We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900
Open access books available

185,000
International authors and editors

200M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Chapter

The Diversity of Endophytic *Aspergillus*

Vo Thi Ngoc My and Nguyen Van Thanh

Abstract

In plants, endophytic fungi and plant are closely related, endophytic fungi can use substances in plants as nutrients to survive. In return, they bring many benefits to the plant, playing an important role in protecting the host plant against the harmful effects of insects, harmful microorganisms or environmental disadvantages. Recently, secondary fungi metabolites, especially endophytic fungi, are gaining interest because they can produce many bioactive metabolites with antibacterial, anticancer and antioxidant properties. Some endophytic fungi are noted as *Aspergillus, Penicllium, Fusarium* due to the production of many metabolites for biological effects such as antibacterial, antiviral, anticancer, etc. in which *Aspergillus* species product many compounds have properties antibacterial such as terrequinon A, terrefuranon, Na-acetyl aszonalemin, etc.

Keywords: endophytic fungi, *Aspergillus*, endophyte, secondary metabolites, biological activity

1. Introduction

1.1 Endophytic microorganisms

Endophytic microorganisms are microorganisms that live in the plant tissue beneath the epidermal cell layers without harming or infecting the host plant, endophytic microorganisms that live in the intercellular space of tissues and thereby they can invade living cells [1].

1.2 Endophytic fungi

Endophytic fungi account for a high percentage of the current group of endophytic plant microorganisms. They are considered a source of many new substances, including many active substances with interesting biological effects. These fungal forms can be detected incidentally in the deep tissues of normally growing host plants. They are endogenous to the host plant and, thanks to their strong biosynthetic capacity, are able to produce a large number of metabolites. This may lead to the emergence of new bioactive substances and promises to develop production on an industrial scale. In addition, the substances produced by endophytic fungi are considered as an agent to help balance the microflora on the host plant to prevent pathogens [2, 3].

1.3 Relationship between endophytic fungi and plants

Endophytic fungi can be easily isolated from a surface-sterilized piece of plant tissue. The number of endophytic fungi found was also very variable when examining different plant samples, this number can range from one to several hundred strains.

The presence of endophytic fungi in plant tissues can be explained in many different ways. But perhaps the most plausible is the hypothesis that endophytic fungi arose from some plant pathology in the evolution of plants. The tree also has a microflora, in which there are strains that exist dormant and cause disease only when the tree is old and weak or facing adverse living conditions. The interaction between the host plant and the pathogenic microorganism during long-term development has resulted in genetic mutations from the pathogenic microorganisms to yield useful strains of endophytic fungi without causing disease [1].

Between endophytic fungi and host plants there is a symbiotic relationship, mutualism or mutualism, etc. The symbiotic or mutualistic relationship between endophytic fungi and plants is shown quite closely. At times they are closely linked as a single individual and contribute to the distinctive character of the tree.

Endophytic fungi promote ecological adaptation of host plants. In some plant species with endophytic fungi, it has been found that they have increased drought tolerance or tolerance of aluminum toxicity in water sources, in habitats, etc. In addition to protecting plants against a number of factors detrimental to the host such as herbivores or insects, many natural products produced by endophytic fungi have also been observed, monitored and concluded on the ability to prevent, inhibit or kill many different pathogens that invade plant tissues. That is also the reason why some endogenous fungal strains can produce phytochemicals that give the host plant a unique and distinctive character [3, 4].

For example: in the early 1990s, a novel taxol-producing endophytic fungus, *Taxomyces andreanae*, was isolated from *Taxus brevifolia*. This set the stage for a more comprehensive examination of the ability of other *Taxus* species and other plants to yield endophytes producing taxol. There is an endophytic fungi strain that produces taxol, an important active substance of great significance in the field of medicine.

1.4 Basic principles for selecting plants to isolate endophytic fungi

Young plant tissues are more suitable for isolating endophytic fungi than mature tissues because adult tissues often contain many different types of fungi, making isolation difficult. Collected plant samples should be stored at 4°C until endophytic fungi are isolated, and isolation should be carried out as soon as possible to avoid airborne bacterial contamination.

To obtain endophytic fungi with biological activity, it is necessary to select plant species that are outstanding in terms of biology, age, endemism, botanical history, and habitat of the host plant. Many studies have shown that medicinal plants and plants living in special environments are frequently studied to screen for endophytic fungi that produce antibiotic substances [1].

1.4.1 Plants live in unusual biological environments

With these plants, the unusual environment and harsh natural conditions force the tree to survive, a special element is needed to make the plant highly resistant. And one would expect that factor to be beneficial endophytic fungi [4].

For example: showed that an aquatic plant, *Rhyncholacis penicillata*, which lives in harsh aquatic environment which may be constantly wounded by passing rocks and

other debris, resists infection by common oomyceteous fungi that cause disease. The possibility that endophytes associated with this aquatic plant may produce antifungal agents that protect the plant from attack by pathogenic fungi is feasible. A novel antioomycetous compound, oocydin A was discovered from the endophytic strain *Serratia marcescens* from this plant.

1.4.2 Plants are used as folk medicine

A number of plants have been used according to folk experience, from generation to generation for wound healing, antifungal, antibacterial, etc.

For example: A study of endophytic fungi producing novel bioactive substances in Brazil. It is a plant named "Mexican Sunflower" - *Tithonia diversifolia* (Asteraceae) that is often mentioned with many interesting points. For a long time, based on oral experience, people have used this plant to cure a number of diseases such as malaria, diarrhea, viral fever, hepatitis and to heal open wounds. In addition, extracts from *T.diversifolia* with anti-inflammatory, amoebic, antispasmodic, antifungal, antibacterial, and antiviral activities were also mentioned. Based on that information, scientists have isolated and isolated *Phoma sorghina*, an endogenous fungus from the leaves of this "Mexican sunflower". From this, six anthraquinone derivatives were obtained from fungal metabolites, half of which are new known substances [1].

1.4.3 Ecologically specific plants

Plants with unusually long lifespans, growing in areas of great biological change, or living in ancient soils are also ideal research subjects to provide endogenous fungi new. Plants surrounded by plants infected with the pathogen, but not infected, are more likely to harbor endophytic fungi with antimicrobial activity than other host plants.

For example: 2008, Tuntiwachwuttikul et al., found an endogenous fungal that was active against pathogens on banana plant *Colletotrichum musae* (Phyllachoraceae) [5].

1.4.4 Endemic plants

Endemic plant species that have a normal lifespan, or occupy a certain area of land in the wild. *Chaetomium globosum* isolated from leaves of endemic plant *Maytenus hookeri* distributed only in Yunnan regions, China produces chaetoglobosin B which inhibits tuberculosis bacteria [5].

1.5 Diversity of endophytic fungi

Endophytic fungi are very abundant, according to a study by Matsushima in 1971 conducted on some angiosperms and conifers in North America and Panama, which suggested that most of the endophytic fungi belong to the *Ascomycetes* class [4].

2008, Huang et al. also found endogenous fungi present in 27/29 surveyed medicinal plants. The frequency of occurrence of endophytic fungi is relatively high, mainly the genera *Fusarium* (27%), *Colletotrichum* (20%), *Phomopsis* (11%), *Alternaria* (9%), *Aspergillus* (5%), etc. **Figure 1**.

According to the statistics of scientists studying three plant families in Southeast Arizona - USA, forests in North Carolina and Northern forests shows that:

- Surveying the host plant representing the Fagaceae family obtained 44 endogenous fungal strains in which the genus *Sordariomycetes* predominated.

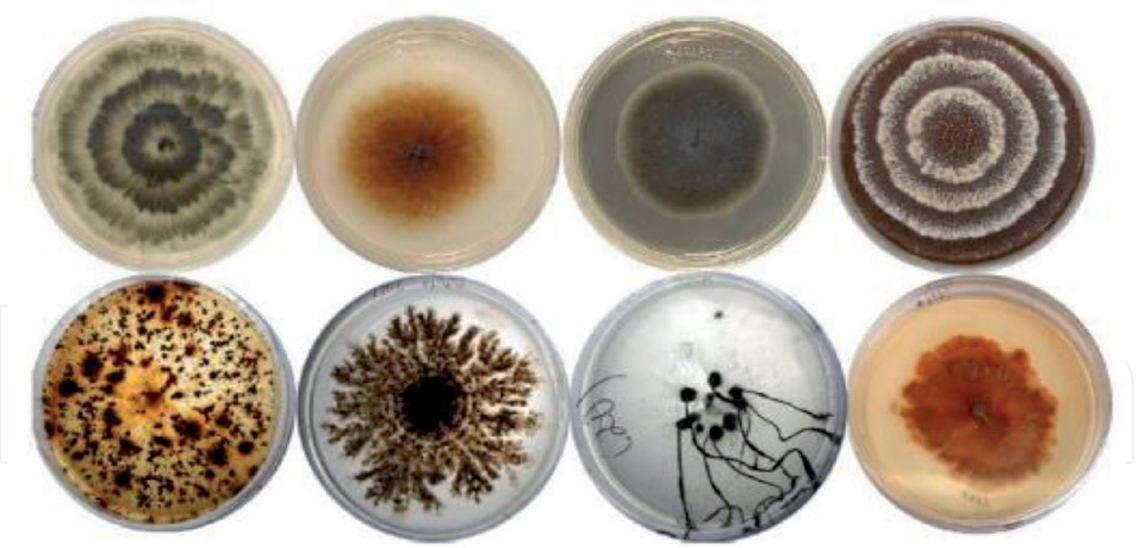


Figure 1.
Strains of class Ascomycetes isolated from leaves of angiosperms and conifers in North America and Panama (source: Selim KA et al., 2012).

- Surveying *Pinus ponderosa* trees representing the Pinaceae family obtained 111 endogenous fungal strains, in which the genus *Leotiomycetes* predominated.

- Surveying plants *Cupressus arizonica* and *Platycladus orientalis* representing the Cupressaceae family obtained 42 strains, in which the genus *Dothideomycetes* prevailed [4].

1.6 Endogenous fungi produce biologically active substances

Many endogenous fungi in plants have been isolated, they have the ability to produce biologically active substances such as antibiotic, antibacterial, antifungal, tumor suppressor, antioxidant and other biological activities.

1.6.1 Endogenous fungi with antibacterial and antifungal properties

Many studies on antibacterial and antifungal activities are produced from endogenous fungi, mainly belonging to the following groups: alkaloids, peptides, steroids, terpenoids, phenols, quinines and flavonoids, etc. These compounds account for only a part small in the total number of active substances produced by endophytic fungal species, they are clearly an excellent and novel potential source for the production of new antibiotics. This holds great promise for solving the problem of drug resistance in bacteria because these antibiotics are novel and highly active compounds **Table 1**.

Besides, *Phomopsis* is an endogenous fungus that produces phomopsichalasin, representing the first group of compounds of cytochalasin type.

1.6.2 Endogenous fungal tumor suppressor

Since 1990, *Taxomyces* andreanae was first isolated from *T. brevifolia*, this fungus produces paclitaxel - an inhibitor of achromatic spindles during cell division, with a mass spectrum similar to paclitaxel extracted from *Taxus*. Subsequently, several paclitaxel-producing fungi have been isolated from many plants and other *Taxus* species **Table 2**.

Endophytic fungi	Isolation source	Antibiotic	Antimicrobial effects	Ref.
Pestralotiopisis microspora	*Torreya axifolia*	Pestalopyrone Hydroxypestalopyrone	Plant antibiotics	[4, 6]
Pestralotiopisis jesteri	Trees that grow in the rivers of Papua New Guinea	Hydroxyl jesterone	Antifungal plant disease	[7]
Colletotrichum gloeosporioides	*Artemisia mongolica*	Acid colletotric	Antimicrobial *Helminthosporium sativum*	[4]
Colletotrichum sp.	*Artemisia annua*	Metabolites	Antibacterial, anti-fungal that causes diseases for humans and plants	[4]
Muscodor albus	*Cinnamomum zeylanicum*	Volatile matter	Inhibits bacteria and fungi	[4]
Fusarium sp.	*Selaginella pallescens*	CR 337: New pentaketide	*Candida albicans*	[4]
Acremonium zeae	*Zea mays* L.	Pyrrocidines A, B	Fungi	[4]
Cryptosporiopsis quercina	*Tripterigeum wilfordii*	Cryptocandin Cryptocin	*C. albicans* *Trichophyton* spp. *Botrytis cinerea* *Pryriaria oryzae*	[4]
Alternaria sp. *Nigrospora oryzae* *Papulospora* sp.	8 types of medicinal plants found in 3 different regions of western India	Extract from fermented juice	*C. albicans*	[4]
Chaetomium globosum	Lead of *Ginkgo biloba*	Chaetoglobosin A and C	*Mucor miehei*	[4, 6]
Talaromyces sp.	Mangroves	7-epiaustdiol Stemphyperylenol Secalonic A	*P. aeruginosa* *Sarcina ventriculi*	[4, 7]

Table 1.
Antibiotic effects of some endogenous fungal species.

No.	Endophytic fungi	Isolation source	Ref.
1	*Pestalotiopsis microspora*	*Taxus wallichiana*	[8]
2	*Pestalotiopsis guepini*	*Wollemia nobilis*	[8]
3	*Seimatoantlerium tepuiense*	*Maguireothamnus sprciosus*	[8]

Table 2.
Some endophytic fungi producing paclitaxel.

1.6.3 Endophytic fungi that are active against insects

Many studies have demonstrated the importance of endophytic fungi in the production of insect repellents, which have many implications for crop protection and increase in agricultural yields **Table 3**.

Endophytic fungi	Isolation source	Compounds	Activities	Ref.
Nodulisporium sp.	*Bontia daphnoides*	Nodulisporic	Insecticide, against larvae of green flies, flies, etc	[4]
Muscodor vitigenus	*Paullina paullinioides*	Napthalene	Except for bed bugs	[4]

Table 3.
Anti-insect effects of some endophytic fungal species.

Endophytic fungi	Isolation source	Metabolites	Biological impact	Ref.
Pestalotiopsis microspora	*Terminalia morobensis*	Pestacine Isopestacine	Strong anti-oxidant Anti-fungal	[9]
Cephalosporium sp. *Microsphaeropsis olivacea*	*Trachelospermum jasminoides* *Pilgerodendron uviferum*	Graphislactone A	Stronger antioxidant than BHT and ascorbic acid	[10]
Xylaria sp.	*Ginkgo biloba*	Phenolic, flavonoid	Strong anti-oxidant	[10]
Phyllosticta sp.	*Guazuma tomentosa*	Metabolites	Strong anti-oxidant	[10]

Table 4.
Antioxidant effects of some endophytic fungal species.

Endophytic fungi	Isolation source	Metabolites	Biological impact	Ref.
Pseudomassaria sp.	Plants in the African Rainforest	Nonpeptidal (L-783,281)	Lowers blood sugar with a mechanism similar to insulin but taken orally	[4]
Fusarium subglutinans	*Trypterygium wifordii*	Subglutinol A Subglutinol B	Decreased B and T lymphocytes (immunosuppression)	[4]
Penicillium sp.	*Limonium tubiflorum*	NF-B inhibitor	Reduce the incidence of cancer	[4]
Pestalotiopsis microspora	*Torreya taxifolia*	Acid torreyanic	Anti-cancer agent	[4]
Fusarium solani	*Camptotheca acuminata*	Camptothecin	Anti-cancer compounds	[4]
Curvularia lunata	*Niphates olemda*	Cytoskyrin	Antimicrobial Potential agent for cancer treatment	[4]
Fusarium sp.	*Kandelia candel*	New isoflavone	Inhibits the growth of Hep-2 and Hep G2 cancer cells	[4]
Phomopsis sp.	*Musa acuminata*	Hexaketide γ-lacton Oblongolides Z	Anti-herpes simplex virus type 1	[4]
Phomopsis sp.	*Excoecaria agallocha*	Phomopsis-H76 A, B and C	Formation of vessels in the sub-intestinal vasculature	[4]

Table 5.
Endogenous fungi producing other biologically active substances.

1.6.4 Endogenous fungi with antioxidant activity

Antioxidants are substances that react with free radicals generated during oxidation, thus preventing or slowing down this process. Antioxidants prevent and treat diseases such as cancer, cardiovascular (atherosclerosis, hypertension, ischemia), diabetes, neurodegenerative diseases (Parkinson's disease), arthritis and aging, etc. Endophytic fungi in higher plants are a source of many new antioxidant active substances **Table 4** [11, 12].

1.6.5 Endogenous fungi produce other biologically active substances

Endogenous fungi are also known as a source of many other biological metabolites, such as anti-inflammatory, antidiabetic, hypoglycemic, immunosuppressive, etc. used to prevent rejection in organ transplants and can be used to treat autoimmune diseases such as rheumatoid arthritis, insulin dependent diabetes also known from endogenous fungi.

Endophytic fungi of the genus *Chaetomium* produce chaetoglobosin, which is a cytochalasin analog that inhibits actin polymerization. The genus *Chaetomium* is able to produce cytostatic metabolites including chaetomin, chaetoglobosin A, C, D and G, chaetoquadrin, oxaspirodion, chaetospiron, orsellide and chaetocyclinon **Table 5**.

2. Introduction of the endophytic *Aspergillus*

Aspergillus is a large genus of fungi and one of the most studied, according to Thom and Church in 1918, the genus is divided into 18 groups, 132 species and 18 orders. They account for a large proportion in the natural environment and are easy to culture in the laboratory. The economic importance of several species has attracted much research on *Aspergillus.* Furthermore, this common genus of fungi is involved in many industrial processes including production of enzymes (such as amylase), chemicals (such as citric acid) and food (such as soy sauce) are one of the plant endogenous fungal genera known for its ability to produce many biologically active substances with many practical applications [13].

2.1 Classify

Aspergillus was first classified in 1809 by the Italian priest and biologist Micheli by observation under a microscope. Nowaday, "*Aspergillum*" is also the name for asexual spores that form the common structure for all species of the genus *Aspergillus*; about a third of species in the genus have a sexual reproduction stage. According to the classification:

Kingdom: Fungi
Division: Ascomycota
Class: Eurotiomycetes
Order: Eurotiales
Family: Trichocomaceae
Genus: *Aspergillus*

2.2 Characteristics of *Aspergillus*

The characteristics of color (black, brown, yellow, red, white, blue, etc), growth rate, edge of mushroom cluster and surface texture of mushroom cluster vary

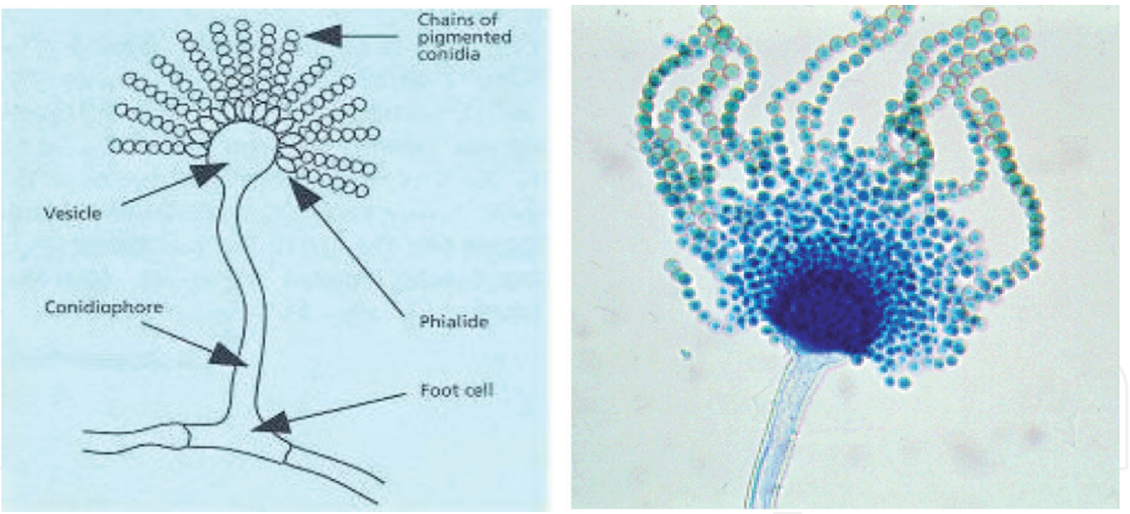


Figure 2.
Structure of the asexual reproductive organs of Aspergillus (source: Doddamani, 2012).

depending on species and growing conditions. The mycelium of *Aspergillus* belongs to the group of colorless, segmented, branched hyphae that can produce many enzymes and some toxins. *Aspergillus* mycelium is vigorous and produces many spores attached to a long vertical spore stalk, which grows from a special cell located in the trophic fiber called a foot cell [14, 15].

The spore-bearing head includes the spores: spore, flask, vesicle and spore stalk. The properties of each component vary from species to species and are characteristics that help identify species. Most species have the same shape, size, and color of spore-bearing heads as the cluster **Figure 2**.

Some common *Aspergillus* species: *A. aculeatus, A. candidus, A. flavus, A. foetidus, A. fumigatus, A.terreus, A. lentus, A. nidulans, A. niger, A. oryzae,* etc.

2.3 Ecological characteristics and distribution

Aspergillus is very aerobic, found in most oxygen-rich environments, usually growing on the surface of a substrate. Normally, fungi grow on carbon-rich substrates such as monosaccharides (glucose) and polysaccharides (amylase).

Aspergillus is widely distributed in the environment and can grow almost anywhere, especially in places with high humidity. *Aspergillus* grows by saprophyte on decaying plants, compost, and humus. Most *Aspergillus* species can live on a variety of substrates such as feces, human tissues, and ancient parchment. *Aspergillus* species grow well and produce many spores at a temperature of about 23–26°C. However, there are some species such as *A. terreus*, *Acronurus carneus*, *A. jcheri* which thrives at 35°C or *A. fumigatus* which grows well at 45°C even up to 50°C. Temperature also affects the shape of the attachment spore tip. *A. janus* species produces two different types of attached spore heads, the ratio of these two forms is affected by temperature, at 18–20°C, most of the spore heads are white, clubhead-shaped, and long spore stalks; but at 30°C, most of the spore heads are dark green, spherical, and short spore stalks.

2.4 Some biologically active substances produced by endophytic *Aspergillus*

Apergillus sp. has the ability to produce many biological active substances such as antibacterial, antiviral, cytotoxic and antioxidant activities, etc. **Table 6**.

Endophytic fungi	Isolation source	Metabolites	Biological impact	Ref.
A. flavus	*Solanum lycopersicum L.*	Chlorophyll, flavonoids, carbohydrates, phenolics, total proteins contents	To improve the growth and the secondary metabolites contents of tomato	[16]
A. flavus	*Sonneratia alba*	Kojic acid	Antibacterial (*Staphylococcus aureus, Escherichia coli*)	[17]
A. flavus IBRL-C8	*Cassia siamea* Lamk	The ethyl acetate extract	Antifungal (*C. albican*)	[18]
A.flavus	*Viscum album*	Lectin	Anti-cancer MCF7	[19]
A. flavus (SS03)	*Moringa oleifera Lam.*	*Fenaclon, (R)(−) 14 methyl-8-hexadecyn-1-ol, Trans-β-farnesene (E)-β-farnesene, 9-Octcadecene,1,1, Dimethoxy*	Antibacteria (*S. aureus, Bacillus, Candida tropicalis*)	[20]
A. flavus *Nigrospora sphaerica*	Tropical Tree Species of India, Tectona	Duroquinone, Adamantine derivative, Dodecanoic acid, tetradecanoic acid, pentadecanoic acid and Myristic acid	Insecticidal	[21]
A. flavus *A. niger*	*Acacia nilotica*	The ethyl acetate extract	Antifungal (*Pythiummyriotylum, Rizoctoniasolani*)	[22]
A. carbonarius *A. niger*	*Zea mays* *Arachis hypogea*	The ethyl acetate extract	Anticancer Promoted plant growth	[23]
A.niger CSR3	*Cannabis sativa*	Gibberellins, indoleacetic acid	Antibacteria	[24]
A.fumigatus	R7	Linoleic acid	Antimicrobial and cytotoxic activities	[25]
A.fumigatus	*riparian plants Myricaria laxiflora*	(Z)-N-(4-hydroxystyryl) formamide (NFA)	Improves drought resistance in rice as an antioxidant	[26]
A.fumigatus	*Cocos nucifera*	Flavonoid, terpenoid and saponin	Antibacteria *(Pseudomonas aeruginosa, E. coli, Bacillus subtilis, S. aureus)*	[27]
A.fumigatus	*Copaifera multijuga*	The compounds into the fermentation broth under specific culture conditions	Antibacteria *(Mycobacterium tuberculosis* H37Rv strain (ATCC 27294))	[28]
A.fumigatiaffinis	*Tribulus terestris*	A new antibacterial polyketide (−) palitantin	Antibacteria (*Enterococcus faecalis* UW 2689, *Streptococcus pneumonia*)	[29]
A. terreus KC 582297	The seaweed	The ethyl acetate extract	*Antimicrobial*	[30]

Endophytic fungi	Isolation source	Metabolites	Biological impact	Ref.
A.terreus (JAS-2)	*Achyranthus aspera*	The ethyl acetate extract	Antibacterial, antifungal and anti-oxidant	[31]
A. terreus	*Ambrosia ambrosoides*	Terrequinon A Terrefuranon Na-Acetyl aszonalemin	Anti-cancer	[32]
A. terreus	*Brickellia* sp.	Dehydrocurvularin 11-methoxycurvularin 11-hydroxycurvularin		
A.japonicus EuR-26	*Euphorbia indica L.*	Improved plant biomass and other growth features under high temperature stress (40◦C)	Modulate host plants growth under heat stress	[33]
A.nomius EF8-RSM	*Aloe vera* Western Ghats of Karnataka India	The ethyl acetate extract	Increases biomass production, increases synthesize different enzymes	[34]
A. iizukae	*Silybum marianum*	Silymarin (Silybin A (1), silybin B (2), and isosilybin A (3))		[35]
A.aculeatus	*Rosa damascena* Mill.	Secalonic acid	Anticancer (TNBC) cells.	[36]
A. tamarii	*Opuntia ficus-indica Mill*	The ethyl acetate extract	Against *Aedes aegypti and Culex quinquefasciatus*	[37]
A.clavatonanicus MJ31	*Mirabilis jalapa L.*	Seven antibiotics	Antimicrobial *(B. subtilis, Micrococccus luteus, S. aureus)*	[38]
A.aculeatinus Tax-6	Taxus yew barks	Taxol	Antitumor	[39]
Aspergillus sp.	*Ficus carica*	The ethyl acetate extract	Antimicrobial *(P. aeruginosa)*	[40]

Table 6.
Endophytic Apergillus sp. producing other biologically active substances.

2.5 Isolation of biologically active endophytic fungus *Aspergillus*

In many plants, the microflora is entirely endophytic fungal. This suggests that endophytic fungi may have a more favorable biological interaction than endophytic bacteria with respect to host plants. The strains of endogenous fungi with active substances are very diverse in both morphology and reproduction, and some strains have very special forms of reproduction.

Identification of *Aspergillus* strains by ITS gene sequencing method and searching on BLAST SEARCH gave similar results as the morphological method, contributing to the confirmation of strains with high biological activity which the subject isolated was *Aspergillus* [16].

Aspergillus spiecies isolated from plants have been shown to be able to produce many secondary metabolites with valuable biological effects such as anticancer, antiviral, antimicrobial compounds. Strains of *Aspergillus* isolated from galangal, turmeric, tangerine, and kumquat plants could produce metabolites with high activity against *S. aureus* and *MRSA*.

Conditions affecting the biological activity of the endophytic fungus Aspergillus

- pH: Importantly affects the growth, metabolism of fungi, enzyme activity, intermediate products, dissociation, dissolution, etc., thus affecting the biosynthesis of active ingredients antibacterial of fungi.

- Temperature: Like other microorganisms, the temperature of the environment also greatly affects the growth and development of fungi.

- Oxygen concentration: Oxygen concentration is very important and necessary for the survival and growth of aerobic microorganisms.

- Carbon source-nitrogen source: The choice of carbon and nitrogen sources greatly affects the activity of secondary substances. Different carbon sources such as dextrose, lactose, sucrose, fructose, starch, molasses and glycerol are believed to be suitable carbon sources for metabolism in various fungi. Organic and inorganic nitrogen sources such as $NaNO_3$, yeast extract, meat extract and soybean meal, NH_4NO_3, $(NH_4)_2SO_4$, etc. can help increase biological activity in fungi [2, 41, 42].

All the optimization was performed based on % inhibition of bacterial growth when challenged with 10 μg/μl metabolite concentration. Among different media used, potato dextrose broth (PDB) and sabouraud's dextrose broth (SDB) proven to be better media for growth of fungus as well as metabolites production 1% yeast extract and 4% dextrose resulted in higher cell inhibition. Ethyl acetate served as good extracting solvent [19].

- Addition of vegetable oil to the environment: Vegetable oil can be used to supplement the carbon source during lovastatin production in *Aspergillus*. Palm oil and soybean oil significantly increased the biomass and lovastatin production of *A. terreus* [43, 44].

- Trace elements: Fe and Zn are necessary for the biosynthesis of some antibiotics. It is possible that these two minerals have a positive effect on the antibiotic biosynthesis of *Aspergillus*.

- Salt concentration: Salt concentration affects the antibacterial activity of *Aspergillus*. For example, strain *A. terreus* has strong antibiotic activity in the range of NaCl salt concentrations from 0 to 1%. When the salt concentration is above 1%, the antibiotic activity of this strain decreases and at a NaCl concentration of 6%, *A. terreus* strain is no longer capable of biologically active substances. *A. terreus* is not only of research interest in terms of antimicrobial activity, but it is well known for its ability to produce lovastatin. According to the study of Pawlak et al. in 2012 on optimal conditions for lovastatin production of *A. terreus,* the authors determined that ventilation is essential for aerobic biological response [45].

Endophytic fungal populations of the genus *Aspergillus* have been isolated from many plants and have been shown to produce a wide range of biologically active substances including antifungal, antibacterial, anticancer, etc. In addition to the characteristics of resistance to *MRSA* and *S. aureus* as published by many studies, some strains of *A. terreus* isolated from soil or from plants have a spectrum of

effects on a number of other bacteria such as *E. coli, P. aeruginosa, Streptococcus faecalis.* This shows the potential to study antibacterial compounds of *Aspergillus*.

2.6 Determination of biological activity of secondary compounds

In the world, there are many studies on the role and application of biologically active substances produced by endogenous fungi. Some endophytic fungal strains have the ability to produce important antibiotics to prevent the invasion of pathogenic organisms to host plants, which are significant in the control of plant diseases and insect pests. Some endogenous fungi are able to synthesize biologically active substances used as anticancer drugs, produce tumor suppressor antibiotics, immunostimulants, and antioxidants, and have biological activities. These compounds mainly belong to the groups of alkaloids, steroids, flavonoids and terpenoid derivatives and other substances, etc. Endogenous fungi also perform a resistance mechanism against plant diseases by producing substance with antibacterial activity. Screening for antimicrobial compounds from endogenous fungi is a way to kill resistant bacteria in humans and plants. In addition, the natural metabolites of endogenous fungi also help to protect natural resources and meet the requirements of pharmaceutical production from plant origin by fermentation. Many biologically active substances are produced by endogenous fungi during growth and development. Finding and discovering those active ingredients is the goal that biopharmaceutical researchers are constantly reaching for.

2.7 The interaction between the host plant and the endophytic fungus *Aspergillus*

There is a complex relationship between endophytic fungi and host plants, the interaction between host and endophytic fungi can be endogenous or symbiotic depending on genetic predisposition, developmental stage, nutritional status and environmental factors.

Commensalism helps the endogenous fungi to survive by being supplied with nutrients without affecting the host plant. Mutual beneficial relationships of endophytic fungi and host plants through the provision of energy, nutrients, shelter as well as protection under environmental stress. On the other hand, endophytic fungi indirectly benefit from host plant growth by producing secondary metabolites that help host plants adapt to abiotic factors such as light, drought and stress such as herbivores, insect and nematode attacks or pathogens.

Schulz and Boyle in 2005, the authors proposed that the endophysis of endophytic fungal is a balanced antagonism between host and endophytic fungi, and provided endogenous virulence and protective capacity of the balanced host plant showed no significant symptoms.

Once the host-endophytic interactions become imbalanced, or disease in the host plant or host defense tissues kills the pathogenic endophytic fungi. Whether the interaction is balanced or unbalanced depends on the host-endophytic condition, virulence of the fungi, host defenses, toxicity, environment, and nutritional status and growth stages of the host plant and endophytic fungi.

Therefore, commensal relationships require a balance between the defense responses of the host plant and the nutritional requirements of the endophytic fungi. In agreement with the 2006 study by Kogel et al., endophytic fungi share structural similarities with pathogens and both have many similar virulence factors, such as production of Metabolites and exoenzymes are required to infect and colonize the host plant, so endophytic fungi are subject to self-recognition, the host

plant can respond to defensive responses as a disease agent. In addition, the cell wall of endogenous fungi is often associated with the production of macromolecular compounds in plants. Thus, endogenous fungi avoid or overcome nonspecific resistance to invasion by programming the invading cells to harbor pathogenic structures and to maintain integrity in the host cell for a long time [4, 46].

3. Conclusion

Isolation of endophytic fungi from medicinal and other plants may result in methods to produce biologically active agents for biological utilization on a large commercial scale as they are easily cultured in laboratory and fermentor instead of harvesting plants and affecting the environmental biodiversity.

Author details

Vo Thi Ngoc My* and Nguyen Van Thanh
Nguyen Tat Thanh University, Ho Chi Minh City, Vietnam

*Address all correspondence to: vtnmy@ntt.edu.vn

IntechOpen

© 2021 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. CC BY

References

[1] Tan RX, Zou WX (2001), "Endophytes: a rich source of functional metabolites", Natural Product Reports, 18, pp. 448 – 459.

[2] Hawksworth DL, Rossman AY (1997), "Where Are All the Undescribed Fungi?", Phytopathology, 87 (9), pp. 888-891.

[3] Strobel G và Daisy B (2003), "Bioprospecting for microbial endophytes and their natural products", *Department of Plant Sciences,* Microbiology and molecular biology, 67(4), pp. 491-502.

[4] Selim KA, El-Beih AA, AbdEl-Rahman TM, El-Diwany AI (2012), "Biology of endophytic fungi", Current Research in Environmental and Applied Mycology, 2(1), pp. 31-82.

[5] Tuntiwachwuttikul P, Taechowisan T (2008), "*Secondary metabolites from Streptomyces sp.*", *SUC1.* Tetrahedron, 64, pp. 7583-7586.

[6] Castillo UF, Strobel G et al. (2000), "Munumbicins, Wide-spectrums antibiotics produced by *Streptomyces* NRRL 30562, endophytic on *Kennedia nigriscans*", Microbiology, 148, pp. 2675 – 2685.

[7] Raviraja NS, Maria GL, Sridhar KR (2006), "Antimicrobial evaluation of endophytic fungi inhabiting medicinal plants of the Western Ghats of India", Engineering In Life Sciences, 6 (5), pp. 515-520.

[8] Tsui TY, Brow GD (1996), "Chromones and Chromanones from Baeckea frutescens", Phytochemistry, 43 (4), pp. 871-876.

[9] Davis EC , Franklin JB , Shaw AJ and Rytas V (2003), "Endophytic Xylaria (Xylariaceae) among liverworts and angiosperms: phylogenetics, distribution, and symbiosis", American Journal of Botany, 90(11), pp. 1661-1667.

[10] Srinivasan K, Jagadish LK (2010), "Antioxidant activity of endophytic fungus *Phyllosticta* sp. isolated from *Guazuma tomentosa*", Journal of Phytology 2 (6), pp. 37-41.

[11] Arora DS, Chandra P (2010), "Assay of antioxidant potential of two *Aspergillus* isolates by different methods under various physio-chemical conditions", Brazilian Journal of Microbiology, 41, pp. 765-777.

[12] Seema D, Sandeep K (2012), "Antioxidant activity of fungal endophytes isolated from salvador oleoides decne", International Journal of Pharmacy and Pharmaceutical Sciences, 4 (2), 380-385.

[13] Thom C, Church MB (1918). "*Aspergillus fumigatus, A. nidulans, A. terreus n.* sp. and their allies", American Journal of Botany, 5 (2), pp. 84-104.

[14] Masayuki M, Katsuya G, Bennett JW (2010), "*Aspergillus*: Molecular biology and genomics", *Caister Academic Press*, pp. 220-238.

[15] Mariana (2013), "Fungal infections *Aspergillus terreus*", *Leading International Fungal Education*, pp. 174-176.

[16] Fatma Abdel-Motaal, Noha Kamel, Soad El-Zayat, Mohamed Abou-Ellail (2020), "Early blight suppression and plant growth promotion potential of the endophyte *Aspergillus flavus* in tomato plant", Annals of Agricultural Sciences, 65, pp. 117-123.

[17] Antonius R. B. Ola, Christina A. P. Soa, YosephSugi, Theo Da Cunha, Henderiana L. L. Belli, Herianus J. D. Lalel (2020), "Antimicrobial metabolite from the endophytic fungi *Aspergillus*

flavus isolated from *Sonneratia alba*, a mangrove plant of Timor- Indonesia", Rasayan J. Chem., 13(1), pp. 377-381.

[18] Darah Ibrahim, Nurhaida, Lim Sheh Hong (2018), "Anti-candidal activity of *Aspergillus flavus* IBRL-C8, an endophytic fungus isolated from *Cassia siamea* Lamk leaf", *Journal of Applied Pharmaceutical Science*, Vol. 8(02), pp. 083-087.

[19] Sadananda TS, Govindappa M, Ramachandra YL, Chandrappa CP, Umashankar T (2016), "*In Vitro* Apoptotic Activity of Endophytic Fungal Lectin Isolated from Endophyte, *Aspergillus flavus of Viscum album* on Human Breast Adenocarcinoma Cell Line (MCF-7)", Metabolomics *6:* 162.

[20] RAJESWARI S., UMAMAHESWARI S., D. ARVIND PRASANTH, RAJAMANIKANDAN K. C. P. (2016), "Bioactive potential of endophytic fungi *Aspergillus flavus* (SS03) against clinical isolates", *International Journal of Pharmacy and Pharmaceutical Sciences*, Vol. 8 (9).

[21] N. Senthilkumar, S. Murugesan, D. Suresh Babu (2014), "Metabolite Profiling of the Extracts of Endophytic Fungi of Entomopathogenic Significance, *Aspergillus flavus* and *Nigrospora sphaerica* Isolated from Tropical Tree Species of India", *Tectona grandis* L., *Journal of Agriculture and Life Sciences,* Vol. 1 (1).

[22] Dipali B. Tribhuvan, Aparna S.Tawre *(*2019), "Antifungal activity of endophyte *Aspergillus flavus* isolated from *Acacia nilotica"*, *International Journal of Current Research*, Vol. 11, (07), pp. 5139-5140.

[23] EDWIN RENE PALENCIA (2012), "Endophytic associations of species in the *Aspergillus section nigri* with maize (*Zea mays*) and peanut (*Arachis hypogea*) hosts and their mycotoxins, *Under the Direction of Charles W. Bacon.*

[24] Lubna, Sajjad Asaf, Muhammad Hamayun, Humaira Gul, In-Jung Lee, Anwar Hussain (2018), "*Aspergillus niger* CSR3 regulates plant endogenous hormones and secondary metabolites by producing gibberellins and indoleacetic acid", Journal of Plant Interactions, 13 (1), pp. 100-111.

[25] Mohamed Shaaban, Hamdi Nasr, Amal Z. Hassan, Mohsen S. Asker (2013), "Bioactive secondary metabolites from endophytic *Aspergillus fumigatus*: Structural elucidation and bioactivity studies", *Rev. Latinoamer. Quím. 41*/1.

[26] Wanggege Qin, Chengxiong Liu, Wei Jiang, Yanhong Xue, Guangxi Wang and Shiping Liu (2019), "A coumarin analogue NFA from endophytic *Aspergillus fumigatus* improves drought resistance in rice as an antioxidant", BMC Microbiology 19:50.

[27] Guerrero, J. J. G., Imperial, J. T., General, M. A., ArenaE. A. A., Bernal, M. B. R. (2020), "Antibacterial activities of secondary metabolites of endophytic *Aspergillus fumigatus*, *Aspergillus* sp. and *Diaporthe* sp. isolated from medicinal plants", Österr. Z. Pilzk*,* 28: 53-61.

[28] Silva, E.M.S.; Silva, I.R.; Ogusku, M.M.; Carvalho, C.M.; Maki, C.S.; Procópio, R.E.L. (2018), "Metabolites from endophytic *Aspergillus fumigatus* and their in vitro effect against the causal agent of tuberculosis", Acta Amazonica 48: 63-69.

[29] Antonius R. B. Olaa,b, Bibiana D Tawoa, Henderiana L. L Bellib, Peter Prokschc, Dhana Tommyc, Euis Holisotan Hakimd (2018), "A New Antibacterial Polyketide from the Endophytic Fungi Aspergillus fumigatiaffinis", *Natural Product Communications,* Vol. 13 (12), pp. 1573-1574.

[30] Suja Mathan, Vasuki Subramanian and Sajitha Nagamony (2013), "Optimization and antimicrobial metabolite production from endophytic

fungi *Aspergillus terreus* KC 582297", Euro. J. Exp. Bio., 3(4):138-144.

[31] Goutam J, Singh S, Kharwar RN, Ramaraj V (2016), "*In vitro* Potential of Endophytic Fungus *Aspergillus terreus* (JAS-2) Associated with *Achyranthus aspera* and Study on its Culture Conditions", Biol Med (Aligarh) 8: 349.

[32] Hedayati MT, Pasqualotto, Warn; Bowyer, Denning (2007),"Aspergillus flavus: human pathogen, allergen and mycotoxin producer"Aspergillus flavus: human pathogen, allergen and mycotoxin producer", Journal of Medical Microbiology, 153 (6), pp. 1677-1692.

[33] Ismail, Muhammad Hamayun, Anwar Hussain, Amjad Iqbal, Sumera Afzal Khan, In-Jung Lee (2018), "Endophytic Fungus Aspergillus japonicus Mediates Host Plant Growth under Normal and Heat Stress Conditions", *BioMed Research International*, Vol. 2018.

[34] Rohit Shankar Mane and Ankala Basappa Vedamurthy (2020), "Physiology of Endophytic *Aspergillus nomius* EF8-RSM Isolated from *Aloe vera* Western Ghats of Karnataka India", Asian Journal of Applied Sciences, 13 (1), pp. 32-39.

[35] El-Elimat T., Raja H.A., Graf T.N., Faeth S.H., Cech N.B., and Oberlies N.H. (2014), "Flavonolignans from *Aspergillus iizukae,* a Fungal Endophyte of Milk Thistle (*Silybum marianum*)", Journal of Natural Products, 77, pp.193-199.

[36] Sadaqat Farooq, Arem Qayum, Yedukondalu Nalli, Gianluigi Lauro, Maria Giovanna Chini (2020), "Discovery of a Secalonic Acid Derivative from *Aspergillus aculeatus*, an Endophyte of *Rosa damascena* Mill.", *Triggers Apoptosis in MDAMB-231 Triple Negative Breast Cancer Cells ACS* Omega, 5, pp. 24296−24310.

[37] Kannan Baskar, Ragavendran Chinnasamy, Karthika Pandy, Manigandan Venkatesan (2020), "Larvicidal and histopathology effect of endophytic fungal extracts of *Aspergillus tamarii* against *Aedes aegypti* and *Culex quinquefasciatus*", Heliyon *6.*

[38] Mishra VK, Passari AK, Chandra P, Leo VV, Kumar B, Uthandi S, et al. (2017), "Determination and production of antimicrobial compounds by *Aspergillus clavatonanicus* strain MJ31, an endophytic fungus from *Mirabilis jalapa L*. using UPLC-ESI-MS/MS and TD-GC-MS analysis", PLoS ONE *12(10).*

[39] Weichuan Qiao, Tianhao T ang, Fei Ling (2020), "Comparative transcriptome analysis of a taxol-producing endophytic fungus, *Aspergillus aculeatinus* Tax-6, and its mutant strain", Scientific Reports, 10:10558.

[40] D. Prabavathy, C. Valli Nachiyar (2011), "Screening and characterisation of antimicrobial compound from endophytic *Aspergillus* sp. isolated from *Ficus carica", Journal of Pharmacy Research*, Vol.4 (6).

[41] Gao, (2007),"Effects of carbon concentration and carbon to nitrogen ratio on the growth and sporulation of several biocontrol fungi", Mycological Research, 111, pp. 87-92.

[42] Pranay J, Ram KP (2010), "Effect of different carbon and nitrogen sources on *Aspergillus terreus* antimicrobial metabolite production", International Journal of Pharmaceutical Sciences Review and Research, 5(3), pp. 72-76.

[43] Sripalakit P, Riunkesorn J, Saraphanchotiwitthaya A (2011), "Utilisation of vegetable oils in the production of lovastatin by *Aspergillus terreus* ATCC 20542 in submerged cultivation", Maejo International Journal of Science and Technology, 5(02), pp. 231-240.

[44] Zaehle C, Gressler M, Shelest E, Geib E, Hertweck C, Brock M (2012), "Microbial transformation of the sesquiterpene lactone tagitinin C by the fungus *Aspergillus terreus*", *Journal of Industrial Microbiology and Biotechnology,* pp. 1214-1216.

[45] Pawlak M, Marcin B (2012), "Kinetic modelling of lovastatin biosynthesis by *Aspergillus terreus* cultivated on lactose and glycerol as carbon sources", Chemical And Process Engineering, 33 (4), pp. 651-665.

[46] Huawei Zhang, Yifei Tang1, Chuanfen Ruan1 and Xuelian Bai (2016), "Bioactive Secondary Metabolites from the Endophytic *Aspergillus* Genus", Rec. Nat. Prod. 10:1, pp. 1-16.

IntechOpen