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Medicinal Fungi

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Abstract

Medicinal fungi are those fungi, which produce medically significant metabolites or can be induced to produce such metabolites using biotechnology. The range of medically active compounds that have been identified include antibiotics, anti-cancer drugs, cholesterol inhibitors, psychotropic drugs, immunosuppressants and even fungicides. Although initial discoveries centered on simple molds of the type that cause spoilage of food, later work identified useful compounds across a wide range of fungi.

Keywords Medicinal, fungi

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List of abbreviation: None

Although fungi products have been used in traditional and folk medicines, probably since pre-history, the ability to identify beneficial properties and then extract the active ingredient started with the discovery of penicillin by Alexander Fleming in 1928. Since that time, many additional antibiotics have been discovered and the potential for fungi to synthesize biologically active molecules, useful in a wide range of clinical therapies, has been extensively exploited.

Pharmacological research has now isolated antifungal, antiviral, and antiprotozoan, isolates from fungi [1].

The fungus with probably the longest record of medicinal use, *Ganoderma lucidum*, is known in Chinese as língzhī "spirit plant", and in Japanese as mannentake "10,000-year mushroom". Traditional Chinese medicine. Notable medicinal mushrooms with a well-documented history of use include *Agaricus subrufescens* [2].

Studies have shown another species of genus *Ganoderma*, *G. applanatum*, contains compounds with anti-tumor and anti-fibrotic properties.

Inonotus obliquus was used in Russia as early as the 16th century, and it featured in Alexandr Solzhenitsyn's 1967 novel Cancer Ward [3].

Applications

Cancer

Paclitaxel is synthesized using *Penicillium raistrickii* and plant cell fermentation. Fungi can synthesize other mitotic inhibitors including vinblastine, vincristine, podophyllotoxin, griseofulvin, aurantiamine, oxaline, and neoxaline [4].

11,11'-Dideoxyverticillin A, an isolate of marine *Penicillium*, was used to create dozens of semi-synthetic anticancer compounds [5]. 11,11'-Dideoxyverticillin A, andrastin A, barceloneic acid A, and barceloneic acid B, are farnesyl transferase inhibitors that can be made by *Penicillium* [6]. 3-O-Methylfunicone, anicequol, duclauxin, and rubratoxin B, are anticancer/cytotoxic metabolites of *Penicillium*. *Penicillium* is a potential source of the leukemia medicine asparaginase [7].

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Antibacterial agents (antibiotics)

Alexander Fleming led the way to the beta-lactam antibiotics with the *Penicillium* mold and penicillin. Subsequent discoveries included alamethicin, aphidicolin, brefeldin A, cephalosporin, cerulenin, citromycin, eupenifeldin, fumagillin, fusafungine, fusidic acid, itaconic acid, MT81, nigrosporin B, usnic acid, verrucarin A, vermiculine and many others. Antibiotics retapamulin, tiamulin, and valnemulin are derivatives of the fungal metabolite pleuromutilin. Plectasin, austrocortilutein, austrocortirubin, coprinol, oudemansin A, strobilurin, illudin, pterulone, and sparassol are antibiotics isolated from basidiomycete species. Rene Dubos had reported the discovery of the first naturally derived antibiotic, tyrothricin, a compound of 20% gramicidin and 80% tyrocidine, from B. brevis. It was one of the first commercially manufactured antibiotics and was very effective in treating wounds and ulcers during World War II [8].

Cholesterol biosynthesis inhibitors

Statins are an important class of cholesterol-lowering drugs; the first generation of statins were derived from fungi [9]. Lovastatin, the first commercial statin, was extracted from a fermentation broth of *Aspergillus terreus* [9]. Industrial production is now capable of producing 70 mg lovastatin per kilogram of substrate [10]. The red yeast rice fungus, *Monascus purpureus*, can synthesize lovastatin, mevastatin, and the simvastatin precursor monacolin J. Nicotinamide riboside, a cholesterol biosynthesis inhibitor, is made by *Saccharomyces cerevisiae*.

Antifungals

Some antifungals are derived or extracted from other fungal species. Griseofulvin is derived from a number of *Penicillium* species, caspofungin is derived from *Glarea lozoyensis* [11]. Strobilurin, azoxystrobin, micafungin, and echinocandins, are all extracted from fungi. Anidulafungin is a derivative of an *Aspergillus* metabolite.

Immunosuppressants

Ciclosporin, was discovered *in Tolypocladium inflatum*. Bredinin was discovered in *Eupenicillium brefeldianum*. Mycophenolic acid was discovered in *Penicillium stoloniferum*. Thermophilic fungi were the source of the fingolimod precursor myriocin. *Aspergillus* synthesizes immunosuppressants gliotoxin and endocrocin. Subglutinols are immunosuppressants isolated *from Fusarium subglutinans* [12]. Other compounds include mizoribine.

Malaria

Codinaeopsin, efrapeptins, zervamicins, and antiamoebin [13] are made by fungi.

Diabetes

Many fungal isolates act as DPP-4 inhibitors, alpha-glucosidase inhibitors, and alpha amylase inhibitors in vitro. Ternatin is a fungal isolate that suppresses hyperglycemia [14]. Aspergillusol A is an alpha-glucosidase inhibitor made by *Aspergillus*. Sclerotiorin is an aldose reductase inhibitor made by *Penicillium*.

Psychotropic effects

A number of fungi have well documented psychotropic effects, some of them severe and associated with sometimes acute and life-threatening side-effects [15]. Well known amongst these is *Amanita muscaria*, the fly agaric. More widely used informally are a range of fungi collectively known as "magic mushrooms", which contain psilocybin and psilocin.

The history of bread-making is also peppered with references to deadly ergotism caused by ergot, most commonly *Claviceps purpurea*, a parasite of cereal crops. A number of therapeutically useful drugs have subsequently been extracted from ergot including ergotamine, pergolide and cabergoline [16].

Psychotropic compounds created from ergot alkaloids also include dihydroergotamine, methysergide, methylergometrine, hydergine, nicergoline, lisuride, bromocriptine, cabergoline, pergolide. Polyozellus

multiplexsynthesizes prolyl endopeptidase inhibitors polyozellin, thelephoric acid, kynapcins. Neurotrophic fungal isolates include L-theanine, tricholomalides, scabronines, termitomycesphins. Many fungi synthesize the partial, non-selective, serotonin receptor agonist/analog psilocin.

A number of other fungal species, including species of *Aspergillus* and *Penicillium*, have been induced to produce ergot alkaloids.

Vitamins

Fungi are a source of ergosterol, which can be converted to vitamin D upon exposure to ultraviolet light to synthesize vitamins D2 (ergocalciferol), D4 (22-dihydroergocalciferol), and D1 (Lumisterol+D2) [17,18].

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