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Antibiotics Production from Fungi

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Abstract

Almost majority of the fungi are responsible for the production of antibiotics, antioxidants bioactive and used as a food source. Specially, filamentous fungi are responsible for different types of antibiotics help to treat against tumour and cancer. Literatures on the antibiotic production of fungi and application have recognized that the natural oxidants and amino acids ergothioneine and polyphenolic produced from fungi sources are phenolic compounds (tocopherol, flavonoids, and phenolic acids), nitrogen compounds (alkaloids, chlorophyll derivatives, amino acids, and amines) or carotenoids as well as ascorbic acid. Several enzymes and secondary metabolites are used against free radicals. *Penicillium notatum* synthesizes cephalosporins, monobactams and carbapenems, the terpenoid fusidic acid is produced by the *Fusidium coccineum. Aspergillus lanosus* and *Penicillium produces* polyketide griseofulvin. Echinocandin B and pneumocandin B is produced by Aspergillus *nidulans* and *Glarea lozoyensis*. The *Hypocladium inflatum* is responsible for cyclosporine (cyclosporine A, CsA). *Taxomyces andreanae* is able manufacture produce paclitaxel. Camptothecin is *Aspergillus* sp. and *Trichoderma atroviride*. Vinblastine and vincristine are Catharanthus *roseus, Alternaria, Fusarium oxysporium*, aryltetralin-type lignan and podophyllotoxin are synthesized by *Phialocephela fortinii*. There is less awareness of the se antibiotics use of tumor and cancer treatment. Furthermore, some of the disease-causing pathogens is resistant to these antimicrobials over a long period of times. Thus, it is important to look for other sources of microbial/fungi isolation other than soil.

Keywords: Fungi; Antibiotics; Antioxidant; Secondary Metabolite; Pathogen.

Abbreviations: AIDS: Acquired Immune Deficiency Syndrome; HBV: Hepatitis B virus

Introduction

Antibiotics derived from microorganisms are used to cure the disease caused by microorganisms themselves. Despite of soil microorganisms are the most known antibiotics producer there are about 5500 antibiotics were discovered [1,2].

Mush rooms can produce both antifungal and anti-bacterial compounds. Fungal components have been recognized to provide several anti-microbial activities against bacterial pathogens, yeasts, mycelial fungi pathogens. Furthermore, antimicrobial compounds isolated from different stages of fungi growth have shown to have antifungal action bacterial, viral and fungal pathogens which are resistant to current therapeutic agents [3]. Anti-bacterial fungi activity can be produced from the mushrooms fruiting bodies, mycelium cultivation and cell wall biological components. For instance, Basidiomycota and Ascomycota have the potential of antibacterial activity [4].

Lentinan Anti-bacterial compounds can be isolated from the fruiting body of *L. edodes* [3] and compounds from the cultured mycelium of *T. versicolor* [1]. Cortinelin mycelial extracts from different strains of L. edodes have anti-microbial activity against *Bacillus cereus, Escherichia coli, Listeria monocytogenes, Salmonella typhimurium* and *Staphylococcus aureus* [3]. Chitin was linked with stimulation of innate immunity and production of pro- and anti-inflammatory cytokines (Rodrigues et al., 2011). *Agaricus bisporus, Lentinus edodes, Flammulina velutipe, Grifola frondosa* and *T. versicolor* can lower blood cholesterol. A glycoprotein of *T. versicolor* can prevent hypertension, thrombosis, blood platelet aggregation, antihyperlipidemic and antiarrhythmic. Furthermore, Pleurotus and Monascus have the potential of lowering blood glucose levels in diabetics [5]. Mycelial biomass and culture liquid of Basidiomycetes and Ascomycetes fungi are also important sources of the antibiotic synthesis. Currently, the production of these fungi antibiotics in industrial scale has got a serious focus for treatment of several cancer and tumour linked disease [6].

Fungal Antioxidant and their Application

Since oxidants responsible for the food spoilage and damage are not easily prevented from animal antioxidant products only, they are satisfied by fungi antioxidant products. Synthetic and natural antioxidants are involved in elimination of free radicals [7] However, natural oxidants produced from fungi sources are phenolic compounds (tocopherol, flavonoids, and phenolic acids), nitrogen compounds (alkaloids, chlorophyll derivatives, amino acids, and amines) or carotenoids as well as ascorbic acid [8]. Several enzymes and secondary metabolites are used against free radicals. For instance, amino acid ergothioneine and polyphenolic compounds found in fungi are phenolic acids and flavonoids, followed by tocopherols, ascorbic acid and carotenoids.

Phenolic compounds, polyketides, terpenes and steroids are some of the antioxidants produced against anti-microbial [4]. Specifically, flavonoids are responsible for antibacterial, antiviral, anti-inflammatory, antiallergic and vasodilatory actions [3]. Pleurotus and other higher Basidiomycetes are responsible for phenolic, terpenoid and polysaccharide content production [9]. *M. purpureus* is also other fungi species involved in Methanolic extracts production were found to possess strong radical scavenging and lipid peroxidation activity.

Metabolites such as polysaccharides, terpenoids, triterpenoids, diterpenoids, sesquiterpenoids and ergosterol are typically produced using submerged liquid fermentation. Used as cancer, acquired immune deficiency syndrome (AIDS) and hypercholesterolemia, suggesting they deserve more serious investigation [10]. A massive drugs and pharmaceutical grade products have been produced from fungi body parts against human disease treatment by screening process. These are (penicillin, tetracycline and erythromycin), antiparasitics (avermectin), antimalarials (quinine, artemisinin), lipid control agents (lovastatin and analogs), immune suppressants (cyclosporine, rapamycins), and anticancer drugs (taxol, doxorubicin) [4]. These antibiotics are taken in human being in the form of a powdered concentrate or extracts in hot water [10].

Antibiotics Production and Application from Fungi

Mycology is the fruit of various anti-pathogenic drugs that are applied as antibiotics, antifungal, immunosuppressive, or cholesterol lowering agents. β-lactam antibiotic penicillin G discovery from the fungus *Penicillium notatum* lead for the discovery of other β-lactam antibiotics, such as cephalosporins, monobactams and carbapenems [11]. The drugs are applied as a bacterial cell wall synthesis inhibition. Recently nine known β-lactam derivatives, including two cephalosporins, six carbapenems and one penem that are used clinically [5].

The terpenoid fusidic acid is produced by the *Fusidium coccineum*, fungal species. Fusidic acid inactivates synthesis of bacterial protein by hinderance of G factor elongation [1]. Fungi also produce drugs used as antifungal agents. *Aspergillus lanosus* and *Penicillium griseofulvum* are filamentous fungi responsible in the manufacture of antifungal polyketide griseofulvin. The drug is beneficial for dermatophytosis and anticancer activity treatment [12]. Echinocandin B and pneumocandin B are also produced from *Aspergillus nidulans* and *Glarea lozoyensis*. The drugs are responsible for fungal cell wall damage [1,2].

The fungus *Hypocladium inflatum* is responsible for the production of the lipophilic cyclic undecapeptide cyclosporine (cyclosporine A, CsA) [6]. Cyclosporine is immunosuppressant and has been widely used for the treatment of transplant rejection, treatment of severe psoriasis [12], potent inhibitor of HIV-1 and HCV replication [5] and development of potent antiviral compounds against HCV, such as alisporivir [6]. In addition, the antimalarial activity of cyclosporine was also identified to prevent *Plasmodium falciparum* [3] and *P. vivax* [3].

Indeed, in the case of grass-inhabiting endophytes, they are known to produce loline alkaloids to protect the plant against herbivores [11]. Most of the Endophytes are involved in a plethora of compounds production. An endophytic fungus *Taxomyces andreanae* is able manufacture produce paclitaxel [11]. In turn, paclitaxel helps to prevent breast and pancreatic cancers [13]. Camptothecin is another antibiotic synthesized from endophytic fungi, including *Aspergillus* sp. and *Trichoderma atroviride* [7]. The antibiotic is used for the treatment of severe bladder toxicity, ovarian cancer and colorectal cancer, respectively [6]. Vinblastine and vincristine are anticancer drugs secreted from Catharanthus *roseus, Alternaria, Fusarium oxysporium* [13], aryltetralin-type lignan and podophyllotoxin are synthesized by Phialocephela fortinii [12]. The drugs are used for the treatment of anticancer disease [14-19], (Table 1).

Table 1: Lists antimicrobial activities established from various filamentous fungi and their preparation.

Species	Preparation	Effective	References
Ganoderma spp.	Methanolic extracts	Bacillus subtilis Gram-positive bacteria; *B. cereus* and *Staphylococcus aureus.* Gram-negative bacteria; *Pseudomonas aeruginosa and Escherichia coli.*	[15,18]
Lentinula. edodes	Culture fluid Lentinan - aqueous and solvent extracts	*Candida albicans, Streptococcus pyogenes, S. aureus* and *B. megaterium* *Streptococcus, Actinomyces spp., Lactobacillus spp., Prevotella spp*. and *Porphyromonas spp*. of bacteria.	[3,14]

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Coprinus spp.	Coprinol isolated from culture fluid	Multi-drug-resistant gram-positive bacteria	[19]
Pleurotus ostreatus	Crude extracts from culture broth, Hexane-dichloromethane extract containing *ρ*-anisaldehyde, Various extracts; two main unidentified compounds	Gram-positive, gram-negative bacteria and *Aspergillus niger B. subtilis, P. aeruginosa, Aspergillus niger* and *Fusarium oxysporum Bacillus spp., E. coli, Vibrio cholera* and *Salmonella typhi*	[3,14,19]
Pleurotus eryngii	Methanolic extracts, Eryngin – an antifungal peptide	*Enterococcus faecium, S. aureus and B. subtilis Fusarium oxysporum* and *Mycosphaerella arachidicola*	[16,9]
Pleurotus sajor-caju	12 kD a ribonuclease	*F. oxysporun, M. arachidicola, P. aeruginosa* and *S. aureus*	[16]
Monascus spp.	Ethanol: n-hexane (1:10) extract-Monascidin A, Pigments: Rubropunctatin and monascorubin Citrinin	*B. subtilis, P. aeruginosa and E. coli. Aspergillus, Penicillium, Mucor, Fusarium, Alternaria* and *Botrytis.* Gram-positive and gram-negative bacteria	[5]
Grifola frondosa	Exopolysaccharide; D-fraction	Hepatitis B virus (HBV)	[14]

Conclusion

There are abundance antibiotics and antimicrobials produced from fungi. However, there is less awareness of the se antibiotics use of tumour and cancer treatment. Furthermore, some of the disease-causing pathogens is resistant to these antimicrobials over a long period. Thus, it is important to look for other sources of microbial/fungi isolation other than soil.

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