2019 <http://www.indexfungorum.org/names/Names.asp>. In this review, the biological activities, potential biotechnological applications, and challenges facing commercializing *Myrothecium* or its products were highlighted in order to encourage more studies on this miraculous fungus.

Myrothecium as Source of Biologically Active Compounds

Myrothecium species are prolific producers of vast of biologically active secondary metabolites such as enzymes, antibiotics, sesquiterpenoids, triterpenes, diterpenoids, cyclopeptides such as verrucamides A-D [11-15]. Additionally, *Myrothecium* species produce many macrocyclic trichothecene mycotoxins such as verrucarins and roridins, [16-18]. More than twenty compounds were reported from *M. roridum*, and around thirty compounds were listed to be originated from *M. verrucaria* [19]. Some *Myrothecium* species, such as *M. verrucaria*, are known for their production of

many enzymes such as lipases, chitinases, laccases, and proteinases [20,21]. The chemical structures of some trichothecene mycotoxins produced by *Myrothecium* species were illustrated in Figures 1 & 2.

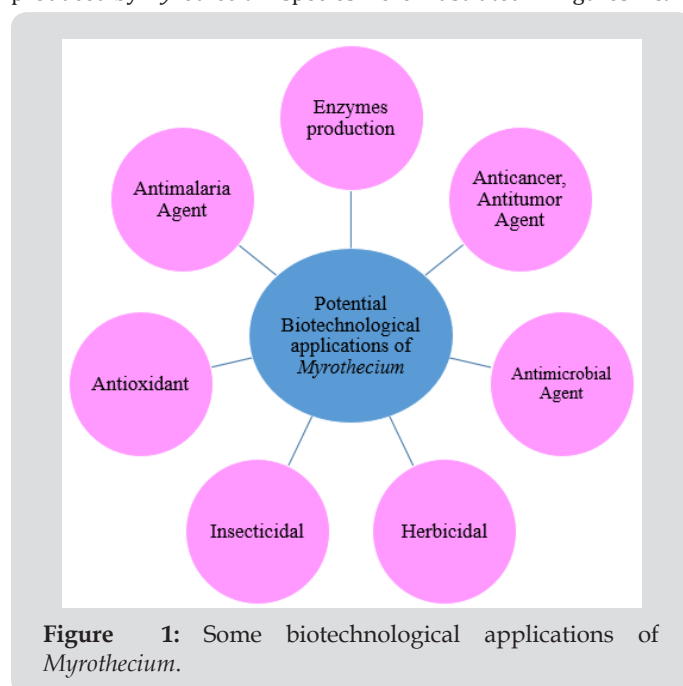


Figure 1: Some biotechnological applications of *Myrothecium*.

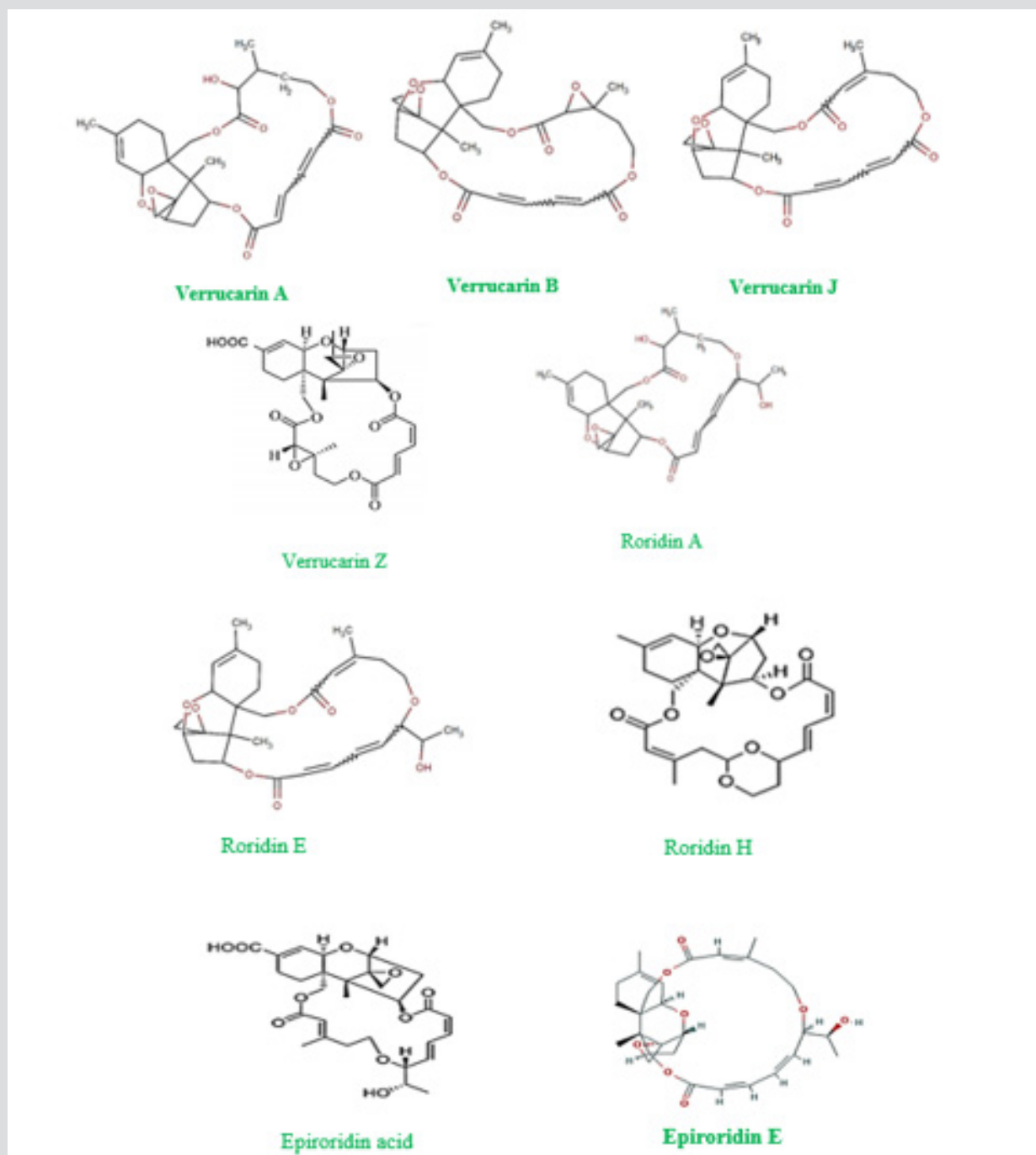


Figure 2: Chemical structures of some biologically active trichothecenes mycotoxins.

Some Biotechnological Applications of *Myrothecium*

Myrothecium uses in Biocontrol of Insects

Thanks to its ability to produce many enzymes, *Myrothecium verrucaria* has a promising insecticidal activity. Those produced enzymes are capable of degrading the extracellular cuticles of insects [20,22,23]. Thus, *M. verrucaria* represents potential tool for the biocontrol of insects such as mosquitoes [22]. Moreover, the activity of *M. verrucaria* as a nematophagous fungus could be used in bio-

controlling losses in crops from nematodes. Different mechanisms of nematodes inhibition by *M. verrucaria* were previously reported, those include affecting hatching of egg, inhibiting development, or through killing the nematode itself [24,25].

Myrothecium Herbicidal Spectrum and Uses

Using synthetic herbicides in natural habitats is not recommended due to its impacts on surrounding ecological systems, and the risk of affecting other plants due to the close association

between harmful plants (targeted to be killed), and the plant to be protected. Hence, using bio-herbicides may offer alternatives to the control of weeds with synthetic compounds including the use of plant pathogens as bioherbicides [26]. *Myrothecium verrucaria* is known as for its virulence against numerous weed plant species and is potentially useful as a bio-herbicide [27]. Spraying crude extract preparations of *M. verrucaria* has proven its pathogenicity against different exotic plants and weed species belonging to different plant families [9] such as plumeless thistle (*Carduus acanthoides* L.) [28]; leafy spurge (*Euphorbia esula* L.) [29]; sicklepod (*Cassia obtusifolia* L.) [27,30]; hemp sesbania [*Sesbania exaltata* Rydb. ex. A.W. Hill] [27]; kudzu [*Puereria lobata* (Willd.) Ohwi] [31,32], many weeds affecting commercial tomato fields such as common purslane, horse purslane, spotted spurge, and prostrate spurge [26], besides many morning-glory species (*Ipomoea* spp.) [33].

Furthermore, *M. verrucaria* present a promising bioherbicide for controlling pre-plant weed [26]. In spite of having desirable bioherbicidal characteristics such as its high virulence capabilities and broad weed host range, there is a serious disadvantage standing in front of commercializing *Myrothecium* traits, which is production of mycotoxins such as the macrocyclic trichothecenes [31,34]. Studies are now trying to reduce or those mycotoxins [12,35]. Approaches conducted to solve such problem include changing Carbon and nitrogen sources and concentrations within the culture media [35], getting rid of spores by washing [35], and preventing spore production during growth of the fungus within the liquid culture medium [36].

Myrothecium Production of Bilirubin Oxidase

Myrothecium verrucaria has been known as a producer of bilirubin oxidase [37-39], which has various biotechnological applications such as manufacturing biobatteries and biosensors, bleaching of clothes, degradation of effluents, and dye decolorization [40-43].

Myrothecium Antimicrobial Activities

The antibacterial activity of *Myrothecium* crude extracts has been previously reported against wide range of pathogenic bacteria such as *Escherichia coli*, *Salmonella Typhi*, *Klebsiella pneumoniae* and *Bacillus cereus* [44, 45]. A study by Ruma et al. [46] revealed promising antibacterial activities against *Bacillus subtilis*, *Klebsiella pneumoniae*, *Shigella flexneri*, while moderate activities were recorded against *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella typhi* [46]. The cyclic tetradecapeptides, verrucamides A-D were responsible for antibacterial activity against *Staphylococcus aureus* [14], whereas some quinone sesquiterpenes were reported to exhibit activity against *Staphylococcus aureus* and *Bacillus cereus* [47]. An extract of *Myrothecium verrucaria* fermentation culture containing the cyclopeptides Verrucamides A-D, showed promising antibacterial activity against *Staphylococcus aureus* [9,14]. On the other hand, many fungi showed susceptibility to *Myrothecium* crude extracts such as *Sclerotinia sclerotiorum* [48]; *Candida albicans* [46]. A novel triterpene glycoside named FR227244 exhibits *in vitro*

antifungal activity against *Aspergillus* sp., *Trichophyton* sp., *Candida utilis*, and *Candida parapsilosis* [49].

Other Biological Activities Exerted by Myrothecium Species

Ruma et al. [46] have reported the antioxidant activity of some *Myrothecium* species crude extracts when assessed by DPPH and ABTS radical scavenging methods. Extracts of some *Myrothecium* Species exhibited protection of DNA at a concentration of 50 mg/mL [46]. The macrocyclic trichothecene mycotoxins verrucarins A, verrucarins J, roridin A, and roridin E isolated from the freeze-dried culture filtrate of *M. verrucaria* BCC 112 exerted strong antimalarial activity against *Plasmodium falciparum* (K1 strain) [50]. The diterpene antibiotic, myrocin C, exhibited an antitumor activity that moderately increased the life span of Ehrlich ascites tumor-bearing mice [51]. *Myrothecium* spp. have been investigated for the management of cancer due to cytotoxic impacts [52]. *Myrothecium* species showed also ability to fight some tumours and inhibit liver cancer [53]. The list of potential applications of *Myrothecium* itself or compounds originated from *Myrothecium* is steadily increasing. Some potential biotechnological applications of *Myrothecium* is illustrated in Figure 1.

Harmful sides of Myrothecium

Generally, *Myrothecium* species are commonly found in the environment as endophytes and/or saprophytes on dead and decaying plant tissue [54,55], except for some species such as the famous plant pathogen *Myrothecium roridum* Tode [56], and the weak pathogen *M. verrucaria* Ditmar [8]. The development of plant diseases caused by *Myrothecium* is generally related to wet soil conditions, that's why it is important to take care of watering and soil sanitation in order to reduce crops losses [57]. *Myrothecium* species have been reported previously infecting coffee [58], seeds of rice and soybean [59], mulberry [52,60], chilli seed [61], rubber fig (*Ficus elastic*) [62]. Moreover, species *Myrothecium* were found infecting different economically important crops such as causing leaf blight in cotton [63], Peanut [4]; root rot in red clover [64], leaf spot in sunflower [65], potato [66], and leaf spot pepper [67].

Although the observed phyto-pathogenicity of some *Myrothecium* species may cause threaten to some crops, especially economically important crops, but it can be directed toward the field of biological control. On the other hand, some species of *Myrothecium* were reported as indoor air contaminant or growing inside houses which represent potential health hazard due to their ability to produce mycotoxins [68]. Nevertheless, no study has evaluated *Myrothecium* risk to humans [68]. *Myrothecium* species produce many mycotoxins such as roridins produced by both *M. roridum* and *M. verrucaria*. Roridins are lethal to some plants even in very small concentrations, and they cause myrotheciotoxicosis, sudden death in cattle and sheep accompanied with pulmonary congestion and edema, in addition to necropsy lesions

of abomasitis, hepatitis [69-75]. However, many of these trichothecenes mycotoxins exhibited promising biological activities as

shown in Table 1. The chemical structure of these trichothecenes mycotoxins were illustrated in Figure 2.

Table 1: Some biologically active trichothecenes mycotoxins.

Mycotoxin	Application	Reference
Roridin A	Antimalarial agent	Isaka et al. [50]
	Nematicidal activity	Nguyen et al. [70]
Roridin E	Antimalarial agent	Isaka et al. [50]
Roridin H	Phytotoxic, and cytotoxic to mammalian cell lines	Abbas et al. [31]
Verrucarin A	Inhibits proliferation and induces apoptosis in prostate cancer cells by inhibiting prosurvival Akt/NF-kB/mTOR signaling.	Liu et al. [71]
	Antimalarial agent	Isaka et al. [50]
	Nematicidal activity	Nguyen et al. [70]
Verrucarin B	Antifungal activity	Mondol et al. [72]
Verrucarin J	Antimalarial agent	Isaka et al. [50]
	Inhibits ovarian cancer	Carter et al. [73]
Verrucarin Z	Motility inhibitory and zoospicidal activity against <i>Phytophthora nicotianae</i>	Mondol et al. [72]
Epiroridin E	cytotoxic activities against human glioma, breast adenocarcinoma, non-small cell lung cancer, and hepatoma cell line	Liu et al. [74]
Epiroridin acid	cytotoxic activities against human glioma, breast adenocarcinoma, non-small cell lung cancer, and hepatoma cell line	Liu et al. [74]

Conclusion

Every study conducted on *Myrothecium* resulted in discovery of new metabolites or pointing to a possible application, which made *Myrothecium* species potential source of pharmaceuticals and attracted attention for further investigations of their medical properties. On the other hand, those fungi have various applications in large scale production of industrial enzymes, antibiotics, bioherbicides, and insecticides. Challenges of mycotoxins production by those fungi can be overcome as previously mentioned besides via conducting more studies.

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