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REVIEW

Secondary metabolites isolated from fungi of the *Xylaria* genus and their antibacterial properties – a review

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Abstract

Fungi, as living organisms, offer a vast potential for synthesizing natural compounds. Many of these compounds are highly valued as nutraceuticals and pharmaceuticals due to their medicinal properties and economic significance. Fungi are known to produce a wide range of secondary metabolites with bioactive properties, including antimicrobial and antioxidant activities, which contribute significantly to human health and well-being. In an age, when microbial antibiotic resistance increases, searching for new therapies to combat bacterial infections is in demand. Due to their ubiquitous nature, fungi are often chosen as promising candidates in the search for new antimicrobial agents. Among them, the genus *Xylaria* stands out. Widely distributed in subtropical and temperate regions, *Xylaria* species occupy various ecological niches, including decaying wood, living plant tissues as endophytes, and even the guts of termites, making their isolation both challenging and intriguing. This article reviews the literature on antibacterial compounds derived from *Xylaria* species, with a particular focus on those with confirmed antibacterial activity and potential applications in therapeutic protocols.

Keywords

Xylaria; secondary metabolites; antibiotics

1. Introduction

Shortly after the introduction of the first antibiotic into widespread use, the primary antibiotic-resistant microorganisms occurred, while the last decade has brought a significant increase in the proportion of pathogens that are not susceptible to various types of drugs (Roca et al., 2015; Kozińska & Sitkiewicz, 2017; Popowska, 2017). Antimicrobial resistance (AMR) occurs when microorganisms such as bacteria or fungi can adapt and grow in the presence of antibiotics that have inhibited them in the past (Dadgostar, 2019). This is attributed to the development of several novel mechanisms underlying multidrug resistance, which can lead to serious clinical infections, prolonged hospitalization, and increased healthcare expenses (Chandra Deb et al., 2023). Increasing multidrug resistance forces searching the new antibiotic compounds, however, the discovery of new antibiotics has slowed significantly (Xie et al., 2023). The search for new antibiotics extends across a wide range of environments and organisms, including mushrooms. In recent years, these organisms have been rediscovered as valuable sources of diverse and medically significant compounds,

particularly relevant to healthcare and pharmaceutical applications. One notable group of fungi known for their rich production of secondary metabolites is the genus *Xylaria* belonging to Xylariaceae family.

The Xylariaceae family includes 41 already accepted genera (Rogers et al., 2002). However the number of them may be at least 75 (Tang et al., 2009), the largest of which is the genus *Xylaria*. The genus *Xylaria* contains at least 300 species, although, this genus is considered to be composed of over 500 or even 800 species, however, these numbers are not confirmed (Tang et al., 2009; Suwannasai et al., 2023). Xylariaceae commonly occur throughout the temperate, subtropical and tropical regions and are inhabitants of plant organs, like wood, branches, seeds, fruits, leaves, dung and soil. Some of them cause wood decaying and many are phytopathogenic, however, they usually serve as plant debris decomposers. Among them plant endophytes also exist, and some of them are associated with termite or ant nests. Many members of the Xylariaceae, including *Xylaria* spp., are often associated with dry habitats (Fournier et al., 2011; Ma et al., 2022; Ju & Hsieh, 2023; Suwannasai et al.,

2023). Some species of the genus *Xylaria* are difficult to identifying and classifying because they exhibit considerable morphological variations, which means that they often differ in color, size, and also in the overall shape of the stromata (Lee et al., 2000). Living in a natural environment requires fungi to protect their mycelia from infecting by other microorganisms. One of the most important defense mechanisms is the production of antimicrobial compounds. For example, ethanolic extracts of *Xylaria hypoxylon* have been shown to inhibit the growth of certain medically significant bacteria, such as *Bacillus subtilis* ATCC 6633, *B. subtilis* DSMZ 1386, *Enterococcus faecium*, *Listeria monocytogenes* ATCC 7644 and *Staphylococcus aureus* ATCC 25923. However, some microorganisms were not sensitive to this extract e.g., *Candida albicans* DSMZ 1386 or *Escherichia coli* CFAI (Canli et al., 2016). Despite the various susceptibilities of bacteria to *Xylaria*-derived compounds, this genus presents an interesting source for biologically active substances. Substances isolated from *Xylaria* spp. fungi are very diverse in structure, mode of action, and biological effectiveness (Table 1).

Compounds derived from the fungi of the genus *Xylaria* are widely isolated using various chemical methods. Among the procedures of isolation of antimicrobial substances, mostly used are screening methods based on spectroscopic analysis of fungal crude extracts and then chromatographic separation and structural elucidation. The methods used result in the precision of the isolation and the number of the isolated compounds. Research methods used in searching for biologically active compounds should be carefully selected and adapted according to the part of the fungus (e.g. mycelium, stromata, fruiting bodies) used in the laboratory procedures. Most studies begin by culturing fungi on an appropriate medium to obtain mycelium and eventually fructification and sporulation, followed by morphological and molecular identification (Tarman et al., 2011, Ariantari et al., 2023). Bioactive compounds, including antimicrobial or cytotoxic ones, may be found in culture filtrates as well as in crude mycelia. Extraction of the compounds may also be carried from whole fruiting bodies and stromata, which before extraction are usually dried and optionally grounded (Gebreyohannes et al., 2019; Nagam et al., 2021; Fathoni et al., 2022). Methods typically used in testing antimicrobial properties include the disc-diffusion method, agar diffusion test, agar plug method, spectrometric assays, and TLC bioautography.

The *Xylaria* fungi provide a vibrant and diverse range of secondary metabolites with industrial, agricultural, pharmaceutical, and medical applications, such as antimalarial, cytotoxic, anti-inflammatory, antioxidant, anticancer, nematocidal, phytotoxin, antimicrobial, and antifungal (Klaiklay et al., 2012; Sawadstang et al., 2015; Chen et al., 2018). Moreover, they have the ability to produce a variety of antimicrobial constituents, that can affect such hard-to-control bacteria like methicillin-resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli* (Keekan et al., 2022; Zheng, 2018b). Among numerous *Xylaria* spp. strains unidentified to the genus level many of them produce a wide range of bio-compounds, including some described for the first

time or exclusively isolated only from one strain/species. The review aims to present the antibacterial properties of the genus *Xylaria* fungi-produced chemical compounds.

2. Cyclic peptides and other compounds from endophyte *Xylaria* spp.

Peptides are common cell constituents with various roles, from fundamental components to essential physiological compounds, that are necessary for many biochemical processes, including peptide hormones. This makes them interesting as bioactive compounds with a possible antimicrobial use. Nonribosomal peptides represent a unique class of natural products and are of great interest as therapeutic compounds, e.g. as antimicrobials. *Xylaria ellisii*, a leaf and stem endophyte of *Vaccinium angustifolium*, was a source of eight new proline-containing cyclic nonribosomal peptides named ellisiimides A–H. Among them, ellisiimide A presented the moderate antimicrobial activity against *Escherichia coli* BW25113 with the MIC of 100 µg/ml. This activity underscores its potential use against Gram-negative bacteria, a remarkable finding for compounds in this structural class. However, it was not active against *Saccharomyces cerevisiae* B4741 and *Candida albicans* ATCC# 9002. Also other tested ellisiimides C–D did not present any bioactivity against all tested microorganisms (Ibrahim et al., 2020; Xu et al., 2017) presented results on two new cyclic peptides, Xylapeptide A and Xylapeptide B (Table 1), isolated from *Xylaria* GDG-102 strain, which existed as an endophyte of an herbal plant *Sophora tonkinensis*, which is used in traditional Chinese medicine to treat throat and laryngeal diseases (Zhang et al., 2021, Liang et al., 2022). Xylapeptide A exhibited strong antimicrobial activity against *Bacillus subtilis* and *B. cereus*, with a MIC of 12.5 µg/mL. Xylapeptide B exhibited a wider range of antibacterial and antifungal activity than Xylapeptide A (Xu et al., 2022). Growth inhibition was observed in *Bacillus subtilis*, *B. cereus*, *B. megaterium*, *Micrococcus luteus*, *Staphylococcus aureus*, and *Shigella castellani*, with MIC values ranging from 12.5 µg/mL to 6.25 µg/mL depending on the bacterium species. The authors observed a difference in antimicrobial activity, which may be attributed to structural dissimilarities. Specifically, the presence of L-Pipecolic or L-Proline residues in the substance's structure. The identification of these structures was made possible through the use of NMR, MS, and X-ray crystallography.

3. Coumarins, Lactones and compounds with lactone structures

Lactones are cyclic esters widely distributed in nature, with significant importance in food aromas and pharmaceutical applications. They contribute to the primary odor notes in various fruits and are present in over 120 food products (Dufossé et al., 1994). Lactones exhibit diverse biological activities, ranging from antimicrobial to anti-neoplastic effects, depending on their functional groups (Konaklieva & Plotkin, 2005). Coumarins are chemical compounds belonging to the class of benzopyrones, and their basic chemical structure is 1,2-benzopyrone (e.g. benzene fused with α -pyrone lactone).

An Amazonian endophytic fungus, *Xylaria feejeensis* produced a nonenolide compound with lactone ring – xyolide (Table 1) (Baraban et al., 2013). The antimicrobial activity of xyolide was determined against a Chromistan plant pathogen *Pythium ultimum*. The lowest concentration of xyolide with a detectable activity against that phytopathogen was 425 µM. Xyolide represents a new member of the nonenolides – a small class of fungal natural products containing 10-membered lactone rings. Members of this family have diverse bioactivity, including antibacterial, antifungal, herbicidal, and cytotoxic activity (Baraban et al., 2013).

Zhang et al. (2024) isolated 18 compounds from the fungus *Xylaria* sp. Z184, and then evaluated *in vitro* antimicrobial activity of 13 of them against *S. aureus* subsp. *aureus*. Only three of these compounds showed weak activity at a concentration of 100 µM against this bacterium, they were: pestalothiopyrone M (growth inhibition rate of 25.9%), xylariaopyrone A (growth inhibition rate of 31.5%) and xylariaopyrone H (growth inhibition rate of 25.3%).

Quang et al. (2006) isolated from the dried stromata of the fungus *X. intracolorata* the chemical compound 3,5-dimethoxy-2-(6-oxo-5-pentyl-6H-pyran-3-carbonyl)-benzoic acid, known as coloratin A. Its antimicrobial activity was evaluated *in vitro* using the disk-diffusion method, with discs containing 50 µg of the compound, against seven microorganisms species: *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, *S. enteritidis*, *E. coli*, *A. niger* and *C. albicans*. Coloratin A was shown to exhibit potent antibacterial and antifungal activity, comparable to the effectiveness of antibiotics (gentamicin and nystatin) used against these pathogens.

Gan et al. (2023) evaluated the antimicrobial activities of 2 non-lactone compounds from *Xylaria* sp. KYJ-15 – xylarsteroid A, xylarsteroid B, and two lactone compounds xylarglycoside A, and xylarglycoside B (Table 1) against various microorganisms including *B. subtilis*, *E. coli* and *S. aureus*. Xylarglycosides A and B showed significant activity against *B. subtilis* with MIC values of 2 µg/mL, and against *S. aureus* with MIC values of 4 µg/mL (xylarglycoside A) and 2 µg/mL (xylarglycoside B). These results indicate the potential of these compounds as antimicrobial agents.

Various strains of the genus *Xylaria* were tested by many researchers indicating numerous active substances. Depending on strain origin, growth conditions, and isolation methods, as well as, methods used in testing the antimicrobial activity they obtained different results. The compounds extracted by Guo et al. (2018) from a strain of *Xylariales* species belonged to the λ-pyrone and dihydropyrone-2-ones. These compounds were isolated and purified using various chromatographic techniques, including reversed-phase silica gel column chromatography and preparative HPLC. The compounds were named xylariaopyrones A–D (Table 1). They exhibit antimicrobial activity and may inhibit the production and release of bacterial signaling molecules that could support cell-to-cell communication. The antimicrobial activity of these compounds was tested using the well diffusion method. MIC values ranged from 20.5 to

50.6 µg/mL, indicating significant inhibitory activity against the tested microorganism – *Erwinia carotovora* (Guo et al., 2018).

The group of 10 molecules obtained by Mo et al. (2021) included three lactones: 6-heptanoyl-4-methoxy-2H-pyran-2-one, xylarphthalide A, 5-carboxymellein (Table 1). However, their antibacterial activity was not proven in this study. Zheng et al. (2018a) proved the activity of 6-heptanoyl-4-methoxy-2H-pyran-2-one against *E. coli* and *S. aureus*. Xylarphthalide A, 5-carboxymellein, and 5-methymellein were obtained from the *Xylaria* sp. GDG-102 in a study conducted by Zheng et al. (2018b) (Table 1). All these three substances exhibited antimicrobial activity against *S. aureus*, *B. subtilis*, *B. megaterium*, *E. coli*, and *S. dysenteriae*.

Other lactone compounds, myrotheciumone A and (3aS,6aR)-4,5-dimethyl-3,3a,6,6a-tetrahydro-2H-cyclopenta[b]furan-2-one, were isolated from *X. curta* E10 strain (Table 1). Their antimicrobial activity was tested against *S. aureus* NBRC 13276 and *P. aeruginosa* ATCC 15442 by disc-diffusion method, showing moderate activity against selected bacteria at a concentration of 100 µg/disk (Tchoukoua et al., 2017).

An endophyte *Xylaria curta* YSJ-5 isolated from *Alpinia zerumbet* resulted in two α-pyrone derivatives xylarpyrones A–B. One of them, 6-pentyl-4-methoxy-pyran-2-one, displayed significant antibacterial activity against *Staphylococcus aureus* and methicillin-resistant *S. aureus* with minimal inhibitory concentration value of 6.3 µg/mL (Wei et al., 2024).

Coumarins represent a highly promising class of bioactive heterocyclic compounds, synthesized through various biosynthetic pathways. A fungus *Xylaria* sp. YX-28 was a source of the chemical compound 7-amino-4-methylcoumarin. Its antimicrobial activity was evaluated against group of microorganisms, such as *S. aureus*, *E. coli*, *S. typhi*, *S. typhimurium*, *S. enteritidis*, *Shigella* sp., *Aeromonas hydrophila*, *Yersinia* sp., *Vibrio anguillarum*, *V. parahaemolyticus*, *C. albicans*, *P. expansum* and *Aspergillus niger*. The efficacy of 7-amino-4-methylcoumarin was compared with three antibiotics: ampicillin, tetracycline and gentamicin. The compound showed a broader spectrum of antimicrobial activity compared to the reference antibiotics. 7-amino-4-methylcoumarin showed the highest efficacy against *A. hydrophila* (MIC value: 4 ± 0.45 µg/ml), *Shigella* sp. (MIC: 6.3 ± 0.28 µg/ml) and *S. enteritidis* (MIC: 8.5 ± 0.46 µg/ml) (Liu et al., 2008).

Yang et al. (2022) isolated eight α-pyrone derivatives from the fungus named “*Xylariales* sp. (HM-1)”, five of which were new compounds, designated as xylariaopyrones E–I. The α-pyrone structure is characteristic for coumarin ring system. The antimicrobial activity of these compounds was evaluated against four bacterial strains: *Erwinia carotovora* subsp. *carotovora*, *E. coli*, *S. aureus* and *P. aeruginosa*. Streptomycin was used as a positive control. Three of the new compounds, xylariaopyrones E–G, showed moderate activity against three of tested bacteria, namely – *E. coli*, *S. aureus* and *P. aeruginosa*, with MIC values in the range of 25.4–64.5 µg/ml. In contrast, all the tested compounds showed a weak activity against *E. carotovora* subsp. *carotovora*.

Another compound, 7-amino-4-methylcoumarin (Table 1) was isolated from the endophytic fungus *Xylaria* sp. YX-28 (Liu et al., 2008). The compound showed strong antibacterial activity against *S. aureus*, *E. coli*, *Salmonella typhi*, *S. typhimurium*, *S. enteritidis*, *Aeromonas hydrophila*, *Yersinia* sp., *Shigella* sp., *Vibrio anguillarum*, and *V. parahaemolyticus*. It also presented antifungal activity against *Candida albicans*, *Penicillium expansum*, and *Aspergillus niger*. The MIC value of the compound against all microorganisms ranged from 4 to 40 µg/mL, giving hope for its use in treating food-borne diseases. Authors, Liu et al. (2008), also suggested its potential application as a substance to combat food spoilage.

4. Polyketides

Polyketides are a diverse class of natural products synthesized by polyketide synthases through iterative condensation of simple acyl units, primarily derived from acetic acid (Hertweck, 2009; Baerson & Rimando, 2007). These compounds exhibit a wide range of biological activities and have significant pharmaceutical importance (Baerson & Rimando, 2007). The structural diversity of polyketides arises from complex biosynthetic mechanisms involving various enzymatic modifications. They are produced by various organisms, including bacteria, fungi, plants, and animals. These compounds often serve as novel structures for use as antibiotics (Hertweck, 2009).

In a study of Rakshith et al. (2016), they isolated the polyketide compound 3-O-methylcellin from the fungus *Xylaria sidii* FPL-52(S). The antimicrobial activity of this compound was evaluated using the disk-diffusion method and the broth microdilution method. 3-O-methylmellein exhibited a broad spectrum of antimicrobial activity, including both Gram-positive and Gram-negative bacteria, as well as antifungal activity. The highest efficacy was observed against the bacteria *B. subtilis*, *E. coli*, *S. flexneri* and *P. aeruginosa* (MIC: 6.25 µg/ml). In addition, 3-O-methylmellein showed significantly stronger antifungal activity than the reference compounds (nystatin and miconazole) against all tested fungal strains: *A. fumigatus*, *A. niger*, *F. verticillioides* (MIC: 1.56 µg/ml), *A. flavus* (MIC: 3.12 µg/ml), *M. canis* and *M. gypseum* (MIC: 0.39 µg/ml), *C. albicans* (MIC: 0.78 µg/ml) and *F. oxysporum* (MIC: 6.25 µg/ml).

Seven new polyketides were isolated from the endophytic fungus *Xylaria* sp. NCY2, isolated from the medicinal plant *Torreya jackii*, seven new polyketides were isolated: 1-(xylarenone A) xylariate A, xylarioic acid B, xylariolide A, xylariolide B, xylariolide C, methyl xylariate C, and xylariolide D, also with taiwapyrone which was previously described in literature was also isolated. Antitumour and antimicrobial studies performed on the isolated compounds showed their antimicrobial activity against *Escherichia coli* ATCC 25922, *Bacillus subtilis* ATCC 9372 and *Staphylococcus aureus* ATCC 25923, with minimum inhibitory concentrations (MIC) values above 10 mg/ml. In contrast, the compounds showed no effect on the growth of yeasts such as *S. cerevisiae* ATCC 9763 and *Candida albicans* As 2.538, at concentrations of 10 mg/ml. MIC determination was carried

out by the microtiter method using 96-well plates, incubating the bacteria in media containing different concentrations of the test compounds (Hu et al., 2010).

Another *Xylaria*-originated polyketide compound, coriloxin (Table 1), is a secondary metabolite isolated from an unidentified species of *Xylaria* sp. NBRTSB20 by Nuthan et al. (2020), that showed antimicrobial activity against several microorganisms. MICs were determined against Gram-negative bacteria such as *P. aeruginosa* and *E. coli*, and Gram-positive bacterium *S. aureus*. MIC values ranged from 0.195 to 1.56 µg/mL for *S. aureus* and 0.390–1.56 µg/mL for Gram-negative bacteria. The efficacy of the compound was compared to gentamicin (MIC 0.048–0.781 µg/mL). The hemolytic activity of coriloxin was also evaluated and showed no hemoglobin leakage even at concentrations above the MIC, indicating low systemic toxicity.

Endophytic fungus *X. curta* E10 was a source of eleven new dimeric chromanones (Wei et al., 2022). The absolute configurations of these compounds were determined using experimental spectroscopic methods, single crystal X-ray diffraction, and equivalent circulating density (ECD) calculations. During the antimicrobial activity tests, polyketide compounds designed as peacillin L and paecillin N (Table 1) exhibited antimicrobial activity against the Gram-negative bacterium *E. coli*, with a MIC value of 16 µg/mL (Tchoukoua et al., 2017). This strain, *X. curta* E10, was also the source of two new cytochalasins, curtachalasin A and curtachalasin B. Cytochalasins are fungal-derived natural compounds with a perhydro-isoindolone core fused with a macrocyclic ring, included into polyketide group. Typically, they present a wide spectrum of bioactivity and a high structural diversity. Both compounds, curtachalasin A and B, were tested for antimicrobial activity against various bacteria and fungi. In an experiment conducted by Wang et al. (2018), these compounds showed weak activity at a concentration of 200 µM against the fungus *M. gypseum* with an inhibition rate of $70.3 \pm 0.4\%$, for curtachalasin A, and $68.4 \pm 0.7\%$ for curtachalasin B. These compounds did not show antibacterial activity against the tested bacteria.

Polyketide – xylarophilone from the isolate *Xylaria* sp. GDG-102 exhibited antimicrobial activity against seven bacterial species: *B. subtilis*, *B. megaterium*, *S. aureus*, *B. anthracis*, *Shigella dysenteriae*, and *E. coli* (Mo et al., 2021).

5. Alkaloids and their derivatives

Xylaria sp. DAP KRI-5 was a source of another bioactive compound – cytochalasin D (Table 1). The antibacterial activity of cytochalasin D was evaluated using two Gram-positive bacteria (*S. aureus*-InaCC B4 and *B. subtilis*-InaCC B1) and two Gram-negative bacteria (*E. coli*-InaCC B5 and *P. aeruginosa*-InaCC B3). The minimum inhibitory concentration (MIC) of cytochalasin D against the tested bacteria was determined to be 2 µg/ml for *S. aureus*, 4 µg/mL for *B. subtilis*, 8 µg/ml for *E. coli*, and 32 µg/ml for *P. aeruginosa*. The antibacterial activity of cytochalasin D was compared to commercial antibiotics, including chloramphenicol, streptomycin, and vancomycin, showing comparable or better activity of that compound against the tested bacteria (Fathoni & Augusta, 2019).

The antimicrobial activity of compounds isolated from the fungus *Xylaria* sp. PSU-F100 by Rukachaisirikul et al. (2009) was evaluated against *S. aureus* and a methicillin-resistant strain (MRSA). All compounds isolated from that *Xylaria* strain showed MIC activity against both bacterial strains at the level of 200 µg/mL, which means that they have low activity against these bacteria. The crude extract showed weaker, than single compounds, activity against tested microorganisms. The activity towards *S. aureus* was 320 µg/mL and it was without activity against MRSA. The main compound of this study was xylarisin, an alkaloid compound included in the group of cytochalasins, which usually presented good or even strong antimicrobial activity (Fathoni & Augusta, 2019; Mo et al., 2021).

Xylaria longipes was another source of antimicrobial substances – high conjugation alkaloids – xylaridines A and B, obtained as racemates from that fungus. Xylaridin A showed weak antibacterial activity against *P. aeruginosa* with MIC of 128 µg/ml, xylaridin B showed weak antibacterial activity against *Salmonella enterica* with MIC of 93 µg/ml. Authors also proposed a biosynthetic pathway with individual biosynthetic steps, which also may be a source of substances with potential antimicrobial activity (Li et al., 2019).

Xylaria sp. GDG-102, when cultivated on rice medium or in potato dextrose broth (PDB), produced a variety of novel compounds. Among these, two exhibited notable antimicrobial activity: the alkaloid cytochalasin K and 2-methoxy-6-methyl-1,4-benzoquinone (Table 1). These compounds demonstrated antimicrobial effects against seven bacterial species, including *B. subtilis*, *B. megaterium*, *S. aureus*, *B. anthracis*, *Shigella dysenteriae*, and *E. coli* (Xu et al., 2017; Mo et al., 2021).

6. Terpenoids

Terpenoids, a largest class of natural compounds, play crucial roles in various aspects of human life, from pharmaceuticals to perfumes (Sell, 2003). These molecules are classified based on their carbon content, ranging from monoterpenes (C₁₀) to sesterterpenes (C₂₅) (Wang et al., 2005). Terpenoids exhibit diverse biological activities, including anticancer, antimalarial, and anti-inflammatory properties (Huang et al., 2012).

Three new sesquiterpenoids – xylarenone A and B and xylarenic acid were isolated from the fungus *Xylaria* sp. NCY2. These compounds inhibited bacterial growth at a concentration of 50 mg/ml against *E. coli*, *B. subtilis* and *S. aureus*. The test of activity against yeast did not show the effectiveness of these compounds. The fungus was isolated from *Torreya jackii*, a conifer plant of the family Taxaceae, for which *Xylaria* sp. NCY2 is an endophytic fungus (Hu et al., 2008).

Four new triterpenoid glycosides, named kolokosides A–D, isolated from the fungus *Xylaria* sp. (MYC-1736). Kolokoside A showed antimicrobial activity against *B. subtilis* (ATCC 6051) and *S. aureus* (ATCC 29213) indicated by diffusion-disk tests with a dose of 200 µg/disk. The inhibition zones achieved diameters of 16 and 12 mm, respectively,

after 48 hours of incubation. However, no activity of kolokoside B was observed in these tests. Kolokosides A and B were also tested for activity against *E. coli* (ATCC 25922) and *Candida albicans* (ATCC 14053) at the same concentration, and both were inactive (Deyrup et al., 2007). Other sesquiterpenoid compounds, also with no antimicrobial activity were isolated from *Xylaria curta* YSJ-5 from *Alpinia zerumbet*. This group of compounds included xylarcurenes A–E, one norsesquiterpene xylarcurene F. Despite they presented no antimicrobial activity, they still present a potential in other types of biological activity (Wei et al., 2024).

Xylaria sp. SNB-GTC250, an endophytic fungus obtained from leaves of *Bisboecklera microcephala* was the source of two isopimarane diterpenoids, xylabisboeins A and B, both new to the literature. For this fungus, it was shown that ethyl acetate extract from its cultures exhibited significant antibacterial activity against *S. aureus* (MIC = 8 µg/ml). Both new compounds, xylabisboeins A and B, exhibited antimicrobial activity with MIC at concentration of above 128 µg/ml against *S. aureus*, *Trichophyton rubrum* and *Candida albicans* (Sorres et al., 2015).

Xylaria hypoxylon was a source of sesquiterpene – eremoxylarin D, F, G, and I (Table 1) (Miral et al. 2023). They were evaluated against Gram-positive bacteria, including *S. aureus* (MRSA) and *S. epidermidis*. The minimum inhibitory concentration (MIC) for these compounds ranged from 0.39 to 12.50 µg/ml. Eremoxylarin I showed the strongest activity against Gram-positive bacteria – its MIC ranged from 0.39 to 1.56 µg/ml. In contrast, Gram-negative bacteria, i.e. *E. coli* and *P. aeruginosa*, were insensitive to the compounds. Eremoxylarin D showed the weakest effect, which may be related to its structure, as it was characterized by the shortest aliphatic chain, which may be directly related to the correlation between aliphatic chain length and antimicrobial activity of these compounds (Miral et al., 2023).

Lin et al. (2016) investigated the antimicrobial activity of compounds isolated from the endophytic fungus *Xylaria* sp. against *E. coli*, *B. subtilis*, and *S. aureus*. The antimicrobial activity was evaluated by measuring the percentage decrease in optical density of the suspension at 560 nm after incubation of the microorganisms for 18 hours. The final concentration of the drug solutions was 50 µg/ml. A monoterpene compound 3,7-dimethyl-9-(2,2,5,5-tetramethyl-1,3-dioxolan-4-yl)nona-1,6-dien-3-ol (Table 1), belonging also to the alcohols, showed strong inhibitory activity against three strains (*B. subtilis*, *B. pumilus*, *S. aureus*), and indicating its potential use in the treatment of these microorganisms. On the other hand, another compound, nalgiovensin (Table 1), exhibited strong inhibition against *B. subtilis*, with a 48.1% of the decrease in bacterial growth (Lin et al., 2016).

Xylaria sp. GDG-102 grown on a rice medium resulted in production a terpenoid compound – xylareremophil. Xylareremophil was tested in an experiment presented by Liang (2019) and was found to inhibit the growth of *Micrococcus luteus* and *Proteus vulgaris*.

7. Other compounds and crude extracts

Xylaria sp. FPL-25(M) was a source of xylobovid 9-methyl ester (Rakshith et al., 2020). The antimicrobial activity of this compound was evaluated by the disc diffusion method against a panel of human and phytopathogenic bacteria. The ethyl acetate extract of *Xylaria* sp. FPL-25(M) was tested at a concentration of 100 µg/disc and the zone of inhibition was measured against gentamicin and nystatin used as controls. The microorganisms tested included both Gram-positive and Gram-negative bacteria, as well as some fungi species. The study showed that the compound exhibited a broad spectrum of antimicrobial activity, with Gram-positive bacteria and fungi being more susceptible than Gram-negative bacteria. However, the activity of the crude extract was lower than in controls, usually close to half of them. The difference could come from the inadequate (not comparable concentrations to control antibiotics) of the active compounds in the tested extract. Among Gram-positive bacteria well controlled by tested extract were: *B. subtilis*, *Listeria monocytogenes*, *S. aureus*, and *Staphylococcus epidermidis*. In the case of Gram-negative bacteria, satisfactory inhibition zones were obtained for *Vibrio parahaemolyticus*, *Shigella flexneri*, and *E. coli*. Other tested bacteria, *Salmonella typhi*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *P. aeruginosa* were controlled less effectively. The better activity of the crude acetate extract was observed against tested fungi *Aspergillus flavus*, *A. fumigatus*, *A. niger*, *Candida albicans*, *Fusarium moniliforme*, *Microsporium canis*, and *M. gypseum*. The extract was more efficient than nystatin and miconazole. The last compound was almost not effective against tested fungi. The experiment showed the new source of antifungal compounds, mostly xylobovid 9-methyl ester (Table 1), which was detected as the main active compound of the extract. This suggests that the compound may have potential as a new bioactive molecule with a broad antimicrobial properties.

Another *Xylaria* sp. compound was helvolic acid. Its antimicrobial activity was evaluated by Ratnaweera et al. (2014) against Gram-positive bacteria such as *B. subtilis* and *S. aureus*. MIC value of helvolic acid towards *B. subtilis* was 2 µg/ml and against *S. aureus* – 4 µg/ml, while the MIC of the positive controls, polymyxin B and rifamycin, were 8 µg/ml and 0.015 µg/ml respectively. This result indicates good efficacy of helvolic acid against *B. subtilis*. Studies have shown a possible mechanism of action of helvolic acid on bacteria by destroying the cell membrane of the microorganism, leading to inhibition of basic cellular processes and ultimately death. This means that helvolic acid shows significant inhibitory activity for *B. subtilis* and for *S. aureus*, and may be used to keep under control these bacteria (Ratnaweera et al., 2014).

A *Xylaria* sp. strain unidentified to the species level was investigated by Sun et al. (2017). It was the source of 5,8-epidioxyergosta-6,22E-diene-3-ol (Table 1). The compound showed antimicrobial activity against 3 of the 7 microorganisms tested. The alcoholic compound showed activity against *E. coli*, *Pseudomonas putida*, and *Kocuria rhizophila* with

MIC values of 3.13, 1.56 and 6.25 µM, respectively. As a positive control served ciprofloxacin, which showed slightly better efficacy with concentrations 0.39, 0.78, and 1.56 µM.

Yu et al. (2019) extracted four compounds from the fungus *Xylaria* sp. HDN13-249: penixylarin B, penixylarin C, 1,3-dihydroxy-5-(12-hydroxyheptadecyl)benzene, and 1,3-dihydroxy-5-(12-sulfoxyheptadecyl)benzene (Table 1). These compounds were tested as potential antibacterial agents against three bacteria species, *Mycobacterium phlei*, *B. subtilis*, and *Vibrio parahaemolyticus*. The minimal inhibitory concentrations (MIC) of these substances ranged from 6.25 to 100 µM. However, the most significant activity presented penixylarin C against *M. phlei*, indicating its potential use in the treatment of tuberculosis.

The antimicrobial activity of 1-(xylarenone A)xylariate A was evaluated by Hu et al. (2010) using the microdilution method in broth (Table 1). Minimum inhibitory concentrations (MICs) were determined against a panel of microorganisms including Gram-positive bacteria such as *S. aureus* and *B. subtilis*, and Gram-negative bacteria such as *E. coli* and *P. aeruginosa*. MIC values for this compound ranged from 16 to 64 µg/mL, indicating moderate antimicrobial activity against three of the four pathogens: *E. coli*, *B. subtilis*, and *S. aureus*.

Ramesh et al. (2015) conducted a study on the antimicrobial activity of an extract from *Xylaria* sp. R006. Its activity was evaluated *in vitro* using the disk-diffusion method against 10 strains of *S. aureus* and 8 strains of *P. aeruginosa*. The extract showed stronger activity against all *S. aureus* strains compared to the reference antibiotics (penicillin, methicillin and vancomycin), with the highest efficacy observed for strains 1 and 6 (MIC value: 75 µg/ml). Similarly, the extract showed stronger antimicrobial activity against *P. aeruginosa* than the four antibiotics tested (cefotaxime, ciprofloxacin, ofloxacin and amikacin), with the highest efficacy against strain 3 (MIC value: 70 µg/ml).

The antimicrobial activity of compounds isolated from *Xylaria feejeensis* was evaluated by microdilution assays against various microorganisms, including *B. subtilis* and methicillin-resistant *S. aureus* (MRSA). Good inhibitory properties were found for integric acid (Table 1). MIC values for this compound were determined to be 16 µg/ml for *B. subtilis* and 64 µg/ml for MRSA, while the positive control was ciprofloxacin used in dose 10 µg/disc (Rajendran et al., 2023). However in earlier tests of Srisapoomi et al. (2015), the integric acid presented a weak antimicrobial activity against Gram-positive bacteria – *B. subtilis* ATCC 6633, *S. saprophyticus* ATCC 15305, *S. aureus* ATCC25923, MRSA DMST 20654, and *E. faecalis* ATCC 29212. Nevertheless, the compound was efficient against the malarial parasite *Plasmodium falciparum* K1 with IC₅₀ value of 6.91 µM.

In a study by Keekan et al. (2022), the acetone extract of *X. longipes*, was subjected to thin-layer chromatography (TLC) separation and bioautography, which showed strong activity against MRSA at the level of R_f = 0.69 ± 0.28. The bioactive compound present in this point of TLC was partially characterized by FTIR spectroscopy (Fourier-transform infrared spectroscopy) and liquid chromatography

coupled to mass spectrometry (LC-MS/MS), suggesting that the activity against MRSA may be due to integric acid, eremoxylarin C or a related compound.

Xylaranic acid isolated from *Xylaria primorskensis* was tested for antimicrobial activity against bacteria – *S. aureus*, *S. typhi*, and *S. flexneri*. In addition, to enhance the antimicrobial activity, silver nanoparticles were synthesized in combination with xylaranic acid, which enhanced the targeted antimicrobial activity. Both xylaranic acid and xylaranic acid silver nanoparticles (AgNPs) showed better activity than gentamycin, which served as a positive control (Adnan et al., 2018).

Xylaria cubensis PSU-MA34 was used as a source of metabolites to be used against *S. aureus* and its methicillin-resistant MRSA strain (Klaiklay et al., 2012). The compound, 2-chloro-5-methoxy-3-methylcyclohexa-2,5-diene-1,4-dione, presented the MIC value to be 128 µg/ml, on the contrary, vancomycin's MIC was 1 µg/ml. From the study, it can be concluded that 2-chloro-5-methoxy-3-methylcyclohexa-2,5-diene-1,4-dione has even less than mild activity against both bacteria (Klaiklay et al., 2012).

The endophytic fungus *Xylaria* sp. SNB-GTC2501 isolated from leaves of *Bisboeckelera microcephala* was a source of three previously described substances, (-)-5-methylmellein, mellein-5-carboxylic acid and ergosterol peroxide. The MIC of the substances in each case was above 128 µg/ml against *S. aureus*, *Trichophyton rubrum* and *Candida albicans*, which may suggest the formation of unknown interactions causing an increased antimicrobial effect (Sorres et al., 2015).

One approach that may accelerate new antimicrobial molecules discovered put forward by Gokhale et al. (2017) was a study of bioactive molecules of the endophytic fungus *Xylaria* sp. from *Nyctanthes arbor-tristis*. In this study, eleven compounds from the fungal extract were identified. The crude *Xylaria*-extract showed strong inhibitory activity against three pathogenic bacteria: *Micrococcus luteus* (68.2 mm clear zone), *Citrobacter freundii* (59.16 mm clear zone) and *Chromobacterium violaceum* (39.96 mm clear zone). These new substances detected by GC-MS, can be the start for further studies, in which the antibacterial or antimicrobial effects of individual substances that are part of the extract, may be determined (Gokhale et al., 2017).

8. A termite derived *Xylaria escharoidea* compounds

The crude extract of *Xylaria escharoidea*, obtained from termite *Macrotermes barneyi*, was tested against pathogenic bacteria and fungi (Nagam et al., 2021). The compound 4,8-dihydroxy-3,4-dihydronaphthalene-1(2H)-one (Table 1), isolated from the extract, exhibited good antimicrobial activity at a dose of 6.25 µg against bacteria *P. aeruginosa*, *S. aureus*, and *B. subtilis*. It was also able to inhibit pathogenic fungus *C. albicans*. The mode of action of that compound was due to the clear interaction with key residues on protein A (agrA C), which regulates the helper gene, confirming its antimicrobial activity (Nagam et al., 2021).

Table 1 Compounds with antimicrobial activity derived from various species and strains of the genus *Xylaria*.

Fungal species	Compound	Susceptible bacteria	Source
1	2	3	4
<i>Xylaria cubensis</i> PSU-MA34	2-chloro-5-methoxy-3-methylcyclohexa-2,5-diene-1,4-dione	<i>S. aureus</i> , MRSA	Klaiklay et al., 2012
<i>Xylaria curta</i>	Paecilin L	<i>E. coli</i> , <i>S. eternitidis</i>	Wei et al., 2022
	Paecilin N	<i>E. coli</i> , <i>S. eternitidis</i>	
	Myrotheciumone A	<i>S. aureus</i> , <i>P. aeruginosa</i>	
	(3as,6ar)-4,5-dimethyl-3,3a,6,6a-tetrahydro-2Hcyclopenta [b]furan-2-one	<i>S. aureus</i> , <i>P. aeruginosa</i>	Tchoukoua et al., 2017
<i>Xylaria ellisii</i>	Ellisiamide A	<i>E. coli</i>	Ibrahim et al., 2020
<i>Xylaria escharoidea</i>	4,8-dihydroxy-3,4-dihydronaphthalen-1(2H)-one	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>B. subtilis</i>	Nagam et al., 2021
<i>Xylaria feejeensis</i>	6',7'-didehydrointegric acid	<i>B. subtilis</i> , <i>S. saprophyticus</i> , <i>S. aureus</i> , MRSA, <i>E. faecalis</i>	Srisapoomi et al., 2015 Rajendran et al., 2023
	Xylolide	<i>P. ultimum</i>	Baraban et al., 2013
<i>Xylaria hypoxylon</i>	Eremoxylarins D, F, G, I	<i>S. aureus</i> , MRSA, <i>S. epidermidis</i>	Miral et al., 2023
<i>Xylaria intracolorata</i>	Coloratins A	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>K. pneumoniae</i> , <i>S. enteritidis</i> , <i>E. coli</i>	Quang et al., 2006

Table 1 Compounds with antimicrobial activity derived from various species and strains of the genus *Xylaria* (cd.).

1	2	3	4
<i>Xylaria longipes</i>	Eremoxylarin C	<i>S. aureus</i>	Keekan et al., 2022
	Integric acid		Rajendran et al., 2023
	Xylaridin A Xylaridin B	<i>P. aeruginosa</i> , <i>Salmonella enterica</i>	Li et al., 2019
<i>Xylaria primorskensis</i>	Xylaranic acid	<i>S. aureus</i> , <i>S. typhi</i> , <i>S. flexneri</i>	Adnan et al., 2018
<i>Xylaria sidii</i> FPL-52(S)	3-O-methylcellin	Gram-positive and Gram-negative bacteria <i>B. subtilis</i> , <i>E. coli</i> , <i>Shigella flexneri</i> , <i>P. aeruginosa</i> <i>Aspergillus fumigatus</i> , <i>A. niger</i> , <i>A. flavus</i> , <i>Fusarium verticillioides</i> , <i>F. oxysporum</i> , <i>Microsporium canis</i> , <i>M. gypseum</i> , <i>Candida albicans</i>	Rakshith et al., 2016
Strains of <i>Xylaria</i> spp.	Xylariaopyrones A-D	<i>Erwinia carotovora</i>	Guo et al., 2018
	Xylariaopyrones E-G	<i>E. coli</i> , <i>S. aureus</i> and <i>P. aeruginosa</i>	Yang et al., 2022
	Nalgiovensin	<i>S. aureus</i> , <i>B. subtilis</i> , <i>B. pumilus</i> , <i>E. coli</i>	Lin et al., 2016
	3,7-dimethyl-9-(-2,2,5,5-tetramethyl-1,3-dioxolan-4-yl)nona-1,6-dien-3-ol	<i>B. subtilis</i> , <i>B. pumilus</i> , <i>S. aureus</i>	Lin et al., 2016
	Helvolic acid	<i>B. subtilis</i> , MRSA	Ratnaweera et al., 2014
	5,8-epidioxy-ergosta-6,22E-diene-3-ol	<i>E. coli</i> , <i>Pseudomonas putida</i> , <i>Kocuria rhizophila</i>	Sun et al., 2017
<i>Xylaria</i> sp. DAP KRI-5	Cytochalasin D	<i>S. aureus</i> , <i>B. subtilis</i> , <i>E. coli</i> , <i>P. aeruginosa</i>	Fathoni & Agusta, 2019
<i>Xylaria</i> sp. FPL-25	Xylobovide 9-methyl ester	<i>B. subtilis</i> , <i>L. monocytogenes</i> , <i>S. aureus</i> , <i>S. epidermidis</i> , <i>E. coli</i> , <i>E. aerogenes</i> , <i>K. pneumonia</i> , <i>P. mirabilis</i> , <i>P. aeruginosa</i> , <i>S. flexneri</i> , <i>S. typhi</i> , <i>V. parahaemolyticus</i> , <i>X. campestris</i>	Rakshith et al., 2020
<i>Xylaria</i> sp. GDG-102	Xylapeptide A	<i>Bacillus subtilis</i> and <i>B. cereus</i>	Xu et al., 2017
	Xylapeptide B	<i>B. subtilis</i> , <i>B. cereus</i> , <i>B. megaterium</i> , <i>Micrococcus luteus</i> , <i>Staphylococcus aureus</i> , and <i>Shigella castellani</i>	Xu et al., 2017
	Cytochalasin K	<i>S. aureus</i> , <i>E. coli</i>	Mo et al., 2021
	Xylariphilone	<i>B. megaterium</i>	
	2-methoxy-6-methyl-1,4-benzochinon	<i>B. subtilis</i> , <i>B. megaterium</i>	
	6-heptanoyl-4-methoxy-2H-pyran-2-one	<i>E. coli</i> , <i>S. aureus</i>	Zheng et al., 2018a
	Xylareremophil	<i>M. luteus</i> , <i>P. vulgaris</i>	Liang et al., 2019
	Mairetolides B		
	Mairetolides G		
	Xylarphthalide A	<i>S. aureus</i> , <i>E. coli</i> , <i>S. dysenteriae</i>	Zheng et al., 2018b
	(-)-5-carboxymellein		Sorres et al., 2015
	(-)-5-methylmellein (also from <i>Xylaria</i> sp. SNB-GTC2501)		
	xylarophilone	<i>B. subtilis</i> , <i>B. megaterium</i> , <i>S. aureus</i> , <i>B. anthracis</i> , <i>Shigella dysenteriae</i> , <i>E. coli</i>	Mo et al., 2021

Table 1 Compounds with antimicrobial activity derived from various species and strains of the genus *Xylaria* (cd.).

1	2	3	4
<i>Xylaria</i> sp. GDGJ-77B	Xylarchalasin B	<i>B. subtilis</i> , <i>E. coli</i>	Xu et al., 2022
<i>Xylaria</i> sp. Z184	pestalothiopyrone M xylariaopyrone A xylariaopyrone H	<i>S. aureus</i> subsp. <i>aureus</i>	Zhang et al., 2024
<i>Xylaria</i> sp. HDN13-249	Penixylarin B Penixylarin C 1,3-dihydroxy-5-(12-hydroxyheptadecyl)benzene 1,3-dihydroxy-5-(12-sulfoxyheptadecyl)benzene (R)-(2)-mellein methyl ether (R)-(2)-5-carboxymellein (R)-(2)-5-hydroxymethylmellein (4) 6-[(1R)-1-hydroxypentyl]-4-methoxy-2H-pyran-2-one (2E,4S)-2,4-dimethyloct-2-enoic acid Piliformic acid	<i>Mycobacterium phlei</i> , <i>B. subtilis</i> , <i>Vibrio parahemolyticus</i>	Yu et al., 2019
<i>Xylaria</i> sp. KYJ-15	Xylarsteroid A Xylarsteroid B Xylarglycosides A Xylarglycosides B	<i>B. subtilis</i> <i>B. subtilis</i> , <i>E. coli</i> , <i>S. aureus</i>	Gan et al., 2023
<i>Xylaria</i> sp. NBRTSB-20	Coriloxin	<i>E. coli</i> , <i>S. aureus</i>	Nuthan et al., 2020
<i>Xylaria</i> sp. NCY2	1-(xylarenone A)xylariate A	<i>E. coli</i> , <i>B. subtilis</i> , <i>S. aureus</i>	Hu et al., 2010
<i>Xylaria</i> sp. PSU-F100	Xylarisin	<i>S. aureus</i> , MRSA	Rukachaisirikul et al., 2009
<i>Xylaria</i> sp. YX-28	7-amino-4-methylcoumarin	<i>S. aureus</i> , <i>E. coli</i> , <i>S. typhia</i> , <i>S. typhimurium</i> , <i>S. enteriditis</i> , <i>A. hydrophila</i> , <i>Yersinia</i> sp., <i>Vibrio anguillarum</i> , <i>Shigella</i> sp., <i>V. parahaemolyticus</i>	Liu et al., 2008
<i>Xylaria</i> sp. (MYC-1736)	Kolokoside A	<i>B. subtilis</i> (ATCC 6051), <i>S. aureus</i> (ATCC 29213)	Wei et al., 2024
<i>Xylaria</i> sp. SNB-GTC250	Xylabisboeins A and B	<i>S. aureus</i> , <i>Trichophyton rubrum</i> , <i>Candida albicans</i>	Sorres et al., 2015
<i>Xylaria</i> sp. FPL-25(M)	xylobovid 9-methyl ester		Rakshith et al., 2020

9. Conclusions

There are many interesting and effective compounds with antimicrobial activity isolated from fungi of the genus *Xylaria*. Numerous studies have confirmed the antimicrobial properties of extracts derived from the fruiting bodies and mycelia of fungi belonging to the genus *Xylaria*. These

extracts have demonstrated efficacy against a broad range of pathogenic microorganisms, indicating their potential applications in medicine and pharmacology (Ho et al., 2012; Klaiiklay et al., 2012; Sawadsitang et al., 2015; Jin et al., 2017; Chen et al., 2018). However, most of these investigations focus primarily on the overall activity of crude extracts; other researches are aimed at the identification

and analysis of the individual bioactive compounds responsible for the antimicrobial effects. Many compounds derived from the *Xylaria* genus present a potential source for new antibiotics and more strategic and efficient use of natural resources in combating microbial infections – an urgent priority in the context of rising antibiotic resistance. A thorough understanding of the structures and properties of crude extract-derived substances in the future may allow the development of new therapies and antibiotics that can help fight antibiotic-resistant bacteria.

References

- Adnan, M., Patel, M., Reddy, M. N., & Alshammari, E. (2018). Formulation, evaluation and bioactive potential of *Xylaria primorskensis* terpenoid nanoparticles from its major compound xylaranic acid. *Scientific Reports*, 8(1). Article 1. <https://doi.org/10.1038/s41598-018-20237-z>
- Ariantari, N. P., Putra, I. P. Y. A., Leliqia, N. P. E., Yustiantara, P. S., Proborini, M. W., Nugraheni, N., ... & Meiyanto, E. (2023). Antibacterial and cytotoxic secondary metabolites from endophytic fungi associated with *Antidesma bunius* leaves. *Journal of Applied Pharmaceutical Science*, 13(7), 132–143.
- Baerson, S. R. & Rimando, A. M., (eds.) (2007). Polyketides: biosynthesis, biological activity, and genetic engineering. *American Chemical Society*.
- Baraban, E. G., Morin, J. B., Phillips, G. M., Phillips, A. J., Strobel, S. A., & Handelsman, J. (2013). Xyolide, a bioactive nonenolide from an Amazonian endophytic fungus, *Xylaria feejeensis*. *Tetrahedron Letters*, 54(31), 4058–4060. <https://doi.org/10.1016/j.tetlet.2013.05.093>
- Canli, K., Akata, I., Altuner, E. M. (2016). In vitro antimicrobial activity screening of *Xylaria hypoxylon*. *African Journal of Traditional Complementary and Alternative Medicines*, 13(4), 42–46. <https://doi.org/10.21010/ajtcam.v13i4.7>. PMID: 28852719; PMCID: PMC5566152
- Chandra Deb, L., Jara, M., & Lanzas, C. (2023). Early evaluation of the Food and Drug Administration (FDA) guidance on antimicrobial use in food animals on antimicrobial resistance trends reported by the National Antimicrobial Resistance Monitoring System (2012–2019). *One Health*, 17, 100580. <https://doi.org/10.1016/j.onehlt.2023.100580>
- Chen, R., Tang, J.-W., Li, X.-R., Liu, M., Ding, W.-P., Zhou, Y.-F., Wang, W.-G., Du, X., Sun, H.-D., & Puno, P.-T. (2018). Secondary Metabolites from the Endophytic Fungus *Xylaria* sp. Hg1009. *Natural Products and Bioprospecting*, 8(2), 121–129. <https://doi.org/10.1007/s13659-018-0158-x>
- Dadgostar, P. (2019). Antimicrobial Resistance: Implications and Costs. *Infection and Drug Resistance*, 12, 3903–3910. <https://doi.org/10.2147/IDR.S234610>
- Deyrup, S. T., Gloer, J. B., O'Donnell, K., & Wicklow, D. T. (2007). Colocosides A–D: Triterpenoid glycosides from a Hawaiian isolate of *Xylaria* sp. *Journal of Natural Products*, 70(3), 378–382.
- Dufossé, L., Latrasse, A., & Spinnler, H. E. (1994). Importance des lactones dans les arômes alimentaires: structure, distribution, propriétés sensorielles et biosynthèse. [Importance of lactones in food flavours: structure, distribution, sensory properties and biosynthesis]. *Sciences des aliments; Food Science: An International Journal of Food Science and Technology* 14, 17–50.
- Fathoni, A., & Agusta, A. (2019). Bioproduction of cytochalasin D by endophytic fungus *Xylaria* sp. DAP KRI-5. *Journal of Applied Pharmaceutical Science*, 9(3), 105–110. <https://doi.org/10.7324/JAPS.2019.90315>
- Fathoni, A., Ilyas, M., Praptiwi, Wulansari, D., & Agusta, A. (2022). Antibacterial and Antioxidant Activities of Fungal Endophytes Isolated from Medicinal Plants in Simeulue Island, Aceh. *HAYATI Journal of Biosciences*, 29(6), 720–732. <https://doi.org/10.4308/hjb.29.6.720-732>
- Fournier, J., Flessa, F., Peršoh, D., & Stadler, M. (2011). Three new *Xylaria* species from southwestern Europe. *Mycological Progress*, 10(1), 33–52. <https://doi.org/10.1007/s11557-010-0671-8>
- Gan, D., Li, C., Shu, Y., Wang, J., Wang, C., Zhu, L., Yang, Y., Liu, J., He, B., Cai, L., & Ding, Z. (2023). Steroids and dihydroisocoumarin glycosides from *Xylaria* sp. By the one strain many compounds strategy and their bioactivities. *Chinese Journal of Natural Medicines*, 21(2), 154–160. [https://doi.org/10.1016/S1875-5364\(23\)60394-2](https://doi.org/10.1016/S1875-5364(23)60394-2)
- Gebreyohannes, G., Nyerere, A., Bii, C., & Berhe Sbhatu, D. (2019). Determination of Antimicrobial Activity of Extracts of Indigenous Wild Mushrooms against Pathogenic Organisms. *Evidence-Based Complementary and Alternative Medicine*, 2019, 1–7. <https://doi.org/10.1155/2019/6212673>
- Gokhale, M., Verma, M., Faraz, R., & Raj, D. (2017). Bioactive Molecules (GC-MS) of Endophytic Fungi, *Xylaria* from *Nyctanthes arbor-trists* (Linn). *Journal of Advanced Microbiology*, 3(1), 43–53.
- Guo, Z.-Y., Lu, L.-W., Bao, S.-S., Liu, C.-X., Deng, Z.-S., Cao, F., Liu, S.-P., Zou, K., & Proksch, P. (2018). Xylariaopyrones A–D, four new antimicrobial α -pyrone derivatives from endophytic fungus *Xylariales* sp. *Phytochemistry Letters*, 28, 98–103. <https://doi.org/10.1016/j.phytol.2018.09.014>
- Hertweck, C. (2009). The biosynthetic logic of polyketide diversity. *Angewandte Chemie International Edition*, 48(26), 4688–4716.
- Ho, M. Y., Chung, W. C., Huang, H. C., Chung, W. H., & Chung, W. H. (2012). Identification of endophytic fungi of medicinal herbs of Lauraceae and Rutaceae with antimicrobial property. *Taiwania*, 57(3), 229–241.
- Huang, M., Lu, J. J., Huang, M. Q., Bao, J. L., Chen, X. P., & Wang, Y. T. (2012). Terpenoids: natural products for cancer therapy. *Expert Opinion On Investigational Drugs*, 21(12), 1801–1818.
- Hu, Z. Y., Li, Y. Y., Huang, Y. J., Su, W. J., & Shen, Y. M. (2008). Three new sesquiterpenoids from *Xylaria* sp. NCY2. *Helvetica Chimica Acta*, 91(1), 46–52.
- Hu, Z.-Y., Li, Y.-Y., Lu, C.-H., Lin, T., Hu, P., & Shen, Y.-M. (2010). Seven Novel Linear Polyketides from *Xylaria* sp. NCY2. *Helvetica Chimica Acta*, 93(5), 925–933. <https://doi.org/10.1002/hlca.200900323>
- Ibrahim, A., Tanney, J. B., Fei, F., Seifert, K. A., Cutler, G. C., Capretta, A., Miller, J. D., & Sumarah, M. W. (2020). Metabolomic-guided discovery of cyclic nonribosomal peptides from *Xylaria ellisii* sp. Nov., a leaf and stem endophyte of *Vaccinium angustifolium*. *Scientific Reports*, 10(1), 4599. <https://doi.org/10.1038/s41598-020-61088-x>
- Jin, Z., Li, D., Liu, T., Yu, F., Zhang, Z., Su, C., Wang, Y., Guo, Q., & Liu, Z. (2017). Cultural endophytic fungi associated with *Dendrobium officinale*: identification, diversity estimation and their antimicrobial potential. *Current Science*, 112(8), 1690–1697.
- Ju, Y.-M., & Hsieh, H.-M. (2023). *Xylaria* species associated with fallen leaves and petioles. *Botanical Studies*, 64(1), 19. <https://doi.org/10.1186/s40529-023-00377-w>

- Keekan, K. K., Ranadive, K. R., Naik, P., Sendker, J., & Padmaraj, S. R. (2022). Anti-Methicillin-Resistant *S. aureus* Activity of Fruiting Body and Mycelial Culture Extracts of *Xylaria longipes* Nitschke (Ascomycota). *Pharmaceutical Chemistry Journal*, 56(7), 958–965. <https://doi.org/10.1007/s11094-022-02733-9>
- Klaiklay, S., Rukachaisirikul, V., Sukpondma, Y., Phongpaichit, S., Buatong, J., & Bussaban, B. (2012). Metabolites from the mangrove-derived fungus *Xylaria cubensis* PSU-MA34. *Archives of Pharmacal Research*, 35(7), 1127–1131. <https://doi.org/10.1007/s12272-012-0701-y>
- Konaklieva, M. I., & Plotkin, B. J. (2005). Lactones: generic inhibitors of enzymes? *Mini Reviews in Medicinal Chemistry*, 5(1), 73–95.
- Kozińska, A., & Sitkiewicz, I. (2017). „Nowe” i „Stare” antybiotyki – mechanizmy działania i strategie poszukiwania leków przeciwbakteryjnych. [In Polish. “New” and “Old” antibiotics – mechanisms of action and complementary antibacterial strategies]. *Kosmos*, 66(1), 109–124.
- Lee, J. S., Ko, K. S., & Jung, H. S. (2000). Phylogenetic analysis of *Xylaria* based on nuclear ribosomal ITS1-5.8S-ITS2 sequences. *FEMS Microbiology Letters*, 187(1), 89–93. <https://doi.org/10.1111/j.1574-6968.2000.tb09142.x>
- Li, J., Wang, W. X., Chen, H. P., Li, Z. H., He, J., Zheng, Y. S., Sun, H., Huang, R., Yuan, Q. X., Wang, X., Feng, T., & Liu, J. K. (2019). (±)-Xylaridines A and B, Highly Conjugated Alkaloids from the Fungus *Xylaria longipes*. *Organic Letters*, 21(5), 1511–1514. <https://doi.org/10.1021/acs.orglett.9b00312>
- Liang, Y., Xu, W., Liu, C., Zhou, D., Liu, X., Qin, Y., Cao, F., Li, J., Yang, R., Qin, J. (2019). Eremophilane sesquiterpenes from the endophytic fungus *Xylaria* sp. GDG-102. *Natural Product Research*, 33(9), 1304–1309. <https://doi.org/10.1080/14786419.2018.1472597>
- Liang, J. J., Zhang, P. P., Zhang, W., Song, D., Wei, X., Yin, X., Zhou, Y. Q., Pu, X., & Zhou, Y. (2022). Biological activities and secondary metabolites from *Sophora tonkinensis* and its endophytic fungi. *Molecules*, 27(17), 5562.
- Lin, X., Yu, M., Lin, T., & Zhang, L. (2016). Secondary metabolites of *Xylaria* sp., an endophytic fungus from *Taxus mairei*. *Natural Product Research*, 30(21), 2442–2447. <https://doi.org/10.1080/14786419.2016.1198350>
- Liu, X., Dong, M., Chen, X., Jiang, M., Lv, X., & Zhou, J. (2008). Antimicrobial activity of an endophytic *Xylaria* sp. YX-28 and identification of its antimicrobial compound 7-amino-4-methylcoumarin. *Applied Microbiology and Biotechnology*, 78(2), 241–247. <https://doi.org/10.1007/s00253-007-1305-1>
- Ma, H., Song, Z., Pan, X., Qu, Z., Yang, Z., Li, Y., & Zhu, A. (2022). Four New Pale-Spored Species of *Xylaria* (Xylariaceae, Xylariales) with a Key to Worldwide Species on Fallen Fruits and Seeds. *Biology*, 11(6), 885. <https://doi.org/10.3390/biology11060885>
- Miral, A., Ferron, S., Rouaud, I., Slyambayev, D., Bousarghin, L., Camuzet, C., Belouzard, S., Séron, K., Le Pogam, P., Tranchimand, S., & Tomasi, S. (2023). Eremoxylarins D–J, Antibacterial Eremophilane Sesquiterpenes Discovered from an Endolichenic Strain of *Xylaria hypoxylon*. *Journal of Natural Products*, 86(4), 730–738. <https://doi.org/10.1021/acs.jnatprod.2c00881>
- Mo, T.-X., Liu, X.-B., Duan, L.-H., Zhang, X.-M., Xu, Z.-L., Qin, X.-Y., Li, B.-C., Li, J., & Yang, R.-Y. (2021). Secondary Metabolites of the Endophytic Fungus *Xylaria* sp. GDG-102 from *Sophora tonkinensis*. *Chemistry of Natural Compounds*, 57(4), 764–766. <https://doi.org/10.1007/s10600-021-03470-3>
- Nagam, V., Aluru, R., Shoaib, M., Dong, G. R., Li, Z., Pallaval, V. B., & Ni, J. F. (2021). Diversity of fungal isolates from fungus-growing termite *Macrotermes barneyi* and characterization of bioactive compound from *Xylaria escharoidea*. *Insect Science*, 28(2), 392–402.
- Nuthan, B. R., Rakshith, D., Marulasiddaswamy, K. M., Rao, H. C. Y., Ramesha, K. P., Mohana, N. C., Siddappa, S., Darshan, D., Kumara, K. K. S., & Satish, S. (2020). Application of Optimized and Validated Agar Overlay TLC–Bioautography Assay for Detecting the Antimicrobial Metabolites of Pharmaceutical Interest. *Journal of Chromatographic Science*, 58(8), 737–746. <https://doi.org/10.1093/chromsci/bmaa045>
- Popowska, M. (2017). Antybiotykooporność w środowisku naturalnym—Przyczyny i konsekwencje. [Antibiotic resistance in the natural environment – causes and consequences]. *Kosmos*, 66(1), 81–91.
- Quang, D. N., Bach, D. D., Hashimoto, T., & Asakawa, Y. (2006). Chemical constituents of the Vietnamese inedible mushroom *Xylaria intracolorata*. *Natural Product Research*, 20(4), 317–321. <https://doi.org/10.1080/14786410600650354>
- Rajendran, S., Robertson, L. P., Kosgahakumbura, L., Fernando, C., Göransson, U., Wang, H., Hettiarachchi, C., & Gunasekera, S. (2023). Antibacterial eremophilane sesquiterpenoids from *Xylaria feejeensis*, an endophytic fungi of the medicinal plant *Geophila repens*. *Fitoterapia*, 167, 105496. <https://doi.org/10.1016/j.fitote.2023.105496>
- Rakshith, D., Gurudatt, D. M., Yashavantha Rao, H. C., Chandra Mohana, N., Nuthan, B. R., Ramesha, K. P., & Satish, S. (2020). Bioactivity-guided isolation of antimicrobial metabolite from *Xylaria* sp. *Process Biochemistry*, 92, 378–385. <https://doi.org/10.1016/j.procbio.2020.01.028>
- Rakshith, D., Santosh, P., Pradeep, T. P., Gurudatt, D. M., Baker, S., Yashavantha Rao, H. C., Pasha, A., & Satish, S. (2016). Application of bioassay-guided fractionation coupled with a molecular approach for the dereplication of antimicrobial metabolites. *Chromatographia*, 79, 1625–1642.
- Ramesh, V., Santosh, K., Anand, T. D., Shanmugaiah, V., Kotamraju, S., Karunakaran, C., & Rajendran, A. (2015). Novel bioactive wild medicinal mushroom – *Xylaria* sp. R006 (Ascomycetes) against multidrug resistant human bacterial pathogens and human cancer cell lines. *International Journal of Medicinal Mushrooms*, 17(10).
- Ratnaweera, P. B., Williams, D. E., De Silva, E. D., Wijesundera, R. L. C., Dalisay, D. S., & Andersen, R. J. (2014). Helvolic acid, an antibacterial nortriterpenoid from a fungal endophyte, *Xylaria* sp. of orchid *Anoectochilus setaceus* endemic to Sri Lanka. *Mycology*, 5(1), 23–28. <https://doi.org/10.1080/21501203.2014.892905>
- Roca, I., Akova, M., Baquero, F., Carlet, J., Cavaleri, M., Coenen, S., Cohen, J., Findlay, D., Gyssens, I., Heure, O. E., Kahlmeter, G., Kruse, H., Laxminarayan, R., Liébana, E., López-Cerero, L., MacGowan, A., Martins, M., Rodríguez-Baño, J., Rolain, J.-M., Segovia C., Sigauque B., Tacconelli E., Wellington E. & Vila, J. (2015). The global threat of antimicrobial resistance: Science for intervention. *New Microbes and New Infections*, 6, 22–29. <https://doi.org/10.1016/j.nmni.2015.02.007>
- Rogers, J. D, Y.-M. Ju, M. J. Adams (2002). Home of The Xylariaceae, accessed: October 2024,

- <https://mycology.sinica.edu.tw/Xylariaceae/acceptgenera.asp?qrySectionName=Xylariaceae>
- Rukachaisirikul, V., Khamthong, N., Sukpondma, Y., Pakawatchai, C., Phongpaichit, S., Sakayaroj, J., & Kirtikara, K. (2009). An [11]Cytochalasin Derivative from the Marine-Derived Fungus *Xylaria* sp. PSU-F100. *Chemical and Pharmaceutical Bulletin*, 57(12), 1409–1411. <https://doi.org/10.1248/cpb.57.1409>
- Sawadsitang, S., Mongkolthanaruk, W., Suwannasai, N., & Sodngam, S. (2015). Antimalarial and cytotoxic constituents of *Xylaria* cf. *cubensis* PK108. *Natural Product Research*, 29(21), 2033–2036. <https://doi.org/10.1080/14786419.2015.1017724>
- Sell, C. S. (2003). A fragrant introduction to terpenoid chemistry. Cambridge: Royal Society of Chemistry.
- Sorres, J., Nirma, C., Touré, S., Eparvier, V., & Stien, D. (2015). Two new isopimarane diterpenoids from the endophytic fungus *Xylaria* sp. SNB-GTC2501. *Tetrahedron letters*, 56(31), 4596–4598.
- Srisapoomi, T., Ichiyanagi, T., Nakajima, H., Aimi, T., Boonlue, S. (2015). Biosynthesis of integric acid isolated from the wood-decay fungus *Xylaria feejeensis* 2FB-PPM08M. *Current Microbiology*, 70(4), 550–5. <https://doi.org/10.1007/s00284-014-0759-5>
- Sun, D.-W., Cao, F., Liu, M., Guan, F.-F., & Wang, C.-Y. (2017). New Fatty Acid From a Gorgonian-Derived *Xylaria* sp. Fungus. *Chemistry of Natural Compounds*, 53(2), 227–230. <https://doi.org/10.1007/s10600-017-1958-7>
- Suwannasai, N., Sangvichien, E., Phosri, C., McCloskey, S., Wangsawat, N., Thamvithayakorn, P., Ruchikachorn, N., Thienhirun, S., Mekkamol, S., Sihanonth, P., Whalley, M. A., Whalley, A. J. S. (2023). Exploring the Xylariaceae and its relatives. *Botanical Studies*, 64, 15. <https://doi.org/10.1186/s40529-023-00389-6>
- Tang, A. M. C., Jeewon, R., and Hyde, K. D. (2009). A re-evaluation of the evolutionary relationships within the Xylariaceae based on ribosomal and protein-coding gene sequences. *Fungal Diversity* 34, 127–155.
- Tarman, K., Lindequist, U., Wende, K., Porzel, A., Arnold, N., & Wessjohann, L. A. (2011). Isolation of a New Natural Product and Cytotoxic and Antimicrobial Activities of Extracts from Fungi of Indonesian Marine Habitats. *Marine Drugs*, 9(3), 294–306. <https://doi.org/10.3390/md9030294>
- Tchoukoua, A., Ota, T., Akanuma, R., Ju, Y.-M., Supratman, U., Murayama, T., Koseki, T., & Shiono, Y. (2017). A phytotoxic bicyclic lactone and other compounds from endophyte *Xylaria curta*. *Natural Product Research*, 31(18), 2113–2118. <https://doi.org/10.1080/14786419.2016.1277352>
- Wang, G., Tang, W., Bidigare, R. R. (2005). Terpenoids As Therapeutic Drugs and Pharmaceutical Agents. In: Zhang, L., Demain, A. L. (eds.). *Natural Products. Humana Press*. https://doi.org/10.1007/978-1-59259-976-9_9
- Wang, W. X., Li, Z. H., Feng, T., Li, J., Sun, H., Huang, R., Yuan, Q. X., Ai, H. L., & Liu, J. K. (2018). Curtachalasin A and B, two cytochalasins with a tetracyclic skeleton from the endophytic fungus *Xylaria curta* E10. *Organic Letters*, 20(24), 7758–7761.
- Wei S.-S., Lai, J.-Y., Chen, C., Zhang, Y.-J., Nong, X.-M., Qiu, K.-D., Duan, F.-F., Zou, Z.-X., Tan, H.-B. (2024). Sesquiterpenes and α -pyrones from an endophytic fungus *Xylaria curta* YSJ-5. *Phytochemistry*, 220, 114011. <https://doi.org/10.1016/j.phytochem.2024.114011>
- Wei, P.-P., Ai, H.-L., Shi, B.-B., Ye, K., Lv, X., Pan, X.-Y., Ma, X.-J., Xiao, D., Li, Z.-H., & Lei, X.-X. (2022). Paecilins F–P, new dimeric chromanones isolated from the endophytic fungus *Xylaria curta* E10, and structural revision of paecilin A. *Frontiers in Microbiology*, 13, 922444. <https://doi.org/10.3389/fmicb.2022.922444>
- Xie, J., Liu, X., & Liu, G. (2023). A new track for antibacterial treatment: Progress and challenges of using cytomembrane-based vesicles to combat bacteria. *Particuology*, 78, 136–146. <https://doi.org/10.1016/j.partic.2022.10.006>
- Xu, W. F., Hou, X. M., Yao, F. H., Zheng, N., Li, J., Wang, C. Y., ... & Shao, C. L. (2017). Xylapeptide A, an antibacterial cyclopentapeptide with an uncommon L-pipecolic acid moiety from the associated fungus *Xylaria* sp. (GDG-102). *Scientific Reports*, 7(1), 6937. <https://doi.org/10.1038/s41598-017-07331-4>
- Xu, Z.-L., Li, B.-C., Huang, L.-L., Lv, L.-X., Luo, Y., Xu, W.-F., & Yang, R.-Y. (2022). Two new cytochalasins from the endophytic fungus *Xylaria* sp. GDGJ-77B. *Natural Product Research*, 1–7. <https://doi.org/10.1080/14786419.2022.2153362>
- Yang, W. W., Lu, L. W., Zhang, X. Q., Bao, S. S., Cao, F., Guo, Z. Y., Deng, Z. S., & Proksch, P. (2022). Xylariaopyrones E–I, five new α -pyrone derivatives from the endophytic fungus Xylariales sp. (HM-1). *Natural Product Research*, 36(9), 2230–2238.
- Yu, G., Sun, Z., Peng, J., Zhu, M., Che, Q., Zhang, G., Zhu, T., Gu, Q., & Li, D. (2019). Secondary Metabolites Produced by Combined Culture of *Penicillium crustosum* and a *Xylaria* sp. *Journal of Natural Products*, 82(7), 2013–2017. <https://doi.org/10.1021/acs.jnatprod.9b00345>
- Zhang, S. N., Li, X. Z., Tan, L. Y., & Zhu, K. Y. (2021). A review of pharmacological and toxicological effects of *Sophora tonkinensis* with bioinformatics prediction. *The American Journal of Chinese Medicine*, 49(02), 359–389.
- Zhang, Y., Jin, Y., Yan, W., Gu, P., Zeng, Z., Li, Z., Zhang, G., Wei, M. & Xue, Y. (2024). New Pyranone Derivatives and Sesquiterpenoid Isolated from the Endophytic Fungus *Xylaria* sp. Z184. *Molecules*, 29(8), 1728.
- Zheng, N., Liu, Q., He, D.-L., Liang, Y., Li, J., & Yang, R.-Y. (2018a). A New Compound from the Endophytic Fungus *Xylaria* sp. from *Sophora tonkinensis*. *Chemistry of Natural Compounds*, 54(3), 447–449. <https://doi.org/10.1007/s10600-018-2376-1>
- Zheng, N., Yao, F., Liang, X., Liu, Q., Xu, W., Liang, Y., Liu, X., Li, J., & Yang, R. (2018b). A new phthalide from the endophytic fungus *Xylaria* sp. GDG-102. *Natural product research*, 32(7), 755–760. <https://doi.org/10.1080/14786419.2017.1311892>