Putative Anticancer Compounds from Plant-Derived Endophytic Fungi: A Review

Md. Hridoy 1,2,*, Md. Zobayer Hossain Gorapi 3, Sadia Noor 3,4, Nargis Sultana Chowdhury 5, Md. Mustafizur Rahman 6, Isabella Muscari 7, Francesco Masia 7, Sabrina Adorisio 8, Domenico V. Delfino 8,*, and Md. Abdul Mazid 1,4,*

Abstract: Endophytic fungi are microorganisms that exist almost ubiquitously inside the various tissues of living plants where they act as an important reservoir of diverse bioactive compounds. Recently, endophytic fungi have drawn tremendous attention from researchers; their isolation, culture, purification, and characterization have revealed the presence of around 200 important and diverse compounds including anticancer agents, antibiotics, antifungals, antivirals, immunosuppressants, and antymycotics. Many of these anticancer compounds, such as paclitaxel, camptothecin, vinblastine, vincristine, podophyllotoxin, and their derivatives, are currently being used clinically for the treatment of various cancers (e.g., ovarian, breast, prostate, lung cancers, and leukemias). By increasing the yield of specific compounds with genetic engineering and other biotechnologies, endophytic fungi could be a promising, prolific source of anticancer drugs. In the future, compounds derived from endophytic fungi could increase treatment availability and cost effectiveness. This comprehensive review includes the putative anticancer compounds from plant-derived endophytic fungi discovered from 1990 to 2020 with their source endophytic fungi and host plants as well as their antitumor activity against various cell lines.

Keywords: endophytic fungi; anticancer compounds; living plants

1. Introduction

In 1866, de Bary introduced the term “endophyte” [1]. An endophyte may be a fungal or bacterial microorganism that colonizes various interior parts of plants causing no apparent pathogenic effects on its host plants. The endophytes, most commonly endophytic fungi, are believed to help plants adapt to abiotic factors (high temperature and salinity, drought, metal toxicity, and harmful effects of light) as well as biotic factors (herbivores, insects, nematodes, and pathogens). This is mainly achieved by the secondary bioactive metabolites produced by the endophytic fungi. In their symbiotic relation, the endophytes are fed and protected by the host plant, and in return, these microorganisms produce bioactive secondary metabolites, enhancing the growth of the host plant and protecting the plant from pathogens and herbivores [2]. Therefore, endophytic fungal metabolites can also be exploited as drugs for the treatment of various types of human diseases, including cancer [3].
This group of microorganisms has drawn tremendous attention from researchers since the isolation, culture, purification, and characterization of this fascinating group of microorganisms revealed the presence of hundreds of important and diverse chemical classes of compounds. The interest of scientists in endophytes is also growing as they are a good reservoir of bioactive metabolites [4,5]. Until now, many cytotoxic agents including paclitaxel (also known as Taxol) [6] have been isolated from endophytes. Secondary metabolites with cytotoxic properties have the potential to be explored as anticancer drugs.

Recent studies revealed that naphthoquinone derivatives fusarubins including anhydrofusarubin and fusarubin (FUS) produced by endophytic fungi Cladosporium species [7] and Fusarium species [8] showed promising cytotoxicity against cancer cells. Although FUS was reported earlier to have antibacterial activity, its cytotoxic activity was reported recently. Very recently, for the first time, we have revealed the molecular mechanism of cytotoxic action of fusarubin isolated from a Cladosporium species inhabiting the leaves of Rauwolfia serpentina. We have reported that fusarubin and anhydrofusarubin inhibit proliferation and increase apoptosis in leukemias and other hematological tumor cells lines in different manners through the p21/p53-mediated pathway [9]. Our findings urge us to write this review on endophytic fungal metabolites as a fascinating group of bioactives or putative anticancer compounds. Many of these putative anticancer compounds have very promising cytotoxicity against a broad spectrum of cancer cell lines; some compounds are already used as treatments for different cancer types such as breast, bladder, colorectal, esophageal, lung, ovarian, prostate, melanoma, testicular, leukemia, and lymphoma.

2. Anticancer Activity of Endophytic Fungi

Endophytic fungi have been a known source of anticancer agents since the discovery of the valuable drug Taxol (also known as paclitaxel, a diterpenoid) isolated for the first time from an endophytic fungus Taxomyces andreanae obtained from the Pacific Yew bark (Taxus brevifolia) [6]. Since then, other anticancer drugs have been isolated from endophytic fungi, and among these 9-methoxycamptothecin and 10-hydroxycamptothecin from Fusarium solani [10], camptothecin from Entrophospora infrequens [11]; the anticancer lead compounds podophyllotoxin from Phialocephala fortinii [12] and deoxypodophyllotoxin from Aspergillus fumigatus [13] fueled further research on endophytic fungi to discover many other important known and novel anticancer compounds. According to this review, until now, more than 100 different fungal species have been identified to produce more than two hundred putative anticancer compounds (Figures 1 and 2) reported to possess antiproliferative and/or cytotoxic properties against more than 60 different cell lines (Tables 1–3). Figure 1 indicates that endophytic fungal-derived anticancer agents gained attention from scientists over the past three decades. Meanwhile, Figure 2 represents the abundance of different chemical classes and diversity of fungal metabolites. The anticancer compounds isolated from endophytic fungi are effective against diverse cell lines that could be helpful in combating any particular type of cancer (Table 1).

### Table 1. Different cell lines against which endophytic fungal derived metabolites showed cytotoxicity.

| Cell Lines                | Cell Lines               |
|---------------------------|--------------------------|
| A2780S                    | Ovarian tumor cell line  |
| A2058                     | Human melanoma           |
| A549                      | Lung carcinoma epithelial|
| A431                      | Skin carcinoma           |
| ACHN                      | Renal cells              |
| AsPC-1                    | Human pancreatic cancer cells |
| B16F10                    | Skin carcinoma           |
| BC                        | Human breast cancer cell line |
| BC-1                      | Breast cancer            |
|                           |                          |
|                           | Human intestine cancer   |
|                           | T cell leukemia          |
|                           | Human nasopharyngeal epidermoid tumor |
|                           | Human leukemia cells     |
|                           | Mouse lymphoma cells     |
|                           | Pancreatic carcinoma     |
|                           | Pancreatic cancer        |
|                           | Breast cancer cell line  |
|                           | Human breast cancer cell line |
Table 1. Cont.

| Cell Lines | Cell Lines       |
|------------|------------------|
| BEL-7402   | Human hepatocellular carcinoma/human hepatoma cell line | MFC | Gastric cancer cells in mice |
| BEL-7404   | Human hepatocellular carcinoma/human hepatoma cell line | MCF-7 | Breast cancer cell line |
| BGC-823    | Gastric carcinoma | MOLT-4 | Lymphoblastic leukemia |
| BT-220     | Breast cancer cell line | MRC-5 | Fibroblast-like fetal lung cells |
| BT474      | Human breast cancer | MV4-11 | Human FLT3-ITD mutant AML cell line |
| CHO        | Chinese hamster ovary | NCI-H187 | Human small-cell lung cancer |
| DU145      | Human prostate carcinoma | NCI-H460 | Non-small-cell lung cancer |
| EAC        | Ehrlich ascites carcinoma | NEC | Colorectal neuroendocrine cell carcinoma |
| H116       | Human colon adenocarcinoma | OVCAR-5 | Human ovarian cancer |
| HeLa       | Cervical cancer | PANC-1 | Human pancreatic carcinoma |
| Hep2       | Human liver cancer | P388 | Murine leukemia cells |
| HepG2      | Human hepatocellular liver carcinoma | PC-3 | Prostate cancer |
| Hep3B      | Human hepatoma cell line | PC-3 M | Metastatic prostate cancer |
| HM2        | Human gastric carcinoma | RAW264.7 | Mouse macrophage cell |
| HL-60      | Human promyelocytic leukemia cell line | SF-268 | CNS glioma |
| HL251      | Human lung cancer | SW-480 | Human colon cancer cells |
| HL-7702    | Normal hepatocyte | SW-620 | Colon tumor cell line |
| HLK 210    | Human leukemia | SW1116 | Human colon cancer cell line |
| HCT-8      | Human colorectal adenocarcinoma | SW1990 | Human pancreatic cancer cells |
| HCT-116    | Colon tumor cell line | T24 | Bladder carcinoma |
| H22        | Hepatic cancer cells in mice | T47D | Breast cancer |
| H1975      | Non-small-cell lung cancer cells/human lung adenocarcinoma | THP-1 | Human monocytic cell line |
| HS22-T1    | Non-small cell lung cancer | WI-38 | Normal human fibroblast cells |
| HT-29      | Human colon cancer line | U2OS | Human osteosarcoma cells |

Table 2. Anticancer compounds from plant-derived endophytic fungi.

| Compounds | Chemical Class | Fungal Endophytes | Host Medicinal Plant | Activity Against Cell Lines | IC50 Values | Ref. |
|-----------|----------------|-------------------|----------------------|-----------------------------|-------------|-----|
| Leucinostatin A | Peptide | Acremonium spp. | Taxus baccata twig | BT-20 | 2 nM (LD50) | [14] |
| Allantopyrone A | α-Pyrone | Allantophomopsis l. KS-97 | A549 cells, HL-60 | >32, 0.32 μM | [15] |
| Alternariol, Alternusin, Alternariol 5-O-sulfate, Alternariol 5-O-methyl ether, Desmethyllatenensin | Polyketide | Alternaria spp | Polygonon senegalense leaves | L5178Y | <1 × 10^{-6}, 1 × 10^{-5}, 1 × 10^{-5}, 1 × 10^{-5} g/mL | [16] |
| Lapachol | Naphthoquinone | Alternaria spp. | Tabebuia argentea leaf | DU145, HepG2, Hep3B & MCF-7 (β-Lapachone) | 3.5, 3.5, 3.5 & 5 μM | [17–22] |
| Resveratredyes A & B | Stilbenoid (Resveratrol derivatives) | Alternaria spp. R6 | Myoporum bontioides root | MDA-MB-435, HCT-116 | <10 μM | [23] |
| Alterporriol K, Alterporriol L | Quinones | Alternaria spp. ZJ9-6B | Aegiceras corniculatum | MDA-MB-435, MCF-7, HL-60, A549, PC-3, HeLa, A431, MiaPaka-2 and T47D | 26.97, 29.11 & 13.11, 20.04 μM | [24] |
| Alterporriol-10-methyl ether | Polyketide | Alternaria a. | Capsicum annum | DU145, HepG2, Hep3B & MCF-7 (β-Lapachone) | 3.5, 3.5, 3.5 & 5 μM | [25] |
# Table 2. Cont.

| Compounds                          | Chemical Class | Fungal Endophytes | Host Medicinal Plant | Activity Against Cell Lines | IC50 Values | Ref. |
|------------------------------------|----------------|-------------------|----------------------|-----------------------------|-------------|------|
| Camptothecine (CPT), 9-methoxy CPT, 10-hydroxy CPT Chrysin (5,7-dihydroxy flavone) Altermariol 9-methyl ether | Alkaloids      | Alternaria a.      | Miquelia dentata fruit and seed regions | HCT-116, SW-480, MCF-7       | 6.59, 7.2, 10.24 μg/mL (crude fungal ethyl acetate extract) | [26] |
|                                    |                |                   |                      |                             |             |      |
| Dibenzopyranone                    |                | Alternaria a.      | Passiflora incarnata leaves | MCF-7                      | 34.066 μg/mL | [27] |
|                                    |                |                   |                      |                             |             |      |
| Lapachol                           | Naphthoquinone | Alternaria a.      | Tabebuia argentea bark, leaf and stem | DU145, HepG2, Hep3B & MCF-7 (β-Lapachone) | 3.5, 3.5, 3.5 & 5 μM | [17–22] |
|                                    |                |                   |                      |                             |             |      |
| Perylenes                          |                | Alternaria t.      | Erythrophleum foralii bark | HCT-8                      | 1.78 μM     | [29] |
|                                    |                |                   |                      |                             |             |      |
| 1. Flavasperone, 2. Rubrofusarin B, 3. Fonecinone D 9-Deacetoxy fumigaclavine C 1. Fumitremorgin D, 2. 4,8,10,14-tetramethyl-6-acetoxy-1(4H)-acetoxy-19(20,21-dimethyl)-18-ene phenanthrene-1-ene-3,7-dione 3. 12,13-dihydroxy-fumigaclavine C 4. Verruculogen | Alkaloids      | Aspergillus sp.  | Limonia acidissima seeds | 1. Hep 3B and U87 MG 2. SW1116 3. SMMC-7721 and A549 HL-60, KR, Hela, MCF-7 and Spec-A-1 | 1. Between 19.92 and 47.98 μM 2. 4.5 μg/mL 3. >10 μg/mL | [30] |
|                                    |                |                   |                      |                             |             |      |
| Brefeldin A                        | Lactone        | Aspergillus c.     | Torreya grandis bark | K562                        | 3.11 μM     | [32] |
|                                    |                |                   |                      |                             |             |      |
| 9-Deacetoxy fumigaclavine C 1. Fumitremorgin D, 2. 4,8,10,14-tetramethyl-6-acetoxy-1(4H)-acetoxy-19(20,21-dimethyl)-18-ene phenanthrene-1-ene-3,7-dione 3. 12,13-dihydroxy-fumigaclavine C 4. Verruculogen | Alkaloids      | Aspergillus f.     | Cynodon dactylon stem      | K562                        | 3.11 μM     | [32] |
|                                    |                |                   |                      |                             |             |      |
| Sesquiterpenes                     | Naphthopyrones | Aspergillus g.     | Ipomoea batatas plant | Hep-G2, MCF-7               | 41.7 μg/mL   | [34] |
|                                    |                |                   |                      |                             |             |      |
| Pyrones                            |                | Aspergillus n.     | Avicennia marina plant | Hep-G2, MCF-7, A549, SW190, MDA-MB-231 | 61.0 μM  | [35] |
|                                    |                |                   |                      |                             |             |      |
| Rubrofusarin B                     | Naphthopyrones | Aspergillus n.     | Cynodon dactylon stem | SW1116                      | 45 μg/mL    | [36] |
|                                    |                |                   |                      |                             |             |      |
| Lapachol                           | Naphthopyrones | Aspergillus n.     | Diphylecia sinensis mainly roots, rhizomes | HepG2 | 1. 47.5 μM 2. 139.9 μM 3. 4.5 μM 4. 9.8 μM | [33] |
|                                    |                |                   |                      |                             |             |      |
| 1. Sequoiatones A & B 2. Sequoianomacin A & B 3. Butyrolactone I and Butyrolactone V Terrein | Polyketide      | Aspergillus p.     | Sequoia sempervirens inner bark | 1. BC 2. MCF-7, NCI-H460, SF-268 | 1. 4 to 10 μM 2. 19 × 10^{-4}, 4 × 10^{-4}, 15 × 10^{-3} M 34.4, 17.4 & 22.1, 31.9 μM | [37,38] |
|                                    |                |                   |                      |                             |             |      |
| Butenolide                         |                | Aspergillus t.—F7  | Hepatis suaveolens   | MDA-MB-231 and MCF-7        | 121.9 μg/mL | [39] |
|                                    |                |                   |                      |                             |             |      |
| Terrein                            |                | Aspergillus t.     | Achyranthus aspera   | A-549                       | 121.9 μg/mL | [40] |
|                                    |                |                   |                      |                             |             |      |
| 1. Violaceoid A, 2. Violaceoid C, 3. Violaceoid D, 4. Violaceoid F Hydroquinones | Hydroquinones   | Aspergillus v.     | Wild Moss (Bryophyta unidentified species) | 1. HeLa, MCF-7, Jurkat, MOLT-4, HCT116, RAW264.7 BT 220, H116, Int 407, HL, 251 and HLK 210 | 1. 24.6, 14.8, 3.1, 3.0, 5.8, 5.6 μM (LD_{50}) 2. 8.2, 5.9 & 8.3, 6.2 μM (LD_{50}) 3. 6.4, 6.5 μM (LD_{50}) | [41] |
|                                    |                |                   |                      |                             |             |      |
| 1. Sequoiatones A & B 2. Sequoianomacin A & B 3. Butyrolactone I and Butyrolactone V Terrein | Polyketide      | Aspergillus p.     | Sequoia sempervirens inner bark | 1. BC 2. MCF-7, NCI-H460, SF-268 | 1. 4 to 10 μM 2. 19 × 10^{-4}, 4 × 10^{-4}, 15 × 10^{-3} M 34.4, 17.4 & 22.1, 31.9 μM | [37,38] |
|                                    |                |                   |                      |                             |             |      |
| Butenolide                         |                | Aspergillus t.—F7  | Hepatis suaveolens   | MDA-MB-231 and MCF-7        | 121.9 μg/mL | [39] |
|                                    |                |                   |                      |                             |             |      |
| Terrein                            |                | Aspergillus t.     | Achyranthus aspera   | A-549                       | 121.9 μg/mL | [40] |
|                                    |                |                   |                      |                             |             |      |
| 1. Violaceoid A, 2. Violaceoid C, 3. Violaceoid D, 4. Violaceoid F Hydroquinones | Hydroquinones   | Aspergillus v.     | Wild Moss (Bryophyta unidentified species) | 1. HeLa, MCF-7, Jurkat, MOLT-4, HCT116, RAW264.7 BT 220, H116, Int 407, HL, 251 and HLK 210 | 1. 24.6, 14.8, 3.1, 3.0, 5.8, 5.6 μM (LD_{50}) 2. 8.2, 5.9 & 8.3, 6.2 μM (LD_{50}) 3. 6.4, 6.5 μM (LD_{50}) | [41] |
|                                    |                |                   |                      |                             |             |      |
| Taxol                              | Terpene        | Bartalinia r.      | Aegle marmelos leaves |                             |             | [42] |
| Compounds                        | Chemical Class | Fungal Endophytes | Host Medicinal Plant | Activity Against Cell Lines | IC50 Values | Ref. |
|---------------------------------|----------------|-------------------|----------------------|----------------------------|-------------|------|
| Dipsidone 1                     | Dipsidone      | Pseudosphorales    | unidentified plant leaf of the Hala-Bala forest origin | KB, BC         | 6.5, 4.1 µg/mL | [43] |
| 1. Diepoxin δ, Palmarumycin C8  |                |                   |                      |                            |             |      |
| 2. Diepoxins κ & ζ              |                |                   |                      |                            |             |      |
| Verticillin D                   | Peptide        |                   |                      |                            |             |      |
| Stemphyperlenol A               | Sesterterpenoid|                   |                      |                            |             |      |
| Botryarhodine A and B           |                |                   |                      |                            |             |      |
| Cercosporene F                  | Diterpenes     |                   |                      |                            |             |      |
| Ceriponol F, Ceriponol G,       | Sesquiterpenes |                   |                      |                            |             |      |
| Ceriponol K                     |                |                   |                      |                            |             |      |
| Coclidiolinol, Isococlidiolinol | Quinones       | Chaetomium spp.    | Salvia officinalis Stem | L5178Y         | 7.0, 71.5 µg/mL | [51] |
| Chaetococin C                   | Diketopiperazine| Chaetomium spp.    | Cymbidium goeringii root | SW-480         | 0.63 µM      | [52] |
| Chaetococin G                   | Indole diketopiperazines| Chaetomium spp.   | Cymbidium goeringii | MCF-7         | 8.3 mg/mL    | [53] |
| Chaetominine                    | Alkaloids       | Chaetomium g.       | Curcuma wenyujin | H22, MFC      | 3.125, 6.25 µg/mL | [56] |
| Radicicol                       | Lactone         | Chaetomium c.       | Imperata cylindrica stem | KB cell line | 3.0, 40.0, 48.0 & 16.0, 48.0 µM | [57] |
| Chaetoglobosin X                | Alkaloids       | Chaetomium g.       | Curcuma wenyujin | H22, MFC      | 3.125, 6.25 µg/mL | [56] |
| Chaetoglobosin C, E, F & U,     | Alkaloids       | Chaetomium g.       | Imperata cylindrica stem | KB cell line | 3.0, 40.0, 48.0 & 16.0, 48.0 µM | [57] |
| Penochalasin A                  |                |                   |                      |                            |             |      |
| Globosumone A & B               | Ester           | Chaetomium g.       | Ephedra fasciculata | HCT116        | 3.15, 4.43, 5.85, 8.44 µM | [59] |
| Chaetoglobosins A, Fex, Fa & 20-| Alkaloids (cytchalasan mycotoxins) | Chaetomium g. | Ginkgo biloba leaves | HCT116        | 3.15, 4.43, 5.85, 8.44 µM | [59] |
| Anhydrofusarubin and methyl ether of Fusarubin | Naphthoquinones | Cladosporium spp. | Rauvolfia serpentina leaves | K-562         | 3.97 & 3.58 μg/mL | [7]   |
| Taxol                           | Diterpene      | Cladosporium c.     | Taxus media inner bark | MCF-7, BT220, H116, INT-407, HL251, HLK210 | 0.005 to 5 µM | [60,61] |
| Taxol                           | Diterpene      | Cladosporium o.     | Aegle marmelos, Coccinia indica and Moringa oleifera | HCT 15, T47D | 3.5, 2.5 µM | [62,63] |
| Taxol                           | Diterpene      | Clotetrichium c.    | Capsicum annuum fruit | MCF-7, HL 251, HLK 210, BEL7402 | 0.005 to 5 µM | [64,65] |
| Tyrosol C                       | Colletotrichium g. | Pandanus amaryllifolias leaves | A549, HT29, HCT116 | - | [66] |
| Deacetylcytochalasin C          | Cytochalasins   | Cordyceps t.        | unidentified          | 95-D          | 3.67 & 4.04 µM | [67] |
| and Zygosporin D                |                |                   |                      |               |             |      |
| Compounds                        | Chemical Class | Fungal Endophytes | Host Medicinal Plant | Activity Against Cell Lines | IC50 Values                          | Ref.            |
|---------------------------------|----------------|-------------------|-----------------------|------------------------------|--------------------------------------|-----------------|
| 1. Cytospolide P, 2. Cytospolide Q | Lactones       | Cytospora spp.    | *Ilex canariensis*    | 1. A-549, QGY, U973, 2. A-549 | 1. 2.05, 15.82, 28.26 µg/mL, 2. 10.55 µg/mL | [68]            |
| Xylarolide                       |                | Diaporthe t.      | *Glycyrrhiza glabra*  | T47D                         | 7 µM                                 | [69]            |
| Taxol                            | Diterpenes     | Didymostilbe spp. | Taxis chinensis var.  | MCF-7, HL-251, H-280, BEL-402 | 0.005 to 5 µM                        | [64,65]        |
| Camptothecin                     | Alkaloids      | Entrophospora i.   | *Nothapodytes foetida*| A-549, HEP-2, OVCAR-5         | 1. 12, 34, 38, 38 µM, 2. 11, 20, 32, 32 µM | [70]            |
| 1. Eutypellin A, 2. Sesquiterpene|                |                    |                       |                              |                                      |                 |
| 1. γ-Lactone                     |                | Eutypella sp.      | *Etlingera littoralis*|                              |                                      |                 |
| Beauvericin                      | Depsipeptide   | Fusarium o.        | *Miquelia dentata*    |                              | 5.63, 23.5, 10.32 µg/mL (crude fungal ethyl acetate extract) | [26]            |
| Taxol                            | Diterpenes     | Fusarium o.        | *Cinnamomum kuehneae*|                              |                                      |                 |
| Vincristine                      | Alkaloids      | Fusarium o.        | *Catharanthus roseus* |                              |                                      |                 |
| Beauvericin                      | Depsipeptide   | Fusarium o.        | *Cinnamomum kuehneae*|                              |                                      |                 |
| Camptothecine (CPT),             | Alkaloids      | *Fomitopsis* spp.  |                       |                              |                                      |                 |
| 9-methoxy CPT, 10-hydroxy CPT    |                |                    |                       |                              |                                      |                 |
| Beauvericin                      | Depsipeptide   | Fusarium o.        | *Apodytes dimidata*   |                              | 1.41, 1.66, 1.81, 2.29, 3.0, 5.0, 4.7-5.0, 8.8-22.2 µM | [77,76]         |
| Taxol                            | Diterpenes     | Fusarium o.        | *Echinocarpus*        |                              | 1.41, 1.66, 1.81, 2.29, 3.0, 5.0 µM | [77]            |
| Vincristine                      | Alkaloids      | Fusarium o.        | *Echinocarpus*        |                              | 1.41, 1.66, 1.81, 2.29, 3.0, 5.0 µM | [77,78]         |
| Camptothecin                     | Polyketide     | Fusarium o.        | *Echinocarpus*        |                              | 1.41, 1.66, 1.81, 2.29, 3.0, 5.0 µM | [77,78]         |
| Camptothecine (CPT),             | Alkaloids      | Fusarium s.        | *Apodytes dimidata*   |                              | 7, 8.5, 8 & 7, 8.5, 8 µg/mL           | [10,26]         |
| 9-methoxy CPT, 10-hydroxy CPT    |                |                    |                       |                              |                                      |                 |
| Podophyllotoxin                  | Lignans        | Fusarium s.        | *Podophyllum hexandrum*|                              | #                                    | [79]            |
| Camptothecine (CPT),             | Alkaloids      | Fusarium s.        | *Camptotheca acuminata*|                              |                                      | [26,80]         |
| 9-methoxy CPT, 10-hydroxy CPT    |                |                    |                       |                              |                                      |                 |
| Gliocladiolicii A & B            | Epipolythiodi-oxopiperazines | Gliocladium spp. | *Cordyceps sinensis*  |                              | 0.50, 0.50,20 µg/mL (GI50) | [81]            |
| Guignarenone A                   | Tricyclo-       | Guignardia b.      | *Garcinia bombiliana* |                              | 0.38, 2.24 µM                        | [82]            |
| Guignardones Q & S               | Alleloperooids  | Guignardia m.      | *Smilis glabra*       |                              | 83.7 & 92.1 µM                       | [83]            |
| Cajanol (5-hydroxy-3-(4-hydroxy-2-methoxyphenyl)-7-methoxychroman-4-one) | Flavonoids | *Hypocrea l.*    | *Cajanus cajan roots, stems and leaves| 1. A-549, QGY, U973, 2. A-549 | 1. 20.5 µg/mL after 72 h treatment, 24.6 µg/mL after 48 h; and 32.8 µg/mL after 24 h | [84]            |
Table 2. Cont.

| Compounds                  | Chemical Class                  | Fungal Endophytes      | Host Medicinal Plant                  | Activity Against Cell Lines | IC50 Values          | Ref. |
|----------------------------|--------------------------------|------------------------|---------------------------------------|----------------------------|----------------------|------|
| Daldinone C & D           | Benzol[j]fluoranthene          | Hypoxylon t. IFB-18    | Artemisia annua surface-sterilized fresh stems | SW1116                     | 49.5 & 41.0 µM       | [85] |
| 1. * Brefeldin A, trichothecone, 7α-hydroxy-scorpene | | | | | 1. 0.18, 0.04, 0.1; 12.90, 10.06, 11.31 & >75.10, 2.37, 1.73 µM | [86] |
| 2. 8-deoxy-trichothecin, 7α-hydroxy-trichodermol | | | | | 2. >62.81, 0.88, 1.48 & 8.47, 21.53, 27.76 µM | [86] |
| Taxol                      | Diterpenes                     | Lasiodiplodia t.       | Morinda citrifolia leaves             | 1. MCF-7                    | 1. 300 µg/mL         | [60,87] |
| boasted                   | Macrolide                      | Lasiodiplodia t. (MUB-65) | Myrocarphaena urundeva branches     | HCT-116                     | 11.2 µg/mL           | [88] |
| Vincristine                | Alkaloids                      | Myelia s. 97CY (3)     | Catharanthus roseus leaves           | HeLa, MCF7, U251, A549, A431 & HEK293 | 4.2, 4.5, 5.5, 5.5, 5.8 µg/mL | [74,89] |
| Spiromamakone A           | Spirois naphthalene            | Myelia s.              | Knightia excelsa surface-sterilized leaves | P388                       | 0.33 µM              | [90] |
| Cercosporin                | Quinones                       | Mycosphaerella spp.    | Psychotria horizontalis              | MCF7                       | 4.68 µM              | [91] |
| Arundinone B              | Coumarins                      | Microsphaeropsis a.    | Ulmus macrocarpa stems               | T24, A549                    | 35.4, 81.6 µM        | [92] |
| Mycoleptodiscin B         | Alkaloids                      | Mycoleptodiscus spp. F0194 | Inkannabinariosis incomparabilis healthy mature leaves | H460, A2058, H522-T1, PC-3, IMR-90, HepG2, SMMC-7721, A549, MCF-7 cells, QSC-7701, HL-7702 | 0.66, 0.78, 0.63, 0.60, 0.41 µM | [93] |
| Myrotheciumone A          | Lactone                        | Microthecium r.        | Ajuga decumbens                      |                            | 5.36, 6.56, 5.88, 7.56, 16.30, 20.69 µM | [94] |
| Dihydromyrothecine C      | Trichothecone Macrolide        | Microthecium r. IFB-E012 | Artemisia annua                       | KB                          | 44.48 µM             | [95] |
| Camptothecin              | Alkaloids                      | Neurospora c.          | Notopadophyto foetida seed           | A-549, HEP-2, OVCAR-5       | -                   | [11,96] |
| (2R,4R*)-3,4-dihydro-4-methoxy-2-methyl-2H-1-benzopyran-5-ol | | | | | | |
| Pyrans                    | Nodulisporium spp.             | Aquilaria sinensis stem |                            | SF-268                      | -                   | [97] |
| Brefeldin A               | Lactone                        | Paeclomycetes spp.     | 1. Torrega grandis                   | Hl-60, KB, Hela, MCF-7 and Spc-A-1 | 10.0, 9.0, 1.8, 2.0 & 1.0 ng/mL | [31] |
| (22E,24R)-8,14-epoxyergosta-4,22-diene-3,6-dione | Steroids                      | Pupulaspora i.         | 2. Taxus naini bark                  | MDA-MB435, HCT-8, SF295, HL-60 | 3.3, 14.7, 5.0, 1.6 µM | [98] |
| 1. 19-(α-D-glucopyranosyl) |                   | Paraconiothyrium spp. MY-42 | Isopimara-7,15-dien-3β-ol             |izia stem                   | SF-268                      | - | |
| 2. 19-(α-D-glucopyranosyl) |                   | Paraconiothyrium spp. MY-42 | Isopimara-7,15-dien-3β-ol             |izia stem                   | SF-268                      | - | |
| 3. 19-(α-D-glucopyranosyl) |                   | Paraconiothyrium spp. MY-42 | Isopimara-7,15-dien-3β-ol             |izia stem                   | SF-268                      | - | |
| 4. 19-(α-D-glucopyranosyl) |                   | Paraconiothyrium spp. MY-42 | Isopimara-7,15-dien-3β-ol             |izia stem                   | SF-268                      | - | |
| Compounds                        | Chemical Class                           | Fungal Endophytes                  | Host Medicinal Plant | Activity Against Cell Lines | IC50 Values | Ref.   |
|---------------------------------|------------------------------------------|-----------------------------------|----------------------|-----------------------------|-------------|--------|
| Brasilamides E 5-Methyl-8-(3-methylbut-2-enyl) furanocoumarin | Bisabolane Sesquiterpenoids             | Paraconiothyrium b. (M3-3341)     | Acer truncatum branches | MCF-7 and MGC               | 8.4 & 14.7 µM | [100]  |
| 1. Penicillenol A, 2. Penicillenol B1 | Coumarins                                | Penicillium spp. ZH16             | Aviceinia sp. leaves  | KB, KBV200                  | 5.10 µg/mL  | [101]  |
| 1. Leptosphaerone C 2. Penicillenone | Polyketides (tetratomic acids derivatives) | Penicillium spp. GQ-7             | Aegiceras corniculatum inner bark | 1. A-549, BEL-7402, P388, HL-60 | 1. 23.8, 13.03, 8.85, 0.76 µM | [102]  |
| 2. Penifupyrole | Funicone                                | Penicillium spp. JS-HZ-43          | Aegiceras corniculatum inner bark | 1. A549, 2. P388 | 1. 1.45 µM | [103]  |
| Lapachol                         | Naphthoquinone                          | Penicillium spp.                  | Tabebuia argentia     | DU145, HepG2, Hep3B & MCF-7 | (β-Lapachone) | -      |
| 1. Penicillenol A, 2. Penicillenol F | Menoterpenoids                          | Penicillium spp. SXH-65           | Tamaria chinensis     | Hela, HL-60 and K562        | 59.9, 24.2, 36.2 & 44.4, 45.9, 46.6 µM | [105]  |
| 1. Heptaketide 2. Mycotoxin | Periconicin B, Periconicin F   | Penicillium spp.                  | Hertiera littoralis root | HCT-8, Bel-7402, BGC-823, A549, A2780, MCF-7 | >10^{-5} M | [106]  |
| 1. TMC-264, 2. PR-toxin | Citriquinchoman                          | Penicillium ci.                   | Ceratonia siliqua stem | L5178Y | 6.1 µM | [107]  |
| 1. (+)-(3S,6S,7R,8S)-periconone A, 2. (---)-(1R, 4R, 6S, 7S)-2-caroten-4,8-olide | Periconicin B, Periconicin F | Periconia spp.                   | Annona muricata leaves | HeLa and CHO | 8.0 µM | [109]  |
| Periconicin B                    | Periconia a.                             | Xylopia aromatica leaves          | HeLa and CHO         | 8.0 µM | [109]  |
| Pestalopitopsis F                | Diterpene                               | Pestalotopisis spp.              | Rhizophora mucronate leaves | L5178Y | 8.93 µg/mL (EC50) | [110]  |
| Pestalaclam A, Pestalaclam B1 (45,65)-6[(15,2R)-1, 2-dihydroxybutyl]-4-hydroxy-4-methoxytetrahydro-2H-pyran-2-one, 2. (65,2E)-6-hydroxy-3-methoxy-5-oxodec-2-enoic acid, 3. LL-P8808, 4. LL-P8808e, 5. Ergosta-5,7,22-trien-3β-ol, Siccayne [2-(3-Methyl-3-buten-1-ynyl) Hydroquinone] | Alkaloids                       | Pestalotopisis spp.          | Melaleuca quinquenervias stem | MCF-7, NFF | 64.4, 20.2 & 58.5, 12.8 µg/mL | [111]  |
| Pestalone B                      | Monoterpenoids (1,2)                    | Pestalotopisis spp.               | Dendrobium officinale | 1–4 >> HL-60, 1, 2, 4 and 5 >> LOVO | 1–4. 15.24, 30.09, 64.87, 50.75 µM, 12.45, 50.97, 41.91, 68.88 & 65.20 µM | [112]  |
| Molecules                       | Alkyne                                  | Pestalotopisis f.                 | Canella sinensis branches | HeLa, HT29 | 48.2, 33.9 µM | [113]  |
| 1. Pestalofone F, 2. Pestalofone C | Diterpene                               | Pestalotopisis f.                 | Canella sinensis branches | HeLa, MCF-7 | 14.4, 36.4, 36.4, 16.7, 11.9, 33.6, 33.6, 97.5 µM | [114,115] |
| 2. Pestaloficil I, K & L        | 1. Epoxy cyclohexanediol                | Pestalotopisis f.                 | Canella sinensis branches | HeLa, HepG2, U-251 | 12.6, 31.7, 5.4 µg/mL | [116]  |
| Pestalrone B                    | Benzophenones                           | Pestalotopisis k.                 | Camellia sasanqua stems | HeLa, HepG2, U-251 | 12.6, 31.7, 5.4 µg/mL | [117,118] |
| Taxol                           | Diterpene                               | Pestalotopisis m. EF01            | Plectranthus amboecus healthy leaves | Hep G2, MCF-7, BT220, HL251 | 0.5 µg/mL | [117,118] |
Table 2. Cont.

| Compounds                          | Chemical Class | Fungal Endophytes | Host Medicinal Plant | Activity Against Cell Lines | IC50 Values | Ref. |
|------------------------------------|----------------|-------------------|----------------------|-----------------------------|-------------|------|
| Torreyanic acid                    | Quinones       | Pestalotiopsis m. | Torreya taxifolia    | NEC, A549 BT20, H116, INT-407, HL251, HLK210, MCF-7 | 3.5, 45 µg/mL | [119]|
| Taxol                              | Diterpene      | Pestalotiopsis m. | Taxus wallichiana    |                             | 0.005–0.5 µM | [60,120]|
| Taxol                              | Diterpenes     | Pestalotiopsis p. p. | Tabeula pentaphyllia | MCF-7 breast cancer cell line | 350 µg/mL | [121]|
| Photinides A–F, Photipyrene B      | γ-Lactones     | Pestalotiopsis p. | Roystonea regia      | MDA-MB-231 BT20, H116, INT-407, HL251, HLK210, MCF-7 | 10 µg/mL (IC25) | [122,123]|
| Taxol                              | Diterpenes     | Pestalotiopsis t. | Terminalia arjuna leaves |                             | -           | [60,121]|
| Taxol                              | Diterpene      | Pestalotiopsis v., Phialephia f. | Taxus cuspidate leaves and inner bark | MCF-7 breast cancer cell line | - | [73]|
| Podophyllotoxin Phialomustin A–D  | Lignan Azaphilone | Pestalotiopsis v. | Podophyllam pellatun | Topoisomerase 1 T47D | 10, 1, 7, 9.2 µM | [12]|
| Camptothecine (CPT)                | 1. Polyketide 2. Xanthone O-glycoside | Phomopsis spp. | Cinnamomum mollissimum | P388 | 1. 94.6 (%) 2. 48.8 (%) | [125]|
| Camptothecine (CPT)                | Diterpenes     | Phomopsis b.      | Ginkgo biloba leaves | MCF-7, A549, T98G | - | [117]|
| 9-hydroxypodophyllotoxin           | Alkaloids      | Phomopsis spp.    | Miquelia dentata fruit and seed regions | HCT-116, SW-480, MCF-7 | - | [26]|
| 2. 3-O-(6-O-a-L-arabinopyranosyl)-β-D-glucopyranosyl-1,4-dimethoxy-xanthone | 1. Polyketide 2. Xanthone O-glycoside | Phomopsis spp. | Excoecaria agallocha stem | HEP-2 and HepG2 | 32-64 µg/mL (MIC) | [126,127]|
| 1. Deepsidone 2. Isobenzofuranones | Xanthone       | Phomopsis spp.    | Kandelia candel foliage | 1. MDA-MB-435 2. Raji cell line | 1. 63 µM 2. 27, 47 & 18 µM | [128]|
| Phomoxanthone A and B              | Xanthone       | Phomopsis spp.    | Tectona grandis      | KB, BC-1, Vero | 0.99, 0.51, 1.4 & 4.1, 0.70, 1.8 µg/mL | [129]|
| 1. Oblongolide Y                   | Polyketide (hexaketide y-lactone) | Phomopsis spp. | Musa acuminata leaf | 1. BC 2. KB, BC, NCI-H187, Vero | 1. 48 µM 2. 37, 26, 32, 60 µM | [130]|
| 2. Oblongolide Z                   | Cytochalasins  | Phomopsis spp.    | Garcinia kola nut     | HeLa | 8.18, 35.69 & 3.66 µg/mL (LC50) | [131]|
| 18-methoxy-cytochalasin j, Cytochalasins H and I | Ergochromes | Phomopsis l. | Dierandrola frutescens stem | A549, HCT-116 | 7, 1.8, 1 & 7, 1.8, 7 µg/mL (IC100) | [132]|
| Dierandrol A, B & C                | Sesquiterpene Quinone | Phyllosticta s. | Platyelalus orientalis leaf tissue | NCI-H460, PC-3 M, MCF-7, SF-268, MIA Pa Ca-2 | 4.3, 3.5, 1.5, 1.8, 2.8 µM | [133]|
| Tauranin                           | Tauranin Sesquiterpene Quinone | Phyllosticta s. | Platyelalus orientalis leaf tissue | NCI-H460, PC-3 M, MCF-7, SF-268, MIA Pa Ca-2 | 4.3, 3.5, 1.5, 1.8, 2.8 µM | [133]|


| Compounds | Chemical Class | Fungal Endophytes | Host Medicinal Plant | Activity Against Cell Lines | IC50 Values | Ref. |
|-----------|----------------|------------------|----------------------|-----------------------------|-------------|-----|
| Ergoflavin | Ergochrome | PM0651480 | Mimusops elengi | TNF-α, IL-6, ACHN, H460, Panc1, HCT116, and Calu1 | 1.9, 1.2, 1.2, 4, 24, 8, & 1.5 µM | [134] |
| Spiropreussione A | Spirobis naphthalene | Preussia spp. | Aquilaria sinensis | A2780, BEL-7404 | 2.4, 3.0 µM | [135] |
| Cytochalasin 1, 2, 3 and E | Alkaloids | Rhinocladiella spp. | Tristergyrium wilfordii dead tree limbs | A2780S, HCT-116, SW-620 | 3.91, 15.6, 3.91; 15.6, 62.5, 15.6; 3.91, -15.6 & <0.0153, 0.977, 0.244 µg/mL (IC100) | 1.2281 |
| 1. Rhytidones B | Spirobis naphthalenes | Rhytidhysteron spp. | Azima sarmentosa leaves | A2780S, BEL-7404 | 2.4, 3.0 µM | [135] |
| 2. Rhytidones C, MK3018, Palmarumycin CR1 | Spirobis naphthalenes | Rhytidhysteron spp. | Azima sarmentosa leaves | A2780S, BEL-7404 | 2.4, 3.0 µM | [135] |
| TMC-264 | Heptaketide | Rhizopogon v. Nitatf22 | Nicotiana tabacum | HCT-116, HepG2, BGC-823, NCIH1650, and A2780 | 4.2, 5.9, 7.8, 3.2, & 3.6 µM | [138] |
| Rhytidone H & F | Spirobisnaphthalenes | Rhytidhysteron r. AS21B | Azima sarmentosa leaves | Ramos and H1975 | 0.018, 0.252 & 0.048, 1.17 µM | [139] |
| 1. Secalonic acid A, Penicillixanthone A | 2. Hypothemycin | Sphaeropsidin A, Sphaeropsidin D | Diterpenes | Sphaeropsidin A, Sphaeropsidin D | Sphaeropsidin A, Sphaeropsidin D | [140] |
| Taxol | Diterpenes | Stemphylium s. SBU-16 | Taxus baccata inner bark | MCF-7, A549, T98G | 1.33, 2.78, 1.29, 1.73, 0.89 & 1.92, 0.91, 0.90, 1.31, 0.70 µg/mL, 4.2, 4.5, 5.5, 5.5, 5.5 µg/mL | [146] |
| 1. Altersolanol A, 2. Alterporriol G and H | Quinones | Stemphylium g. | Mentha pulegium stem | MCF-7, A549, T98G | 1.33, 2.78, 1.29, 1.73, 0.89 & 1.92, 0.91, 0.90, 1.31, 0.70 µg/mL, 4.2, 4.5, 5.5, 5.5, 5.5 µg/mL | [146] |
| 1. 3-Dehydroxymethylbisde-thio-3,10a-bis(methylthio)gliotoxin | 2. Bisdethiobis(methylthio)Gliotoxin | Talaromyces spp. LGT-2 | Tristergyrium wilfordii | B16 | 86, 82 & 78% at 500 µg/mL | [148] |
| 1. Altersolanol A, 2. Alterporriol G and H | Quinones | Stemphylium g. | Mentha pulegium stem | MCF-7, A549, T98G | 1.33, 2.78, 1.29, 1.73, 0.89 & 1.92, 0.91, 0.90, 1.31, 0.70 µg/mL, 4.2, 4.5, 5.5, 5.5, 5.5 µg/mL | [146] |
| Vincristine and Vinblastine | Alkaloids | Talaromyces r. CrP20 | Catharanthus roseus leaf tissues | MCF-7, A549, A431 | 4.2, 4.5, 5.5, 5.5, 5.5 µg/mL | [74] |
| Taxol | Terpenes | Taxomyces a. | Taxus brevifolia inner bark | INT-407, HL251, MCF-7,98G, T98G | - | [6,60] |
| Hypericin, Emodin | Polyketides | Thielavia s. | Hypericum perforatum stem | MCF-7, MDA-MB-435, HeLa, MDA-MB-231, B16, MCF-7,98G, T98G | 1.33, 2.78, 1.29, 1.73, 0.89 & 1.92, 0.91, 0.90, 1.31, 0.70 µg/mL, 4.2, 4.5, 5.5, 5.5, 5.5 µg/mL | [146] |
| Podophyllotoxin | Lignan | Trametes h. | Podophyllium hexandrum | MDA-MB-435, HeLa, MDA-MB-231, B16, MCF-7,98G, T98G | 1.33, 2.78, 1.29, 1.73, 0.89 & 1.92, 0.91, 0.90, 1.31, 0.70 µg/mL, 4.2, 4.5, 5.5, 5.5, 5.5 µg/mL | [146] |
| Aspocilalin D, Aspocilalin J | Cytochalasan | Trichoderma g. | Panax notoginseng | MDA-MB-231, B16, MCF-7,98G, T98G | 500 µM (LC25), 500 µM (LC50) | [150] |
| Trichothecinol-A | Mycotoxins | Trichothecium spp. XG8D | Phyllanthus amarus | MDA-MB-231, B16, MCF-7,98G, T98G | 500 µM (LC25), 500 µM (LC50) | [150] |
| Merulin A Merulin C | Sesquiterpenes | Xylaria spp. | Xylariopsis granatum plant | BT474, SW620 | 4.98, >10 & 4.84, >10 µg/mL | [151] |
| Eremophilanolide 1,2 & 3 | Sesquiterpenes | Xylaria spp. BCC 21097 | Liciaula spinosa | KB, MCF-7, NCI-H165, Vero cells | 3.8-21 µM | [152] |
**Table 2. Cont.**

| Compounds | Chemical Class       | Fungal Endophytes | Host Medicinal Plant                     | Activity Against Cell Lines | IC50 Values          | Ref. |
|-----------|----------------------|-------------------|------------------------------------------|-----------------------------|----------------------|------|
| 1. 2-Chloro-5-methoxy-3-methylcyclohexa-2,5-diene-1,4-dione | Benzoquinone | Xylaria spp. | *Sandoricum koetjape* | Vero cells | 1.35, >184 µM | [153] |
| 2. Xylariaquinone A | Cytochalasin | Xylaria spp. | *Hypnum sp.* | 1.2 >> NCI-H460, PC-3M, SF-268, MDA-MB-231; 1. >> MCF-7; D: 1.03, 0.22, 0.43, 1.01 µM; C: 1.65, 1.06, 0.96, 1.72 µM; Q: 1.53, 1.51, 1.31, 1.32; 1.44 µM | [154] |
| 1. Cytochalasin D | Alkaloids | Xylaria spp. | *Toona sinensis* | brine shrimp | 2.79 µM (LC50) | [155] |
| 2. Cytochalasin C and Q | Cytochalasins | Xylaria spp. | NC1214 | 1. NCI-H187, KB, Vero cell | 1. 5.95, 3.25, 0.36 µg/mL; 2. NCI-H187, Vero cell | 47.95 µg/mL | [156] |
| 1. Cytochalasin D | Ergosterol peroxide | Xylaria spp. | *Toona sinensis* | PC-3M, SF-268, MDA-MB-231; 1. >> MCF-7; D: 1.03, 0.22, 0.43, 1.01 µM; C: 1.65, 1.06, 0.96, 1.72 µM; Q: 1.53, 1.51, 1.31, 1.32; 1.44 µM | [154] |
| 2. Ergosterol peroxide | 1. Cytochalasins | Xylaria spp. | *Toona sinensis* | brine shrimp | 2.79 µM (LC50) | [155] |
| 1. Xylariacin A | Triterpenes | Xylarialean spp. | *Annona squamosa* phloem | HepG2 | 48, 9.7, 46.7% at 20 µg/mL | [157] |
| 2. Xylariacin B | Steroid | Xylarialean spp. | *Annona squamosa* phloem | HepG2 | 48, 9.7, 46.7% at 20 µg/mL | [157] |
| 3. Xylariacin C | Unidentified | ZSU44 (not better identified) | mangrove plant | HL-60, K562 | 0.38, 0.43 µM | [158] |

* Compounds with IC50 values less than 10 µM are reported.

**Table 3.** Recently (2018–2020) reported potential cytotoxic metabolites isolated from medicinal-plant-associated endophytic fungi.

| Sl | Isolated Metabolites * | Fungus Name | Host Medicinal Plant | Reported Activity | References |
|----|------------------------|-------------|----------------------|-------------------|------------|
| 1  | Penicolinate A          | *Bionectria* spp. | *Raphia taedigera* | Displayed potent cytotoxicity against cells with an IC50 value of 4.1 µM. Shown selective and potent effect towards BT-549, MCF-7, SKOV-3, and HCT-116 cell lines with IC50s 0.09, 0.21, 1.23, and 0.39 µM, respectively | [159] |
| 2  | Fusarthioamide B        | *Fusarium* c. | *Anvillea arcinia* (Burm.f.) DC. | Exhibited potent cytotoxic effect on HepG2 and SMCC-7721 cells with the IC50 values were 0.347 and 0.380 mM, respectively | [160] |
| 3  | 3-(4-nitrophenyl)-5-phenyl isoxazole | *Aspergillus* n. spp. | | Exhibited strong biological effect against MCF7 with a half-maximal inhibitory concentration value at 7.73 ± 0.11 µM | [161] |
| 4  | Spiciferone F           | *Phoma* b. | *Kalidium foliatum* (Pall.) Moq | Displayed cytotoxic activity against human tumor cell lines BGC-823 cells with IC50 values of 1.5 µmol L⁻¹ | [162] |
| 5  | Xylariphthalide A       | *Diapthe* spp. | *Tylophora ouata* | Displayed cytotoxic activity against human tumor cell lines BGC-823 cells with IC50 values of 8.6 µmol L⁻¹ | [163] |
| 6  | *Cis*-4-hydroxy-6-deoxylalone | *Diapthe* spp. | *Tylophora ouata* | Displayed cytotoxic activity against human tumor cell lines BGC-823 cells with IC50 8.6 µmol L⁻¹ | [163] |
| 7  | Xylarolide A            | *Diapthe* spp. | *Datura inoxia* | Showed promisingly inhibited growth of MIA PaCa-2 and PC-3 cells with an IC50 values of 14 µM | [164] |
| 8  | Jammosporin A           | *Rosellinia sanctae-cruciana* | *Albizia lebbeck* | Exhibited promising cytotoxic potential against the human leukemia cancer cell line (MOLT-4) | [165] |
Table 3. Cont.

| Sl | Isolated Metabolites * | Fungus Name | Host Medicinal Plant | Reported Activity | References |
|----|------------------------|-------------|----------------------|-------------------|------------|
| 9  | Pyrrocidine A (Pyridone alkaloid) | Cylindrocarpon spp. | Sapium ellipticum | Showed potent cytotoxicity against the human ovarian cancer cell line A2780 with an IC50 value of 1.7 µM | [166] |
| 10 | Bostrycoindin | Fusarium s. | Cassia alata Linn. plant | Significant cytotoxicity against vero cell line | [8] |
| 11 | Anhydrofusarubin | | | Exhibited cytotoxicity against human lung adenocarcinoma EGFR-TKI-resistant A549 cells with IC50 values of 3.6 µM | |
| 12 | 1-Monolinolein | Streptomyces c. YBQ59 | Cinnamomum cassia plant | | |
| 13 | Bafilomyacin D | Colletotrichum g. A12 | Aquilaria sinensis | Showed activity against EGFR-TKI-resistant A549 cells with IC50 values 6.7 µM | [167] |
| 14 | 3′-Hydroxydaidzein | Colletotricone A | Eucalyptus exserta | Showed activity against EGFR-TKI-resistant A549 cells with IC50 values 7.8 µM | |
| 15 | | | | Inhibited growth of MCF-7, NCI-H460, HepG-2, and SF-268 tumor cells with IC50 values ranging from 15.7 to 46.8 µM | [168] |
| 16 | Mollicellin G | Chaetomium spp. Eef-10 | | Cytotoxic against two human cancer cell lines HepG2 and Hela with IC50 values of 19.64 and 13.97 µg/mL, respectively | [169] |
| 17 | Demethylincisterol A3 | Pestalotiopsis spp. Penicillium spp. (strain ZO-R1-1) | Rhizophora mucronata Zingiber officinale | | |
| 18 | Shearilicine (1), Paspaline-13-ene (2), 7-Hydroxypaxilline-13-ene (3), Shearinine O (6), Shearinine P (7), emindole SB (10), paspaline (18), 7-hydroxy-13-dehydroxypaxilline (19) | | | I showed the most pronounced cytotoxicity against L5178Y (IC50 is 3.6 µM) whereas 1, 6, 10 and 18 displayed pronounced cytotoxicity with IC50 values ranging between 5.3 and 8.7 µM against A549, HT-29, and MCF-7 cancer cells with an IC50 concentration of 9.89 µg/mL, 18 µg/mL, and 54 µg/mL, respectively | [170] |
| 19 | Flavipin | Chaetomium g. | Couroupita guianensis Aubl. leaves | Exhibited cytotoxicity toward A549, HT-29, and MCF-7 cancer cells with an IC50 concentration of 9.89 µg/mL, 18 µg/mL, and 54 µg/mL, respectively | [172] |
| 20 | Bellidisin D | Phoma b. | Tricyrtis maculate leaves | Exhibited significant cytotoxicity against HL-60, A549, SMMC-7721, MCF-7, and SW480 cells with IC50 value ranging from 3.40 to 15.25 µM | [173] |
| 21 | Epicorazine A | Epicoccum n. | Salix sp. | Displayed strong to moderate cytotoxic activities against L5178Y, Ramos, and Jurkat J16 cell lines with IC50 ranging from 1.3 to 28 mM | [174] |
Table 3. Cont.

| Sl  | Isolated Metabolites * | Fungus Name                      | Host Medicinal Plant       | Reported Activity                                                                 | References |
|-----|------------------------|----------------------------------|----------------------------|-----------------------------------------------------------------------------------|------------|
| 22  | Cytochalasin E         | Aspergillus spp.                  | Pinellia ternata tubers    | Exhibited significant cytotoxicity with an IC50 value of 7.8 µM                   | [175]      |
| 23  |                        | Aspergillus A-F (seco-cytochalasins), Asperlactone G-H (asperlactones) Demethylchaetocochin C, dethio-tria(methylthio)chetomin, chaetoperazine A, 4-formyl-N-(30-hydroxyopyridin-20-yl) benzamide |                           | All the compounds showed cytotoxicity against A-549 with IC50 values ranging from 23.3 to 70.2 µM | [175]      |
| 24  |                        | Chaetomium g. 7951               | Panax notoginseng root      | Showed cytotoxicity against MCF-7, MDA-MB-231, H460, and HCT-8 cell lines with IC50 values ranging from 4.5 to 65 µM | [176]      |
| 25  | Chetoseminudin F (1), chaetocochin C (6), ergosterol (8), chetomin A (9), chetomin (12) | Chaetomium spp. SYP-F7950      |                           | 1 displayed more potent cytotoxic activity against MDA-MB-231 cells than paclitaxel with IC50 of 26.49 µM, 6, 8, 9 and 12 exhibited strong cytotoxicity with IC50 values ranging between 2.75 and 8.68 µM against A549 and MDA-MB-231 1 and 3 exhibited moderate cytotoxic activities against MDA-MB-231, MDA-MB-435, NCI-H460, PC-3 & HCT116 cell lines with IC50 values ranging between 4.2 and 7.8 µM. 2 showed cytotoxicity towards the MDA-MB-231 and HCT116 cells with IC50s of 6.6 and 4.5 µM, respectively. Exhibited moderate cytotoxicity towards MDA-MB-231 cell line with an IC50 value of 22.4 ± 1.1 µM. | [177]      |
| 26  | Ascomylactam A to C (1–3) | Didymella spp. CYSK-4             | Pluchea indica healthy branch | 1 and 3 displayed moderate toxicity against SK-MEL and BT-549 cell lines. 2 showed moderate toxicity against BT-549 and LLC-PK11 cell lines. | [178]      |
| 27  | Pleosporalin F         | Pleosporales spp. F46             | Mahonia fortunei           | 1–3 showed selective cytotoxicity against the cell line, MV4–11, with IC50 values of 7.2, 10.0, and 0.22 µM, respectively. Displayed significant specific cytotoxic activity against HL-60 cells with an IC50 of 1.11 µM. Displayed weak cytotoxic activities against MCF-7 and LM3 cells, with IC50 values of 34.4 and 39.2 µM, respectively. Displayed moderate cytotoxicity towards A549, LN229, MGC, LOVO, and MDA231 with IC50 values of 51.45, 23.43, 39.16, 46.97, and 42.85 µg/mL, respectively. | [179]      |
| 28  |                        | Nemania spp. UM10M                | Torreya taxifolia leaf     | 1–3 showed moderate cytotoxicity against the cell line, MV4–11, with IC50 values of 7.2, 10.0, and 0.22 µM, respectively. Displayed significant specific cytotoxic activity against HL-60 cells with an IC50 of 1.11 µM. Displayed weak cytotoxic activities against MCF-7 and LM3 cells, with IC50 values of 34.4 and 39.2 µM, respectively. Displayed moderate cytotoxicity towards A549, LN229, MGC, LOVO, and MDA231 with IC50 values of 51.45, 23.43, 39.16, 46.97, and 42.85 µg/mL, respectively. | [180]      |
| 29  | Gartryprostatins A to C (1–3) | Aspergillus spp. GZWMJZ-258       | Garcinia multiflora fruit   | 1–3 showed selective cytotoxicity against the cell line, MV4–11, with IC50 values of 7.2, 10.0, and 0.22 µM, respectively. Displayed significant specific cytotoxic activity against HL-60 cells with an IC50 of 1.11 µM. Displayed weak cytotoxic activities against MCF-7 and LM3 cells, with IC50 values of 34.4 and 39.2 µM, respectively. Displayed moderate cytotoxicity towards A549, LN229, MGC, LOVO, and MDA231 with IC50 values of 51.45, 23.43, 39.16, 46.97, and 42.85 µg/mL, respectively. | [181]      |
| 30  | 19,20-epoxycytochalasins C (1) and D (2), and 18-deoxy-19,20-epoxy-cytochalasin C (3) | Nemania spp. UM10M | Solanum tuberosum stem tissues | 1–3 showed moderate cytotoxicity against the cell line, MV4–11, with IC50 values of 7.2, 10.0, and 0.22 µM, respectively. Displayed significant specific cytotoxic activity against HL-60 cells with an IC50 of 1.11 µM. Displayed weak cytotoxic activities against MCF-7 and LM3 cells, with IC50 values of 34.4 and 39.2 µM, respectively. Displayed moderate cytotoxicity towards A549, LN229, MGC, LOVO, and MDA231 with IC50 values of 51.45, 23.43, 39.16, 46.97, and 42.85 µg/mL, respectively. | [182]      |
| 31  | Sporulosaldein F       | Paraphaeosphaeria spp. F03        | Paepalanthus planifolius leaves | 1–3 showed moderate cytotoxicity against the cell line, MV4–11, with IC50 values of 7.2, 10.0, and 0.22 µM, respectively. Displayed significant specific cytotoxic activity against HL-60 cells with an IC50 of 1.11 µM. Displayed weak cytotoxic activities against MCF-7 and LM3 cells, with IC50 values of 34.4 and 39.2 µM, respectively. Displayed moderate cytotoxicity towards A549, LN229, MGC, LOVO, and MDA231 with IC50 values of 51.45, 23.43, 39.16, 46.97, and 42.85 µg/mL, respectively. | [183]      |
| 32  | Trichodermin acid      | Penicillium o.                     | Taxus media roots           | 1–3 showed moderate cytotoxicity against the cell line, MV4–11, with IC50 values of 7.2, 10.0, and 0.22 µM, respectively. Displayed significant specific cytotoxic activity against HL-60 cells with an IC50 of 1.11 µM. Displayed weak cytotoxic activities against MCF-7 and LM3 cells, with IC50 values of 34.4 and 39.2 µM, respectively. Displayed moderate cytotoxicity towards A549, LN229, MGC, LOVO, and MDA231 with IC50 values of 51.45, 23.43, 39.16, 46.97, and 42.85 µg/mL, respectively. | [184]      |
Table 3. Cont.

| Sl | Isolated Metabolites * | Fungus Name | Host Medicinal Plant | Reported Activity | References |
|----|------------------------|-------------|----------------------|-------------------|------------|
| 33 | Stemphyperylenol (5), (17R)-4-hydroxy-17-methylincisterol (10) | *Alternaria a.* | *Psidium littorale* Raddi leaves | 5 showed cytotoxicity against MCF-7 and HepG-4 cell lines (IC50 values of 4.2 ± 0.6 and 7.9 ± 0.9 µM, respectively); 10 exhibited cytotoxicity against HepG-4 cell line with an IC50 value of 9.73 ± 1.2 µM. | [185] |
| 34 | Aspergisocoumrins A & B | *Aspergillus* spp. HN15-5D | *Acanthus ilicifolius* fresh leaves | MDA-MB-435 cells (IC50 values of 5.08 ± 0.88 and 4.98 ± 0.74 µM, respectively) | [186] |
| 35 | Phomoxanthone A (1) and Penialidin A (2) | *Coniochaeta* spp. F-8 | *Ageratina adenophora* | 1 showed a stronger cytotoxicity than 2 | [187] |
| 36 | Macrophin | *Phoma m.* | *Glycyrrhiza glabra* Linn | Exhibited prominent cytotoxic activity against all the cancer-cell lines (MDA-MB-231, T47D, MCF-7, and MIAPaCa-2 with IC50 values of 14.8, 8.12, 13.0, and 0.9 µM, respectively). | [188] |
| 37 | Myrothecines D–G (1–4), 16-hydroxymytoxin B (5), and 14′-dehydrovertisporin (6) | *Myrothecium r.* IFB-E008, IFB-E009, and IFB-E012 strains | *Trachelospermum jasminoides* | Showed cytotoxicity against K562 and SW1116 cells (IC50 values ranging between 56 nM and 16 µM). | [189] |
| 38 | Giluterrin | *Aspergillus* t. P63 | *Axonopus leptostachyus* roots | Exhibited cytotoxicity against 786-0 and PC-3 cell lines (IC50 of 22.93 µM and 48.55 µM, respectively). | [190] |
| 39 | 2′-aminodechloromaldoxin (1) and 2′-aminodechlorogeodoxin (2) | *Pestalotiopsis f.* | *Cinnamomum camphora* branches | 1 & 2 displayed moderate cytotoxicity against NCI-H460, SF-268, MCF-7 and PC-3cell lines (IC50 values of 18.63, 20.23, 23.53, 20.48 µM and 16.47, 17.57, 20.79, 19.43 µM, respectively). | [191] |
| 40 | Stachybochartins A, B, C, D and G. (S)-3,6-dihydroxy-8-methoxy-3-methylisochroman-4-one (1a), 6-methoxy-3-methylisochromane-3,8-diol (2) | *Stachybotrys c.* PT2–12 | *Pinellia ternata* | Showed cytotoxicity against MDA-MB-231 and U-2OS cells (IC50 values ranging between 4.5 to 21.7 µM). | [192] |
| 41 | | *Aspergillus f.* | *Cordyceps sinensis* fruiting body | 1a & 2 exhibited moderate growth inhibition against MV4–11 (IC50 values of 38.39 µM and 30.00 µM, respectively). | [193] |
| 42 | Flavoglaucin | *Aspergillus* spp. AV-2 | *Avicennia marina* healthy leaves | Exhibited most potent cytotoxicity against Caco-2 cells (IC50 of 2.87 µM) | [194] |
| 43 | Peniquinone A (1) & peniquinone B (2) | *Penicillium* spp. L129 | *Limonium s.* | 1 showed cytotoxicity against the cell lines, MCF-7, U87, and PC3 (IC50 ranging between 9.01 and 14.59 µM); 2 exhibited relatively weak cytotoxicity against the same cells (IC50 ranging between 13.45 and 25.32 µM). | [195] |
| Sl  | Isolated Metabolites * | Fungus Name          | Host Medicinal Plant | Reported Activity                                                                 | References |
|-----|-----------------------|----------------------|----------------------|-----------------------------------------------------------------------------------|------------|
| 44  | Pestalolide B (1), pestalotether F (4) | Pestalotiopsis spp. | Melaleuca alternifolia leaves | 4 displayed remarkable inhibitory effect against the cell lines, HL60, U87MG, MDA-MB-231, and HEP-3B cells (IC50 ranging from 1.42 to 5.90 \(\mu M\)); 4 exhibited significant inhibitory potency against HL60 (IC50 5.05 \(\mu M\)); 2, 4, and 6 showed cytotoxicity against cell lines, SMMC-7721 & SW-480 (IC50 values ranging between 8.19 and 18.80 \(\mu M\)). Compound 4 also exhibited cytotoxicity against A-549 (IC50 of 11.33 \(\mu M\)). Displayed weak inhibitory activities against SF-268, MCF-7, HepG-2, and A549 cell lines with IC50 values ranging between 30 and 100 \(\mu M\). | [196] |
| 45  | Emeridone B (2), Emeridone D (4), Emeridone F (6) | Emericella spp. Tj29 | Hypericum perforatum root | 2, 4, and 6 showed cytotoxicity against cell lines, SMMC-7721 & SW-480 (IC50 values ranging between 8.19 and 18.80 \(\mu M\)). | [197] |
| 46  | Lithocarin B & C, Tenellone H | Diaporthe l. A740 | Morinda officinalis twigs | All showed significant cytotoxicity against the cell lines, L929 and KB-3-1 (IC50 values ranging between 2.4 to 26 \(\mu g/mL\)). | [198] |
| 47  | Cytosporaquinone A–D, leucomelone | Cytospora spp. CCTU A309 | Juglans (Walnut tree) | 1 showed moderate cytotoxicity against MCF-7 cells (IC50 is 4.79 \(\mu M\)). 4 displayed cytotoxicity against MCF-7, NCI-H460, and SF-268 cells (IC50 values ranging between 5.46 to 8.56 \(\mu M\)). | [199] |
| 48  | Ilanpyrone (1), methyl Asterrate (4) | Annulohypoxylon i. | Cinnamomum sp. | 1, 7 & 15 exhibited cytotoxic activities against L5178Y (IC50 values of 5.0, 8.7, and 24.4 \(\mu M\), respectively). | [200] |
| 49  | Rhinomilisin A (1), Rhinomilisin G (7) and Gliocladic acid (15) | Rhinocladiella s. | Acrostichum aureum | 1 and 2 showed moderate cytotoxicity against HL-60 (IC50 value of 12.7 and 22.3 \(\mu M\), respectively) | [201] |
| 50  | Koninginol B (2), 1R,3R,6S,7R,10S-7-isopropyl-4,10-dimethylbicyclo[4.4.0]dec-4-en-3,10-diol (15), 1R,3R,6S,7R,10S-7-isopropyl-4,10-dimethylbicyclo[4.4.0]dec-4-en-3,10-diol (16) | Trichoderma k. A729 | Morinda officinalis branches | 1 and 2 showed moderate cytotoxicity against HL-60 (IC50 value of 12.7 and 22.3 \(\mu M\), respectively) | [202] |
| 51  | Cytochalasin D1 (1) and C1 (2) | Xylaria cf. cu. | Solanum tuberosum stem tissues | 3, 4, and 6–8 exhibited cytotoxic activities against NCI-H226 and/or MDA-MB-231 (IC50 values ranging between 5.5 to 9.5 \(\mu M\)). Exhibited cytotoxicity against HT-29, HepG2, Caco-2, HeLa, IEC6, and vero cells (IC50 values ranging between 8 to 23.5 \(\mu M\)). | [203] |
| 52  | Bipolahydroquinone C (3), cochlioquinone I (4), cochlioquinones K-M (6–8) | Bipolaris spp. L1–2 | Lycium barbarum fresh leaves | 1 and 2 showed moderate cytotoxicity against HL-60 (IC50 value of 12.7 and 22.3 \(\mu M\), respectively) | [204] |
| 53  | Botrysulfuranol A | Botryosphaeria m. strain E224 | Bixa orellana fresh leaves | 1 and 2 showed moderate cytotoxicity against HL-60 (IC50 value of 12.7 and 22.3 \(\mu M\), respectively) | [205] |
Table 3. Cont.

| Sl | Isolated Metabolites * | Fungus Name                        | Host Medicinal Plant       | Reported Activity                                                                 | References |
|----|------------------------|-----------------------------------|-----------------------------|-----------------------------------------------------------------------------------|------------|
| 54 | Chloroisosulochrin     | Pestalotiopsis t. (N635)          | Camellia sinensis (Theaceae)| Exhibited moderate cytotoxicity towards the HeLa cell line with an IC50 value of 35.2 µM | [206]      |
| 55 | Pestalotether D        |                                   |                             | Exerted cytotoxicity against HeLa and MCF-7 cell lines with IC50 values of 60.8 and 22.6 M, respectively |           |
| 56 | Cytosporins W *        | Pseudopestalotiopsis t.           | Rhizophora racemosa mangrove plants | Exhibited potent cytotoxicity towards mouse lymphoma cell line L5178Y with an IC50 value of 3.0 µM | [207]      |
| 57 | Terezine E and 14-hydroxyterezine D | Mucor spp.                        | Centaurea stoebe            | Showed potent activity against K-562 and HUVEC cell lines | [208]      |
| 58 | Citrinin (CIT) and dicitrinin-A | Penicillium ci.                   | Dichotomaria marginata      | Showed toxicity in A. saline, with LC50 (24 h) 1.71 µg/mL and 2.29 µg/mL, and LC50 (48 h) of 0.54 µg/mL and 0.54 µg/mL, respectively | [209]      |
| 59 | Allantopyrone E        | Aspergillus v.                     | Avicennia marina mangrove   | Exhibited cytotoxic effect on HeLa cells with IC50 = 50.97 µM                      | [210]      |
| 60 | Integracin A and B     | Cytospora spp.                     | Ceriops tagal (Chinese mangrove) | Both compounds showed promising cytotoxicity towards HepG2 Cells with IC50 values of 5.98 ± 0.12 µM and 9.97 ± 0.06 µM, respectively | [211]      |
| 61 | (±)-Asperteretone F (3a/3b) | Aspergillus t.                     | Hypericum perforatum        | Potent cytotoxic activities against human pancreatic cancer cells, including AsPC-1, SW1990 and PANC-1 cells, with IC50 values ranging from 1.2 to 15.6 µM showed moderate to strong cytotoxicity towards A549, BT-549, HepG2, and MCF-7 cells with IC50 values ranging from 5.6 to 14.2 µM | [212]      |
| 62 | Sterigmatocystin       | Pacilamymes spp. TE-540           | Nicotiana tabacum L.        | Exhibited cytotoxicity against MDA-MB-435 cell with an IC50 of 25.96 ± 0.32 µM | [213]      |
| 63 | Methyl 3-chloroasterric acid | Pleosporales spp. SK7.            | Kandelia candel leaves      | Exhibited selective cytotoxicity against NCI-H1650 and BGC823 tumor cells | [214]      |
| 64 | Rhizoperemophilane N   | Rhizopus v.                        | Nicotiana tabacum           | Exhibited strong cytotoxic activities against human lymphoma (Ramos) and leukemia (Jurkat J16) cells with IC50 values of 4.7 and 4.4 µM, respectively | [215]      |
| 65 | Pramanicin A           | Aplosarella j.                     | Orychophragmus violaceus (L.) O. E. Schul | Both the compounds exhibited promising cytotoxicity against SF-268, NCI-H460, and HepG-2 tumor cell lines with the IC50 ranging from 0.0002–16.2 µM and induced apoptosis of HepG-2 cells | [216]      |
| 66 | Myrothecines H and I   | Paramyrothecium r.                | Morinda officinalis         | Exhibited moderate-to-potent cytotoxic activities against MCF7 cells with IC50s of 35.06 and 25.20 µM, respectively | [217]      |
| 67 | Colletotrichalactone A and colletotrichalactone Ca | Colletotrichum spp. JS-0361 | Morus alba | Exhibited moderate-to-potent cytotoxic activities against MCF7 cells with IC50s of 35.06 and 25.20 µM, respectively | [218]      |
Table 3. Cont.

| SI | Isolated Metabolites * | Fungus Name | Host Medicinal Plant | Reported Activity | References |
|----|------------------------|-------------|----------------------|-------------------|------------|
| 68 | Emodin, (an anthraquinone) | *Diaporthe* l. | *Artocarpus heterophyllus* | exhibited cytotoxicity against murine leukemia P-388 cells with an IC50 value of 0.41 µg/mL | [219] |
| 69 | Demethylcisterol A3 | *Aspergillus* l. YP-2. | *Taxus yunnanensis* bark | Showed cytotoxicity against the A549 and HepG2 cell with IC50 values of 5.34 and 12.03 µM, respectively | [220] |
| 70 | Demethylincisterol A5 | | | Showed cytotoxicity against the A549 and HepG2 cell with IC50 values of 11.05 and 19.15 µM, respectively | |

* Compounds with IC50 values less than 10 µM are reported in bold.

Figure 1. Discovery of anticancer agents from endophytic fungi over time.

Figure 2. Relative abundance of anticancer agents from endophytic fungi.
The genera of endophytic fungi containing two or more putative anticancer-agent-producing species are *Acremonium*, *Alternaria*, *Aspergillus*, *Ceriporia*, *Chetomium*, *Colletotrichum*, *Cytospora*, *Emericella*, *Eurotium*, *Eutypella*, *Fusarium*, *Guignardia*, *Hypocrea*, *Penicillium*, *Pestalotiopsis*, *Phomopsis*, *Periconia*, *Stemphylium*, *Talaromyces*, *Thielavia*, and *Xylaria* [4,221]. These endophytic fungi offer an alternative source of bioactive compounds. We may be able to increase their yield of specific anticancer compounds by employing biotechnology and genetic engineering [221].

### 2.1. Anti-Cancer Agents in Clinical Use Shared by Plants and Endophytic Fungi

Plants are prolific sources of anticancer agents. In the area of cancer, of the 175 approved small molecules over the years from the 1940s to 2014, 75% (131) are other than synthetic and 49% (85) are either natural products or their derivatives [222]. Very recently, it was reported that among the approved 321 anticancer molecules from all sources during the period of 1946 to 2019, 35 (10.9%) were unaltered natural products and 65 (20.2%) were natural product derivatives compared to 53 (16.5%) completely synthetic drug molecules. Some of these agents obtained from plants are also found in their corresponding endophytic fungi. The following are some examples of plant/endophytic fungi-derived cancer effective agents [1,6] (Figure 3a,b).

- **Paclitaxel (Taxol®)** is used in combination with other anti-cancer drugs in ovarian, breast, non-small cell lung cancer (NSCLC), and Kaposi sarcoma. An active paclitaxel analogue, docetaxel is used in breast and non-small cell lung cancer (NSCLC) treatment [223]. Even though camptothecin exerted severe bladder toxicity in its clinical trial in the 1970s and therefore, was dropped, its two water-soluble derivatives, topotecan and irinotecan, have been shown to be more effective anti-cancer agents and are being utilized for these purposes [223]. Topotecan (Hycamtin®) was the first CPT derivative that was orally available and has been approved for cervical (when used in combination with cisplatin), ovarian, and non-small cell lung cancer treatment. Irinotecan (Camptosar®) has been approved for colorectal cancer treatment. These agents show cytotoxicity on account of their ability to inhibit a fundamental enzyme, topoisomerase-I, involved in the winding and unwinding process of DNA during replication or protein synthesis [1,223]. The vinca alkaloids, vinblastine and vincristine, and their semi-synthetic analogs, vinorelbine and vindesine, are primarily used in combination with other chemotherapeutic drugs in the treatment of advanced testicular cancer, breast cancer, Kaposi’s sarcoma, lung cancer, leukemias, and lymphomas [223]. Etoposide and teniposide are clinically effective semi-synthetic derivatives of a podophyllotoxin isomer, epipodophyllotoxin, which are used in bronchial cancers, lymphomas, and testicular cancer treatments [223].

### 2.2. Putative Anticancer Compounds from Endophytic Fungi

#### 2.2.1. Alkaloids and Nitrogen-Containing Heterocycles

Camptothecin (CPT) (1), a pentacyclic quinoline alkaloid, was, at first, isolated from the *Camptotheca* acuminata (happy tree) woods showing antileukemic and anti-cancer effects in animals [1]. It exerts its cytotoxicity by inhibition and dissociation of the DNA-topoisomerase-I complex during DNA replication [224,225]. However, recently, CPT has been isolated from some endophytic fungi, *Entrophospora i.*, residing in these plants. Since *Entrophospora i.* also lives inside the inner bark of *Nothapodytes foetida* [11], in 2008, CPT was isolated from a *Nothapodytes foetida* seed endophyte, *Neurospora c.*, and both authentic and fungal CPT exhibited comparable cytotoxic effects in human cancer cell lines HEP-2 (liver cancer), A549 (lung cancer), and OVCAR-5 (ovarian cancer) [96]. In 2009, CPT along with its two derivatives, 9-methoxycamptothecin and 10-hydroxycamptothecin, were isolated from a *Camptotheca acuminata* inner bark endophyte, *Fusarium s.* (Figure 3a). These derivatives are more water soluble and more potent inhibitors of the topoisomerase-I enzyme [80] (Table 2).
Figure 3. Cont.
Figure 3. Anticancer compounds of different chemical classes from endophytic fungi-alkaloidal compounds and their derivatives: (a) (1–8), benzo[j]fluoranthene (9), Chromone (10), coumarin (11),
depsidones (12, 13), depsideptide (14), ergochromes (15, 16), ester (17), lactones (23–24), peptide (25), polykedites (26); (b) polyketides (27–32), quinones (33–39), spirobisnaphthalenes (40–42), terpenes (43–54), xanthones (55), naphthoquinones (56, 57).

Cytochalasins (2a–2d) are fungal metabolites that inhibit cell division by means of inhibiting actin filament polymerization [226]. Four cytochalasins (cytochalasin 1, 2, 3, and E) have been isolated from an endophytic fungus, Rhinocladiella spp. from the Tripterygium wilfordii dead tree limbs and were tested against HCT-116 (colon tumor cell line), A2780S (ovarian tumor cell line), and SW-620 (colon tumor cell line) showing cytotoxic activities [136].

The vinca alkaloid (3a, 3b), vincristine (leurocristine), was isolated from Catharanthus roseus [227]. This alkaloid has also been isolated from some fungal endophytes of Catharanthus roseus such as Fusarium o. (inner bark), Mycelia s. 97CY(3) (Leaves), and Talaromyces r. CrP20 (Leaves) [74,75,89]. Vincristine irreversibly binds to the spindle proteins and microtubules during the S-phase of cell cycle hampering mitotic spindle formation and therefore arresting tumor cell division in the metaphase [1].

Chaetominine (4) was isolated from an endophyte, Chaetomium sp. IFB-E015 from the healthy leaves of Adenophora axilliflora, and it was cytotoxic against K562 (human leukemia cells) and SW1116 (human colon cancer cells) [54].

Cytochalasan-based alkaloids (5a–5c, 6), namely chaetoglobosin C, E, F, U, and penochalasin A (6), were obtained from the endophyte Chaetomium g. IFB-E019 residing inside the Imperata cylindrica healthy stem. Chaetoglobosin U was cytotoxically active against the KB cell line (human nasopharyngeal epidermoid tumor) with an IC50 value of 16.0 µM, whereas chaetoglobosin C (IC50 34.0 µM), E (IC50 40.0 µM), F (IC50 52.0 µM), and penochalasin A (IC50 48.0 µM) were moderately active against the KB cell line [57]. Endophytic fungus Chaetomium g. L18 from the plant Curcuma wenyujin produces chaetoglobosin X that exerted cytotoxic activity against H22 (hepatic cancer cells in mice) and MFC (gastric cancer cells in mice) cell lines [56] (Table 2).

2.2.2. Benzofuranones

Daldinone C (9a) and D (9b) were discovered from an Artemisia annua endophyte, Hypoxylon t. IFB-18, where both agents exerted strong cytotoxic action against the human colorectal cancer SW1116 cell line at IC50 values of 49.5 and 41.0 µM, respectively [85] (Table 2, Figure 3a).

2.2.3. Chromones

A novel chromone, Pestalotiopsone F (10), was isolated from an endophytic fungus Pestalotiopsis spp. associated with a mangrove plant Rhizophora mucronata. Pestalotiopsone F showed moderate cytotoxicity to L5178Y (murine cancer cell line) at an EC50 value of 8.93 µg/mL [110]. Pestaloficiol I, J, K, and L are new isoprenylated chromone derivatives discovered from a Camellia sinensis endophyte, Pestalotiopsis f., that displayed cytotoxicity against HeLa (Cervical cancer) and MCF-7 (Breast cancer) cell lines [115] (Table 2).

2.2.4. Coumarins

Arundinone B (11) was isolated from an endophyte Microsphaeropsis a. associated with Ulmus macrocarpa. The compound showed cytotoxicity to T24 (Bladder carcinoma) and A549 (Lung carcinoma epithelial) cell lines [92] (Table 2).

2.2.5. Depsidesones

Botryorhodines A (12a) and B (12b), two depsidones, were isolated from the endophytic fungus Botryosphaeria r. associated with Bidens pilosa. These compounds exhibited weak antitumor activity against the HeLa cell line at a concentration of 96.97 and 36.41 µM, respectively [48]. Depsidone 1 was discovered from a fungus of the Pleosporales order (BCC 8616) isolated from an unidentified plant leaf of the Hala-Bala forest origin. Depsidone 1
displayed weak cytotoxicity to KB and BC cell lines with IC50 values 6.5 and 4.1 µg/mL, respectively [43] (Table 2).

2.2.6. Depsipeptides

Beauvericin (14), a depsipeptide, was isolated from two fungi, *Fusarium o.* EPH2RAA and *Fusarium o.* associated with the plants *Cylindropuntia echinocarpus* and *Ephedra fasciculate*, respectively. Beauvericin displayed cytotoxicity to NCI-H460 (human non-small cell lung cancer), MIA Pa Ca-2 (human pancreatic carcinoma), MCF-7 (human breast cancer), and SF-268 (human CNS cancer) cell lines with IC50 values of 1.41, 1.66, 1.81, and 2.29 µM, respectively, showing selective cytotoxicity toward MIA PaCa-2 and NCI-H460 (Table 2). Beauvericin also inhibited the metastasis of MDA-MB-231 (Breast cancer) and PC-3M (metastatic prostate cancer) cells at concentrations ranging between 3.0–4.0 and 2.0–2.5 µM, respectively [77]. According to other studies, beauvericin displayed cytotoxicity against A549 (Lung carcinoma epithelial), PC-3 (Prostate cancer), and PANC-1 (human pancreatic carcinoma) cell lines with IC50 values of 10.4 ± 1.6, 49.5 ± 3.8, and 47.2 ± 2.9 µM, respectively [71]. Additionally, in 2006, Ivanova et al. demonstrated the cytotoxicity of beauvericin against Hep-G2 (hepatocellular carcinoma) and MRC-5 (fibroblast-like fetal lung cell line) cells as well [76].

2.2.7. Ergochromes

*Phomopsis l.*, an endophytic fungus of *Dicerandra frutescens*, produced three compounds dicerandrols A, B, and C (15a–15c), structurally related to the ergochromes and secalonic acids as they also have the same tricyclic C15 system with a similar arrangement of substituents. These compounds displayed modest antitumor activities toward A549 (lung adenocarcinoma epithelial cell line) and HCT-116 (colon tumor cell line) cell lines [132] (Table 2).

Secalonic acid D (16), isolated from mangrove plant endophytic fungus no. ZSU44, displayed potent cytotoxicity against HL60 (the human promyelocytic leukemia cell line) and K562 (human leukemia cells) cells with IC50 values of 0.38 and 0.43 µM, respectively. It caused apoptosis in those cell lines and cell cycle arrest in the G(1) phase as well [158].

2.2.8. Esters

Globosumones A (17a) and B (17b), isolated from the endophyte *Chaetomium g.* associated with *Ephedra fasciculate*, were shown to have cytotoxicity to MCF-7 (breast cancer), MIA PaCa-2 (pancreatic carcinoma), NCI-H460 (non-small cell lung cancer), SF-268 (CNS glioma), and WI-38 (normal human fibroblast cells) cell lines [58].

2.2.9. Lactones

The lactone compound Brefeldin A (18) was obtained from two endophytic fungi, *Aspergillus c.* and *Paecilomyces* spp., isolated from the plants *Taxus mairei* and *Torreya grandis*. Brefeldin A exhibited antitumor activities to Hela, HL-60, KB, MCF-7, and Spc-A1 with IC50 values of 1.8, 10.0, 9.0, 2.0, and 1.0 ng/mL [31]. Brefeldin A was also obtained from the endophyte *Acremonium* spp. isolated from the healthy *Knema laurina* twig. It showed cytotoxicity to BC-1 (breast cancer), KB (epidermoid cancer of the mouth), and NCIH187 (human small-cell lung cancer), with IC50 values of 0.04, 0.18, and 0.11 µM, respectively [86] (Table 2).

Radicicol (19) was obtained from *Chaetomium c.* associated with *Ephedra fasciculate* and it is a HSP90 (heat shock protein) inhibitor, which is frequently expressed highly in cancer cells. It also showed cytotoxicity to the MCF-7 (breast cancer) cell line at an IC50 value 0.03 µM [55].

Photinides A–F (20a–20f) were obtained from the endophyte *Pestalotiopsis p.* associated with *Roystonea regia*, and all of these γ-lactones at 10 µg/mL exerted cytotoxicity against the MDA-MB-231 (breast cancer) cell line with inhibitory rates of 24.4, 24.2, 23.1, 24.4, and 24.6%, respectively [123] (Table 2).
Eutypellin A (21), isolated from the endophyte *Eutypella* spp. BCC 13199 associated with *Etlingera littoralis*, showed cytotoxicity to KB, MCF-7NCI-H187 (human small-cell lung cancer cells), and nonmalignant Vero cells with IC50 values of 38, 84, 12, and 88 µM, respectively [70].

2.2.10. Lignans

Podophyllotoxin (22), a precursor to the topoisomerase-I-inhibiting anticancer drugs teniposide (23), etoposide (24), and etoposide phosphate, were isolated from the endophyte *Phialocephala f.* associated with *Podophyllum peltatum* [12]. This was also obtained from the endophyte *Trametes h.* associated with *Podophyllum hexandrum* and from the endophyte *Fusarium s.* associated with *Podophyllum hexandrum* [1,79,148] (Table 2).

2.2.11. Peptides

Leucinostatin A was isolated from the endophyte *Acremonium* spp. associated with *Taxus baccata* and was shown to be effective against BT-20 (breast cancer) cell line with an LD50 value of 2 nM [14]. It inhibits the growth of prostate cancer cells through the suppression of IGF-I (Insulin-Like Growth Factor-I) expression in PrSC (prostate stromal cells) [228] (Table 2).

2.2.12. Polyketides

Two novel oblongolides, Y (26a) and Z (26b) (Figure 3a), are produced by the endophyte *Phomopsis* spp. BCC 9789 housed in *Musa acuminate* (a wild banana). Oblongolide Y exhibited cytotoxicity against BC (human breast cancer) cell line (IC50 48 µM) and Oblongolide Z showed cytotoxicity against BC (human breast cancer), KB (human oral epidermoid cancer), NCI-H187 (small-cell lung cancer), and nonmalignant (Vero) cell lines with IC50 values of 26 µM, 37 µM, 32 µM, and 60 µM, respectively [130] (Table 2). Five tricyclic lactone polyketides, alternariol (27a), alternariol 5-O-sulfate (27b), alternariol 5-O-methyl ether (27c), altenuisatin (28a), and desmethylaltenuisatin (28b) (Figure 3b), were isolated from the endophyte *Alternaria* spp. housed in the leaves of *Polygonum senegalense*. All these compounds manifested significant cytotoxicity against L5178Y (mouse lymphoma cells) with EC50 values of 1.7, 4.5, 7.8, 6.8, and 6.2 µg/mL, respectively [16]. According to another study conducted by Devari et al. in 2014, alternariol 5-O-methyl ether showed antiproliferative activity against HL-60 (human promyelocytic leukemia), A549 (lung cancer), PC-3 (prostate cancer), HeLa (cervical cancer), A431 (skin carcinoma), MiaPaka-2 (pancreatic cancer), and T47D (breast cancer) cell lines. Among all these cell lines, HL-60 (human promyelocytic leukemia) cells were most sensitive (IC50 85 µM) to alternariol 5-O-methyl ether [25].

Two novel polyketides, leptosphaerone C (29) and penicillenone (30), are produced by an endophytic fungus *Penicillium* spp. JP-1, isolated from *Aegiceras corniculatum*. Leptosphaerone C showed cytotoxicity to A549 (lung carcinoma epithelial) with an IC50 value of 1.45 µM, and penicillenone exhibited activity against P388 (leukemia cells) with an IC50 value of 1.38 µM [103].

Bikaverin (31) was isolated from an endophytic fungus *Fusarium o.* strain CECIS associated with *Cylindropuntia echinocarpa* [77]. It exerted cytotoxic activities against cancer cell lines, MIA PaCa-2 (pancreatic carcinoma), NCI-H460 (non-small cell lung cancer), MCF-7 (human breast cancer), and SF-268 (human CNS5 cancer) with IC50 values of 0.26, 0.43, 0.42, and 0.38 µM, respectively, showing selective cytotoxicity toward MIA PaCa-2 and NCI-H460. Bikaverin was also proven to be cytotoxic against EAC (Erlich ascites carcinoma), leukemia L5178, and sarcoma 37 cell lines affecting precursor utilization of nucleic acid and protein synthesis [78].

Sequoiatone A (32a) and B (32b), two novel polyketides (Figure 3b), were isolated from a *Sequoia sempervirens* bark endophyte, *Aspergillus p*. These polyketide compounds were tested against 60 diverse human tumor cell lines, and among them, breast cancer cell lines showed the greatest sensitivity [37] (Table 2).
2.2.13. Quinones

Torreyanic acid (33) (Figure 3b), a dimeric quinine, was isolated from an endophyte of *Torreya taxifolia*, *Pestalotiopsis n.*. It causes cytotoxicity by apoptosis against A549 (lung carcinoma epithelial) and NEC (human colorectal neuroendocrine cell carcinoma) cell lines with IC50 values of 3.5 µg/mL and 45 µg/mL, respectively [119] (Table 2).

Four endophytes, *Alternaria* spp., *Alternaria*, *Aspergillus* n., and *Penicillium* spp., associated with *Tabebuia argentea*, produced the antitumor and anti-metastatic agent lapachol (34) [17,20–22]. It acts by interfering with the bioactivities of the topoisomerase enzymes, which are crucial for DNA replication [22]. β-Lapachone showed activity on DU145 (human prostate carcinoma) and MCF-7 (breast cancer cell line) cell lines [20,22]. Additionally, its antitumor and anti-metastatic activities were evident in HepG2 (human hepatocellular liver carcinoma) and Hep3B (human hepatoma cell line) cell lines [19]. Notably, *Aspergillus n.* can be used to produce lapachol in a large scale within a short time [18].

Two bianthraquinone derivatives, Alterporriol K (35a) and L (35b), are produced by the endophytic fungus *Alternaria* spp. ZJ9-6B associated with the mangrove *Aegiceras corniculatum*. Alterporriol K and L exerted moderate cytotoxicity against MDA-MB-435 and MCF-7 (breast cancer cell line) cell lines with IC50 values between 13.1 and 29.1 µM [24].

2.2.14. Spirobisnaphthalenes

*Mycelia* s., an endophytic fungus isolated from the leaves of *Knightia excelsa*, was shown to produce Spiromamakone A (41) (Figure 3b) that exhibited cytotoxicity to P388 (murine leukemia cell line) at an IC50 value 0.33 µM [90] (Table 2).

A novel spirobisnaphthalene, spiropreussione A (42), was isolated from the endophyte *Preussia* spp. associated with *Aquilaria sinensis*. It displayed cytotoxicity to A2780 (human ovarian carcinoma) and BEL-7404 (human liver carcinoma) cell lines with IC50 values of 2.4 and 3.0 µM, respectively [135].

Diepoxin δ (43), palmarumycin C8 (44), and diepoxins κ and ζ were isolated from the endophytic fungus *Berkleasmium* spp. associated with *Dioscorea zingiberensis*. Diepoxin δ and palmarumycin C8 displayed pronounced cytotoxicity to A-549, A-2780, Bel-7402, BGC-823, and HCT-8 cell lines with IC50 values between 1.28 and 5.83 µM, while diepoxins κ and ζ selectively inhibited A-549 and Bel-7402 cells' growth showing moderate to weak cytotoxicity [44] (Table 2).

2.2.15. Terpenes (Diterpenes, Sesquiterpenes, Triterpenes)

Several terpenes of plant and fungal origin have been established as potential anticancer drugs (Figure 3b, structures 45–54). Among these, paclitaxel (Taxol) (45) was isolated from *Taxus brevifolia* (Pacific yew tree) [230,231]. However, due to less availability of the pacific yew tree and insignificant yield of this metabolite, scientist have set up other approaches, including tissue culture, chemical synthesis, and semi-synthesis [230,232]. However, this diterpenoid was also reported to be produced by an endophytic fungus, *Taxomyces a.* isolated from the *Taxus brevifolia* [6]. Following this report, a number of paclitaxel producing other endophytes were reported. Some of them are *Bartalinia r.* from the leaves of *Aegle marmelos* [42] and *Pestalotiopsis n.* and *Pestalotiopsis v.* from the plant...
**Taxus cuspidate** [73]. This metabolite has been found to induce apoptosis when screened against INT-407, BT220, H116, HL251, and HLK210 cell lines [42] (Table 2).

A fusicoocane diterpene, periconicin B (46), was isolated from a *Xylophia aromatica* endophyte, *Periconia a.* It exerted potent cytotoxicity against HeLa (cervical cancer) and CHO (Chinese hamster ovary) cell lines [109].

Four sesquiterpenes, trichoethocline (47), 7α-hydroxy-scorpene (48), 8-deoxy-trichoethocline (49), and 7α-hydroxytrichodermol (50), were isolated from an endophyte, KLAR 5, housed in the healthy twig of *Knema laurina*. Compounds 47 and 48 were moderately active against BC-1 (human breast cancer cells), KB (Human nasopharyngeal epidermoid tumor), and NCI-H187 (human small-cell lung cancer cells), whereas compounds 49 and 50 showed selective cytotoxic activity against BC-1 and NCI-H187 [86].

Ent-4(15)-eudesmen-11-ol-1-one (51), an eudesmane sesquiterpene, isolated from an *Etlingera littoralis* endophyte, *Eutypella* spp. BCC 13199, showed weak cytotoxicity against KB, MCF7, NCI-H187, and Vero cells with IC50 values of 32, 20, 11, and 32 µM, respectively [70].

Two sesquiterpenes, Merulin A (52a) and Merulin C (52b), are produced by a *Xylocarpus granatum* endophytic fungi, XG8D, where both of them showed significant cytotoxic activity against SW620 (colon cancer) and BT474 (breast cancer) cell lines with IC50 values of 4.84 and 4.11 µg/mL for SW620 and 4.98 and 1.57 µg/mL for BT474, respectively [151].

Three novel eremophilane-type sesquiterpenes (Figure 3b), eremophilanolides 1, 2, and 3 (53a–53c), were isolated from the endophytic fungi *Xylaria* spp. BCC 21097 of the *Licuala spinose* plant and were moderately cytotoxic against KB, MCF-7, and NCI-H187 cell lines [152].

**2.2.16. Xanthones**

Phomoxanthone A (55a) and B (55b) (Figure 3b), isolated from the endophyte *Phomopsis* spp. BCC 1323 associated with *Tectona grandis*, exerted significant cytotoxicity against KB, BC-1, and nonmalignant Vero cells with IC50 values of 0.99, 0.51, and 4.1 µg/mL, respectively, for phomoxanthone A and 4.1, 0.70, and 1.8 µg/mL, respectively, for phomoxanthone B [129] (Table 2).

**2.3. Recently Reported Metabolites with Potential Cytotoxicity and the Case of Fusarubin**

More than one hundred metabolites have been isolated and evaluated for putative anticancer activities in the years 2018 to 2020. Cytotoxic activities of these endophytic metabolites have been summarized in Table 3. Among the reported metabolites, penicillin A isolated from *Bionectria* spp. [159] and pyrrocidine A isolated from *Cylindrocarpon* spp. [166] exhibited potent cytotoxicity against the human ovarian cancer cell line A2780. Fusaritioamide B, a new type benzamide, isolated from *Fusarium c.*, showed potent activity against several cell lines [160]. 3-(4-nitrophenyl)-5-phenyl isoxazole was reported to have a potent effect against HepG2 and SMCC-7721 cells [161], while spiciferone F was reported to have a strong effect against MCF7 [162]. Liu et al. isolated two metabolites, namely xylariphalidiae A and cis-4-hydroxy-6-deoxytalone, and Sharma V. et al. isolated Xylarolide A from *Diaporthe* spp. [163,164]. All these metabolites showed activity towards cancer cells. Three naphthaquinones, anhydrofusarubin, fusarubin, and 3-deoxyfusarubin, and one aza-anthraquinone, bostrycoaidin, have potentiality as bioactive compounds against cytotoxicity on vero cells. These metabolites were isolated from a *Fusarium s.* strain isolated from *Casia alata*. [8]. Monolinolein, bafilomycin D, and 3′-hydroxydaidzein displayed a strong effect against A549 cells. These metabolites were isolated from actinomycete strain...
YBQ59 residing in *Cinnamomum cassia* [167]. *Colletotrichum* g. A12 produced colletotricone A, which showed moderate activity against MCF-7, NCI-H460, HepG-2m and SF-268 tumor cell lines [168]. Mollicellin G, a depsidone, was reported as a moderately active cytotoxic metabolite towards HepG2 and Hela cells [169]. A metabolite of *Pestalotiopsis* spp., named demethylincisterol A3, showed potential cytotoxicity against human cancer cell lines Hela, A549, and HepG [170].

A new type of cytochalin, named jammosporin A, isolated from endophytic fungi *Rosellinia s.-c.* exhibited cytotoxic potential towards MOLT-4 cells [165]. Prenylated diphenyl ethers, namely dioncinol N and analogues isolated from *Arthrinium a.* TE-3, showed moderate cytotoxicity against the human monocytic cell line (THP-1 cell line), with IC50 values of 40.2, 28.3, and 25.9 µM, respectively [233].

An indole diterpenoid, shearilicine, isolated form *Penicillium* spp. (strain ZO-R1-1) of *Zingiber officinale*, showed potent cytotoxicity towards L5178Y cells and A2780 cells [171]. Flavipin from *Chaetomium g.* displayed activity against A549, HT-29, and MCF-7 cells [172]. Emolin, an anthraquinone from *Diaporthe l.*, significantly inhibited the growth of murine leukemia P-388 cells [219].

Recently reported metabolites, namely chloroisosulochrin from *Pestalotiopsis t.* (N635) [206], cytosporin W from *Pseudopestalotiopsis t.* [207], terezine E and 14-hydroxyterezine D from *Mucor* spp. [208], citrinin (CIT) and dicitrinin-A from *Penicillium c.* [209], allantopyrone E from *Aspergillus v.* [210], integracin A and B from *Cytospora* spp. [211], (+)-asperteretone F (3a/3b), and compound 6 (name not established in the paper) *Aspergillus t.* [212], sterigmatocystin, a xanthone, from *Paecilomyces* spp. TE-540 [213], mutolide [234] and pramaninic A from *Aplysorella j.* [216], myrotheceans H and I from *Paramyrotheicum r.* A697 [217], and colletotrichalactone A and colletotrichalactone Ca from *Colletotrichum* spp. JS-0361, exhibited promising activity against different cancer cells [218]. A summary of the putative cytotoxic effects of recently reported endophytic fungal metabolites are summarized in Table 3.

Fusarubin and anhydrofusarubin have been isolated from the endophytic fungi *Cladosporium* residing inside *Rauwolfia* leaves. These compounds inhibited the cell growth of different leukemia cell lines (OCI-AML3, HL-60, U937, and Jurkat) by arresting the cell cycle and augmenting apoptosis. Whereas fusarubin exerted an antiproliferative effect on OCI-AML3 cells by up-regulating p21 in a p53-dependent manner, apoptosis was induced only in a small sub-population of leukemic cells by inducing the production of the Fas ligand (Figure 4) [9].

![Figure 4](image-url) Fusarubin (FUS) and FUS analogues with proposed mechanism of action. (A) Structures of FUS derivatives and (B) Proposed mechanism of action of FUS on OCI-AML3 cells.

### 3. Conclusions

Several hundred endophytic fungal metabolites have been isolated to have cytotoxic and antimicrobial effects. Many metabolites are currently available as drugs on the market. Given that plants host endophytes as part of a symbiotic relationship, some plant metabolites might have an endophytic fungal origin. In fact, increasing evidence indicates that some of these plant metabolites are also produced by fungi. Many of the isolated...
metabolites of endophytic fungi inhabitant medicinal plants have been proved to have cytotoxic effects in vitro. Several of these compounds have been investigated at the molecular level to elucidate the mechanism, since these metabolites are produced in very small quantities by endophytes of plant origin. Due to very insignificant yields and isolation difficulties, these secondary metabolites may not be available to carry out in vivo studies in animal models. Some laboratories applied synthetic approaches to produce natural product derivatives, and one group also tried to synthesize some of these compounds. Optimizing derivatization and synthetic approaches is critical to attain higher yields for animal studies. These approaches will be key for investigating and developing these putative anticancer compounds into treatments.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** Not applicable.

**Informed Consent Statement:** Not applicable.

**Data Availability Statement:** Not applicable.

**Conflicts of Interest:** The authors declare no conflict of interest.

### Abbreviations

| Fungus Name                      | Abbreviation          |
|----------------------------------|-----------------------|
| Allantophomopsis lykopodina      | Allantophomopsis l.   |
| Alternaria alternata             | Alternaria a.         |
| Alternaria tenuissima            | Alternaria t.         |
| Aspergillus clavatus             | Aspergillus c.        |
| Aspergillus fumigatus            | Aspergillus f.        |
| Aspergillus glaucus              | Aspergillus g.        |
| Aspergillus niger                | Aspergillus n.        |
| Aspergillus parasiticus          | Aspergillus p.        |
| Aspergillus terreus              | Aspergillus t.        |
| Aspergillus violaceofuscus       | Aspergillus v.        |
| Bartalinia robillardoides        | Bartalinia r.         |
| Bieneckia ochroleuca             | Bieneckia o.          |
| Bipolaris semiae                 | Bipolaris s.          |
| Botryosphaeria dothidea          | Botryosphaeria d.     |
| Botryosphaeria rhodina           | Botryosphaeria r.     |
| Ceriporia lacerate               | Ceriporia l.          |
| Chaetomium chiversii             | Chaetomium c.         |
| Chaetomium globosum              | Chaetomium g.         |
| Cladosporium cladosporioides     | Cladosporium c.       |
| Cladosporium oxysporum           | Cladosporium o.       |
| Colletotrichum capsici           | Colletotrichum c.     |
| Colletotrichum gloeosporioides   | Colletotrichum g.     |
| Cordyceps taii                   | Cordyceps t.          |
| Diaporthe terebinthifolia        | Diaporthe t.          |
| Entrophospora infrequens         | Entrophospora i.      |
| Fusarium oxysporum               | Fusarium o.           |
| Fusarium solani                  | Fusarium s.           |
| Guignardia bidwillii             | Guignardia b.         |
| Guignardia mangiferae            | Guignardia m.         |
| Hypocrea lixii                   | Hypocrea l.           |
| Hypoxylon truncatum              | Hypoxylon t.          |
| Lasiodiplodia theobromae         | Lasiodiplodia t.      |
| Mycelia sterilia                 | Mycelia s.            |
| Microsphaeropsis arundinis       | Microsphaeropsis a.   |
| Myrothecium roridum              | Myrothecium r.        |
Neurospora crassa
Papulaspora immersa
Paraconiothyrium brasiliense
Penicillium chermesinum
Penicillium citrinum
Periconia atropurpurea
Pestalotiopsis fici
Pestalotiopsis karstenii
Pestalotiopsis microsora
Pestalotiopsis pauciseta
Pestalotiopsis photiniae
Pestalotiopsis terminaliae
Pestalotiopsis versicolor
Phialocephala fortinii
Phialoaphora mustea
Phoma betae
Phomopsis longicolla
Phyllosticta spinarum
Rhizopycnis vagum
Rhytidhysteron rufulum
Setophoma terrestris
Stemphylium sedicola
Stemphylium globuliferum
Talaromyces flavus
Talaromyces radicus
Taxomyces andreanae
Thielavia subthermophila
Trametes hirsuta
Trichoderma gamsii
Xylaria cf. cubensis

References

1. Kumar, V.; Rai, S.; Gaur, P.; Fatima, T. Endophytic Fungi: Novel Sources of Anticancer Molecules. In Advances in Endophytic Research; Verma, V.C., Gange, A.C., Eds.; Springer: New Delhi, India, 2014; pp. 389–422; ISBN 978-81-322-1574-5.
2. Gunatilaka, A.A.L. Natural Products from Plant-Associated Microorganisms: Distribution, Structural Diversity, Bioactivity, and Implications of Their Occurrence. J. Nat. Prod. 2006, 69, 509–526. [CrossRef]
3. Zhang, H.W.; Song, Y.C.; Tan, R.X. Biology and Chemistry of Endophytes. Nat. Prod. Rep. 2006, 23, 509–526. [CrossRef]
4. Aly, A.H.; Debbab, A.; Kjer, J.; Proksch, P. Fungal Endophytes from Higher Plants: A Prolific Source of Phytochemicals and Other Bioactive Natural Products. Fungal Divers. 2010, 41, 1–16. [CrossRef]
5. Staniek, A.; Woerdenbag, H.J.; Kayser, O. Endophytes: Exploiting Biodiversity for the Improvement of Natural Product-Based Drug Discovery. J. Plant Interact. 2008, 3, 75–93. [CrossRef]
6. Sieterle, A.; Strobel, G.; Sieterle, D. Taxol and Taxane Production by Taxomyces Andreanae, an Endophytic Fungus of Pacific Yew. Sci.-N. Y. THEN Wash. 1993, 260, 214. [CrossRef]
7. Khan, M.I.H.; Sohrab, M.H.; Rony, S.R.; Tareq, F.S.; Hasan, C.M.; Mazid, M.A. Cytotoxic and Antibacterial Naphthaquinones from an Endophytic Fungus, Cladosporium sp. Toxicol. Rep. 2016, 3, 861–865. [CrossRef]
8. Khan, N.; Afroz, F.; Begum, N.; Roy Rony, S.; Sharmin, S.; Moni, F.; Mahmood Hasan, C.; Shahe, K.; Sohrab, H. Endophytic Fusarium Solani: A Rich Source of Cytotoxic and Antimicrobial Naphthaquinone and Aza-Anthraquinone Derivatives. Toxicol. Rep. 2018, 5, 970–976. [CrossRef]
9. Adorisio, S.; Fierabracci, A.; Muscari, I.; Liberati, A.M.; Cannarile, L.; Thuy, T.T.; Sung, T.V.; Sohrab, H.; Hasan, C.M.; Ayroldi, E.; et al. Fusarubin and Anhydrofusarubin Isolated from a Cladosporium Species Inhibit Cell Growth in Human Cancer Cell Lines. Toxins 2019, 11, 503. [CrossRef]
10. Shweta, S.; Zuehike, S.; Ramesha, B.T.; Priti, V.; Mohana Kumar, P.; Ravikanth, G.; Spiteller, M.; Vasudeva, R.; Uma Shaanker, R. Endophytic Fungal Strains of Fusarium Solani, from Apodytes Dimidiata E. Mey. Ex Arn (Icacinaceae) Produce Camptothecin, 10-Hydroxycamptothecin and 9-Methoxy camptothecin. Phytochemistry 2010, 71, 117–122. [CrossRef]
11. Puri, S.C.; Verma, V.; Amna, T.; Qazi, G.N.; Spiteller, M. An Endophytic Fungus from Nothapodytes Foetida That Produces Camptothecin. J. Nat. Prod. 2005, 68, 1717–1719. [CrossRef]
12. Eyberger, A.L.; Dondapati, R.; Porter, J.R. Endophyte Fungal Isolates from Podophyllum Peltatum Produce Podophyllotoxin. J. Nat. Prod. 2006, 69, 1121–1124. [CrossRef]
13. Kusari, S.; Lamshöff, M.; Spiteller, M. Aspergillus Fumigatus Fresenius, an Endophytic Fungus from Juniperus Communis L. Horstmann as a Novel Source of the Anticancer pro-Drug Deoxypodophyllotoxin. *J. Appl. Microbiol.* **2009**, *107*, 1019–1030. [CrossRef]

14. Strobel, G.A.; Hess, W.M. Glucosylation of the Peptide Leucinostatin A, Produced by an Endophytic Fungus of European Yew, May Protect the Host from Leucinostatin Toxicity. *Chem. Biol.* **1997**, *4*, 529–536. [CrossRef]

15. Yokoigawa, J.; Morimoto, K.; Shiono, Y.; Uesugi, S.; Kimura, K.; Kataoka, T. Allantopyrone A, an α-Pyrene Metabolite from an Endophytic Fungus, Inhibits the Tumor Necrosis Factor α-Induced Nuclear Factor KB Signaling Pathway. *J. Antibiot.* **2015**, *68*, 71–75. [CrossRef]

16. Aly, A.H.; Edrada-Ebel, R.; Indriani, I.D.; Wray, V.; Müller, W.E.; Totzke, F.; Zirrigebel, U.; Schächtele, C.; Kubbutat, M.H.; Lin, W.H.; et al. Cytotoxic Metabolites from the Fungal Endophyte *Alternaria* sp. and Their Subsequent Detection in Its Host Plant Polygonum Senegalense. *J. Nat. Prod.* **2008**, *71*, 972–980. [CrossRef]

17. Balassiano, I.T.; De Paulo, S.A.; Henriques Silva, N.; Cabral, M.C.; da Gloria da Costa Carvalho, M. Demonstration of the Lapachol as a Potential Drug for Reducing Cancer Metastasis. *Oncoal. Rep.* **2005**, *13*, 329–333.

18. Govindappa, M. First Report of Anticancer Agent, Lapachol Producing Endophyte, *Aspergillus Niger* of Tabebuia Argeteana and Its in vitro Cytotoxicity Assays. *Bangladesh J. Pharmacol.* **2014**, *9*, 129–139. [CrossRef]

19. KIM, S.O.; KWON, J.I.; JEONG, Y.K.; KIM, G.Y.; KIM, N.D.; CHOI, Y.H. Induction of Egr-1 Is Associated with Anti-Metastatic and Anti-Invasive Ability of β-Lapachone in Human Hepatocarcinoma Cells. *Biosci. Biotechnol. Biochem.* **2007**, *71*, 2169–2176. [CrossRef]

20. Lee, J.H.; Cheong, J.; Park, Y.M.; Choi, Y.H. Down-Regulation of Cyclooxygenase-2 and Telomerase Activity by β-Lapachone in Human Prostate Carcinoma Cells. *Pharmacol. Res.* **2005**, *51*, 553–560. [CrossRef]

21. Sadananda, T.S.; Nirupama, R.; Chaithra, K.; Govindappa, M.; Chandrappa, C.P.; Vinay Raghavendra, B. Antimicrobial and Antioxidant Activities of Endophytes from Tabebuia Argeteana and Identification of Anticancer Agent (Lapachol). *J. Med. Plants Res.* **2011**, *5*, 3643–3652.

22. Wuerzberger, S.M.; Pink, J.J.; Planchon, S.M.; Byers, K.L.; Bornmann, W.G.; Boothman, D.A. Induction of Apoptosis in MCF-7:WS8 Breast Cancer Cells by β-Lapachone. *Cancer Res.* **1998**, *58*, 1876–1885.

23. Wang, J.; Cox, D.G.; Ding, W.; Huang, G.; Lin, Y.; Li, C. Three New Resveratrol Derivatives from the Mangrove Endophytic Fungus *Alternaria* sp. *Mar. Drugs* **2014**, *12*, 2840–2850. [CrossRef]

24. Huang, C.-H.; Pan, J.-H.; Chen, B.; Yu, M.; Huang, H.-B.; Zhu, X.; Lu, Y.-J.; She, Z.-G.; Lin, Y.-C. Three Bianthraquinone Derivatives from the Mangrove Endophytic Fungus *Alternaria* sp. *ZJ-6B* from the South China Sea. *Mar. Drugs* **2011**, *9*, 832–843. [CrossRef]

25. Devari, S.; Jaglan, S.; Kumar, M.; Deshidi, R.; Guru, S.; Blushan, S.; Kushwaha, M.; Gupta, A.P.; Gandhi, S.G.; Sharma, J.P.; et al. Capsaicin Production by *Alternaria Alternata*, an Endophytic Fungus from Capsicum Annum; LC-ESI-MS/MS Analysis. *Phytochemistry* **2014**, *98*, 183–189. [CrossRef]

26. Shweta, S.; Gurnumurthy, B.R.; Ravikanth, G.; Ramanan, U.S.; Shivanna, M.B. Endophytic Fungi from Miquelia Dentata Bedd., Produce the Anti-Cancer Alkaloid, Inhibits the Tumor Necrosis Factor α and Anti-Invasive Ability of *Alternaria sp.* *Nat. Prod. Res.* **2008**, *22*, 71–75. [CrossRef]

27. Bangladesh J. Pharmacol. *Horstmann as a Novel Source of the Anticancer pro-Drug Deoxypodophyllotoxin.* *J. Appl. Microbiol. Biochem.* **2015**, *9*, 2840–2850. [CrossRef]

28. Fang, Z.F.; Yu, S.S.; Zhou, W.Q.; Chen, X.G.; Ma, S.G.; Li, Y.; Qu, J. A New Isoflavone from Metabolites of the Endophytic Fungi *Alternaria Tenuissima* (Nees & T. Nees: Fr) Wiltshire. *Chin. Chem. Lett.* **2012**, *23*, 317–320. [CrossRef]

29. Siritwardane, A.M.D.A.; Kumar, N.S.; Jayasinghe, L.; Fujimoto, Y. Chemical Investigation of Metabolites Produced by an Endophytic *Aspergillus* sp. Isolated from Limonia Acidissima. *Nat. Prod. Res.* **2015**, *29*, 1384–1387. [CrossRef]

30. Wang, J.; Huang, Y.; Fang, M.; Zhang, Y.; Zheng, Z.; Zhao, Y.; Su, W. Brefeldin A, a Cytotoxic Produced by *Pacilomyces* sp. and *Aspergillus Clavatus* Isolated from Taxus Mairei and Torreya Grandis. *FEMS Immunol. Med. Microbiol.* **2002**, *34*, 51–57. [CrossRef]

31. Ge, H.M.; Yu, Z.G.; Zhang, J.; Wu, J.H.; Tan, R.X. Bioactive Alkaloids from Endophytic *Aspergillus Fumigatus*. *J. Nat. Prod.* **2009**, *72*, 753–755. [CrossRef]

32. Liang, Z.; Zhang, T.; Zhang, X.; Zhang, J.; Zhao, C. An Alkaloid and a Steroid from the Endophytic Fungi *Aspergillus Fumigatus*. *Molecules* **2015**, *20*, 1424–1433. [CrossRef]

33. Askar, M.; Mohamed, S.F.; Mahmoud, M.G.; Sayed, O.H.E. Antioxidant and Antitumor Activity of a New Sesquiterpene Isolated from Endophytic *Aspergillus Glauces*. *Int. J. PharmTech Res.* **2013**, *5*, 391–397.

34. Liu, D.; Li, X.-M.; Meng, L.; Li, C.-S.; Gao, S.-S.; Shang, Z.; Proksch, P.; Huang, C.-G.; Wang, B.-G. Nigerapyrones A-H, α-Pyrene Derivatives from the Marine Mangrove-Derived Endophytic Fungus *Aspergillus Niger* MA-132. *J. Nat. Prod.* **2011**, *74*, 1787–1791. [CrossRef]

35. Song, Y.C.; Li, H.; Ye, Y.H.; Shan, C.Y.; Yang, Y.M.; Tan, R.X. Endophytic Naphthopyrone Metabolites Are Co-Inhibitors of Xanthine Oxidase, SW1116 Cell and Some Microbial Growths. *FEMS Microbiol. Lett.* **2004**, *241*, 67–72. [CrossRef]

36. Stierle, A.A.; Stierle, D.B.; Bugni, T. Sequoianones A and B: Novel Antitumor Metabolites Isolated from a Redwood Endophyte. *J. Org. Chem.* **1999**, *64*, 5479–5484. [CrossRef]
63. Raj, K.G.; Sambantham, S.; Manikanadan, R.; Arulvasu, C.; Pandi, M. Fungal Taxol Extracted from Cladosporium Oxysporum Induces Apoptosis in T47D Human Breast Cancer Cell Line. *Asian Pac. J. Cancer Prev.* 2014, 15, 6627–6632. [CrossRef]

64. Kumaran, R.S.; Jung, H.; Kim, H.J. In Vitro Screening of Taxol, an Anticancer Drug Produced by the Fungus, *Colletotrichum Capsici*. *Eng. Life Sci.* 2011, 11, 264–271. [CrossRef]

65. Wang, Y.; Tang, K. A New Endophytic Taxol-and Baccatin III-Producing Fungus Isolated from Taxus Chinensis Var. Mairei. *Afr. J. Biotechnol.* 2011, 11, 16379–16386. [CrossRef]

66. Bungihan, M.; Tan, A.M.; Takayama, H.; Cruz, D.E.; Nonato, G.M. A New Macrolide Isolated from the Endophytic Fungus *Colletotrichum sp.* *Philipp. Sci. Lett.* 2013, 6, 57–73.

67. Li, X.-G.; Pan, W.-D.; Lou, H.-Y.; Liu, R.-M.; Xiao, J.-H.; Zhong, J.-J. New Cytochalasins from Medicinal Macrofungus *Cordyceps* Taii and Their Inhibitory Activities against Human Cancer Cells. *Bioorg. Med. Chem. Lett.* 2015, 25, 1823–1826. [CrossRef]

68. Lu, S.; Sun, P.; Li, T.; Kurtan, T.; Mandi, A.; Antus, S.; Krohn, K.; Draeger, S.; Schulz, B.; Yi, Y.; et al. Bioactive Nonanolide Derivatives Isolated from the Endophytic Fungus *Cytospora sp.* *J. Org. Chem.* 2011, 76, 9699–9710. [CrossRef]

69. Yedukondalu, N.; Arora, P.; Wadhwa, B.; Malik, F.A.; Vishwakarma, R.A.; Gupta, V.K.; Riyaz-Ul-Hassan, S.; Ali, A. Diapolic Acid A–B from an Endophytic Fungus, *Diaporthe Terebinthifoli* Depicting Antimicrobial and Cytotoxic Activity. *J. Antibiot.* 2017, 70, 212–215. [CrossRef]

70. Isaka, M.; Palasarn, S.; Lapanun, S.; Chanthaket, R.; Boonyuen, N.; Lumyong, S. γ-Lactones and Ent-Eudesmane Sesquiterpenes from the Endophytic Fungus *Eutypella sp.* BCC 15199. *J. Nat. Prod.* 2009, 72, 1720–1722. [CrossRef]

71. Wang, Q.-X.; Li, S.-F.; Zhao, F.; Dai, H.-Q.; Bao, L.; Ding, R.; Gao, H.; Zhang, L.-X.; Wen, H.-A.; Liu, H.-W. Chemical Constituents from *Endophytic Fusarium Oxysporum*. *Fitoterapia* 2011, 82, 777–781. [CrossRef]

72. Elavarasi, A.; Rathna, G.S.; Kalaiselvam, M. Taxol Producing Mangrove Endophytic Fungi *Fusarium Oxysporum* from Rhizophora Annamalayana. *Asian Pac. J. Trop. Biomed.* 2012, 2, S1081–S1085. [CrossRef]

73. Kumaran, R.S.; Kim, H.J.; Hur, B.-K. Taxol Promising Fungal Endophyte, Pestalotiopsis Species Isolated from *Taxus Cuspidata*. *Molecules* 2022, 27, 296. [CrossRef]

74. Palem, P.P.C.; Kuriakose, G.C.; Jayabaskaran, C. An Endophytic Fungus, *Talaromyces Radicus*, Isolated from Catharanthus Roseus, Produces Vincristine and Vinblastine, Which Induce Apoptotic Cell Death. *PLoS ONE* 2015, 10, e0144476. [CrossRef]

75. Zhang, L.; Guo, B.; Li, H.; Zeng, S.; Shao, H.; Gu, S.; Wei, R. Preliminary Study on the Isolation of Endophytic Fungus of *Catharanthus Roseus* and Its Fermentation to Produce Products of Therapeutic Value. *Chin. Tradit. Herb. Drugs* 2000, 31, 805–807.

76. Ivanova, L.; Skjerve, E.; Eriksen, G.S.; Uhlig, S. Cytotoxicity of Enniatins A, A1, B, B1, B2 and B3 from Fusarium Avenaceum. *Toxicol. Off. J. Int. Soc. Toxicology* 2006, 47, 868–876. [CrossRef]

77. Zhan, J.; Burns, A.M.; Liu, M.X.; Faeth, S.H.; Gunatilaka, A.A.L. Search for Cell Motility and Angiogenesis Inhibitors with Potential Anticancer Activity: Beauvericin and Other Constituents of Two Endophytic Strains of *Fusarium Oxysporum*. *J. Nat. Prod.* 2007, 70, 227–232. [CrossRef]

78. Fuska, J.; Proksa, B.; Fusková, A. New Potential Cytotoxic and Antitumor Substances I. In Vitro Effect of Bikaverin and Its Derivatives on Cells of Certain Tumors. *Neoplasma* 1975, 22, 335–338.

79. Nadeem, M.; Ram, M.; Alam, M.M.; Mohammad, A.; Al-Qurainy, F.; Khan, S.; Abdin, M.Z. *Fusarium Solani Solani*, P1, a New Endophytic Podophyllotoxin-Producing Fungus from Roots of Podophyllum Hexandrum. *Afr. J. Biotechnol.* 2012, 6, 2499–2499.

80. Kusari, S.; Zühlke, S.; Spitterell, M. A New Endophytic Fungus from *Camptotheca Acuminata* That Produces Camptothecin and Analogues. *J. Nat. Prod.* 2009, 72, 2–7. [CrossRef]

81. Chen, Y.; Gou, H.; Du, Z.; Liu, X.-Z.; Che, Y.; Ye, X. Ecology-Based Screen Identifies New Metabolites from a Cordyceps-Colonizing Fungus as Cancer Cell Proliferation Inhibitors and Apoptosis Inducers. *Cell Prolif.* 2009, 42, 838–847. [CrossRef]

82. Sommart, U.; Rukachaisirikul, V.; Trisuwan, K.; Tadpetch, K.; Phongpaichit, S.; Preedanon, S.; Sakayaraj, J. Tricyclicalternarene Derivatives from the Endophytic Fungus *Gygnardia Bidwellii* PSU-G11. *Fitotema.* 2012, 5, 139–143. [CrossRef]

83. Sun, Z.-H.; Liang, F.-L.; Wu, W.; Chen, Y.-C.; Pan, Q.-L.; Li, H.-H.; Ye, W.; Liu, H.-X.; Li, S.-N.; Tan, G.-H.; et al. *Guignardones* P–S, New Meroterpenoids from the Endophytic Fungus *Gygnardia Mangiferae* A348 Derived from the Medicinal Plant *Smilax Glabra*. *Molecules* 2015, 20, 22900–22907. [CrossRef]

84. Zhao, J.; Li, C.; Wang, W.; Zhao, C.; Luo, M.; Mu, F.; Fu, Y.; Zu, Y.; Yao, M. *Hypocrea Lixii*, Novel Endophytic Fungi Producing Anticancer Agent Cajan, Isolated from Pigeon Pea (*Cajanus Cajan* [L.] Millsp.). *J. Appl. Microbiol.* 2013, 115, 102–113. [CrossRef]

85. Gu, W.; Ge, H.M.; Song, Y.C.; Ding, H.; Zhu, H.L.; Zhao, X.A.; Tan, R.X. Cytotoxic Benzo[j] Fluoranthene Metabolites from *Hypoxylon Truncatum* IFB-18, an Endophyte of Artemisia Anna. *J. Nat. Prod.* 2007, 70, 114–117. [CrossRef]

86. Chinworrungse, M.; Wiyakrutta, S.; Sriubolmas, N.; Chuaialu, P.; Suksamarn, A. Cytotoxic Activities of Trichotheccenes Isolated from an Endophytic Fungus *Hypocrea Lixii* to Order Hypocreales. *Arch. Pharm. Res.* 2008, 31, 611. [CrossRef]

87. Pandi, M.; Kumaran, R.S.; Choi, Y.-K.; Kim, H.J.; Muthumary, J. Isolation and Detection of Taxol, an Anticancer Drug Produced from *Lasiodiplodia Theobromae*, a New Endophytic Fungus of the Medicinal Plant *Morinda Citrifolia*. *J. Biotechnol.* 2011, 10, 1428–1435.

88. Sobreira, A.C.M.; Pessoa, O.D.L.; Florêncio, K.G.D.; Wilke, D.V.; Freire, F.C.O.; Gonçalves, F.J.T.; Ribeiro, P.R.V.; Silva, L.M.A.; Brito, E.S.; Canuto, K.M. Resorcylic Lactones from *Lasiodiplodia Theobromae* (MUB65), a Fungal Endophyte Isolated from Myracrodruon Urundeuva. *Planta Med.* 2016, 82, P671. [CrossRef]
89. Yang, X.; Zhang, L.; Guo, B.; Guo, S. Preliminary Study of a Vincristine-Prolonging Endophytic Fungus Isolated from Leaves of Catharanthus Roseus. Chin. Tradit. Herb. Drugs 2004, 35, 79–81.

90. Van der Sar, S.A.; Blunt, J.W.; Munro, M.H.G. Spiro-Mamakone A: A Unique Relative of the Spirobisnaphthalene Class of Compounds. Org. Lett. 2006, 8, 2059–2061. [CrossRef]

91. Moreno, E.; Varughese, T.; Spadafora, C.; Arnold, A.E.; Coley, P.D.; Kursar, T.A.; Gerwick, W.H.; Cubilla-Rios, L. Chemical Constituents of the New Endophytic Fungus Mycosphaerella sp. Nov. and Their Anti-Parasitic Activity. Nat. Prod. Commun. 2011, 6, 835–840. [CrossRef]

92. Luo, J.; Liu, X.; Li, E.; Guo, L.; Che, Y. Arundinols A–C and Arundinones A and B from the Plant Endophytic Fungus Microsphaeropsis Arundinis. J. Nat. Prod. 2013, 76, 107–112. [CrossRef]

93. Ortega, H.E.; Graupner, P.R.; Asai, Y.; Ten Dyke, K.; Qiu, D.; Shen, Y.Y.; Rios, N.; Arnold, A.E.; Coley, P.D.; Kursar, T.A.; et al. Mycoleptodiscins A and B, Cytotoxic Alkaloids from the Endophytic Fungus Mycoceptoblastus sp. F0194. J. Nat. Prod. 2013, 76, 741–744. [CrossRef]

94. Lin, T.; Wang, G.; Shan, W.; Zeng, D.; Ding, R.; Jiang, X.; Zhu, D.; Liu, X.; Yang, S.; Chen, H. Myrotheciumones: Bicyclic Cytotoxic Lactones Isolated from an Endophytic Fungus of Ajuga Decumbens. Biorg. Med. Chem. Lett. 2014, 24, 2504–2507. [CrossRef]

95. Shiono, Y.; Kikuchi, M.; Koseki, T.; Murayama, T.; Kwon, E.; Aburai, N.; Kimura, K. Isopimarane Diterpene Glycosides, Isolated from the Endophytic Fungus Mycosphaerella sp. FICB-E012. J. Antibiot. 2016, 69, 652–655. [CrossRef]

96. Rehman, S.; Shawl, A.S.; Kour, A.; Andrali, R.; Sudan, P.; Sultan, P.; Verma, V.; Qazi, G.N. An Endophytic Neurospora sp. from Nothapodytes Foetida Producing Camptothecin. J. Nat. Prod. 2016, 80, 203–209. [CrossRef]

97. Wu, Z.-C.; Li, L.-D.; Chen, Y.-C.; Zhang, W.-M. A New Isofuranonaphthalenone and Benzopyranos from the Endophytic Fungus Nodulisporium sp. A4 from Aquilaria Sinensis. Helv. Chim. Acta 2010, 93, 920–924. [CrossRef]

98. Borges Coutinho Gallo, M.; Coelho Cavalcanti, B.; Washington Araujo Barros, E.; Odomor de Moraes, M.; Veras Costa-Lotufo, L.; Pessoa, C.; Kenupp Bastos, J.; Tallarico Pupo, M. Chemical Constituents of Papulaspora len mensis, an Endophyte from Smallanthus Sonchifolius (Asteraceae), and Their Cytotoxic Activity. Chem. Biodivers. 2010, 7, 2941–2950. [CrossRef]

99. Shiono, Y.; Yokoi, M.; Koseki, T.; Murayama, T.; Kwon, E.; Aburai, N.; Kimura, K. Isopimarane Diterpene Glycosides, Isolated from the Endophytic Fungus Paraconiothyrium sp. MY-42. Phytochemistry 2011, 72, 1400–1405. [CrossRef]

100. Lin, L.; Chen, X.; Li, D.; Zhang, Y.; Li, L.; Guo, L.; Cao, Y.; Che, Y. Bisabolane Sesquiterpenoids from the Plant Endophytic Fungus Penicillium Chermesinum sp. Nov. Fitoterapia 2011, 82, 746–753. [CrossRef]

101. Huang, Z.; Yang, J.; Cai, X.; She, Z.; Lin, Y. A New Furanocoumarin from the Mangrove Endophytic Fungus Penicillium sp. (ZH16). Nat. Prod. Res. 2012, 26, 1291–1295. [CrossRef]

102. Lin, Z.-J.; Lu, Z.-Y.; Zhu, T.-J.; Fang, Y.-C.; Gu, Q.-Q.; Zhu, W.-M. Penicillinols from Penicillium sp. GQ-7, an Endophytic Fungus Associated with Aegiceras Corniculatum. Chem. Pharm. Bull. 2008, 56, 217–221. [CrossRef]

103. Lin, Z.; Zhu, T.; Fang, Y.; Gu, Q.; Zhu, W. Polyketides from Penicillium sp. JP-1, an Endophytic Fungus Associated with the Mangrove Plant Aegiceras Corniculatum. Phytochemistry 2008, 69, 1273–1278. [CrossRef]

104. Chen, M.-J.; Fu, Y.-W.; Zhou, Q.-Y. Penifypyrone, a New Cytotoxic Funicone Derivative from the Endophytic Fungus Penicillium sp. HSZ-43. Nat. Prod. Res. 2014, 28, 1544–1548. [CrossRef]

105. Sun, X.; Kong, X.; Gao, H.; Zhu, T.; Wu, G.; Gu, Q.; Li, D. Two New Meroterpenoids Produced by the Endophytic Fungus Penicillium sp. SXH-65. Arch. Pharm. Res. 2014, 37, 978–982. [CrossRef]

106. Darsih, C.; Prachyawarakorn, V.; Wiyakrutta, S.; Mahidol, C.; Ruchirawat, S.; Kitakoop, P. Cytotoxic Metabolites from the Endophytic Fungus Penicillium Chermesinum: Discovery of a Cysteine-Targeted Michael Acceptor as a Phamacophore for Fragment-Based Drug Discovery, Bioconjugation and Click Reactions. RSC Adv. 2015, 5, 70595–70603. [CrossRef]

107. El-Neketi, M.; Ebrahim, W.; Lin, W.; Gedara, S.; Badria, F.; Saad, H.-E.A.; Lai, D.; Proksch, P. Alkaloids and Polyketides from Penicillium Citrinum, an Endophyte Isolated from the Moroccan Plant Ceratonia Siliqua. J. Nat. Prod. 2013, 76, 1099–1104. [CrossRef]

108. Ge, H.-L.; Zhang, D.-W.; Li, L.; Xie, D.; Zou, J.-H.; Si, Y.-K.; Dai, J. Two New Terpenoids from Endophytic Fungus Periconia sp. F-31. Chem. Pharm. Bull. 2011, 59, 1541–1544. [CrossRef]

109. Teles, H.L.; Sordi, R.; Silva, G.H.; Castro-Gamboa, I.; da Silva Bolzani, V.; Pfenning, L.H.; de Abreu, L.M.; Costa-Neto, C.M.; Young, M.C.M.; Araújo, Â. Aromatic Compounds Produced by Mycosphaerella Fici sp. F0194. J. Antibiot. 2014, 67, 2686–2690. [CrossRef]

110. Xu, J.; Jier, J.; Sendker, J.; Wray, V.; Guan, H.; Edrada, R.; Lin, W.; Wu, J.; Proksch, P. Chromones from the Endophytic Fungus Pestalotiopsis sp. Isolated from the Chinese Mangrove Plant Rhizophora Mucronata. J. Nat. Prod. 2009, 72, 662–665. [CrossRef]

111. Davis, R.A.; Carroll, A.R.; Andrews, K.T.; Boyle, G.M.; Tran, T.L.; Healy, P.C.; Kalaitzis, J.A.; Shivis, R.G. Pestalactams A–C: Novel Caprolactams from the Endophytic Fungus Pestalotiopsis sp. Org. Biomol. Chem. 2010, 8, 1785–1790. [CrossRef]

112. Liu, S.; Guo, L.; Che, Y.; Liu, L. Pestaloficiolins Q–S from the Plant Endophytic Fungus Pestalotiopsis Fici. Fitoterapia 2013, 85, 114–118. [CrossRef]

113. LIU, S.-C.; YE, X.; GUO, L.-D.; LIU, L. Cytotoxic Isoprenylated Epoxycyclohexanediols from the Plant Endophyte Pestalotiopsis Fici. Chin. J. Nat. Med. 2011, 9, 374–379. [CrossRef]
165. Sharma, N.; Kushwaha, M.; Arora, D.; Jain, S.; Singamaneni, V.; Sharma, S.; Shankar, R.; Bhushan, S.; Gupta, P.; Jaglan, S. New Cytotoxicals from Rosellinia Santsae-Cruciana, an Endophytic Fungus of Albizia Lebbeck. J. Appl. Microbiol. 2018, 125, 111–120. [CrossRef]

166. Kamdem, R.S.T.; Pascal, W.; Rehberg, N.; van Geelen, L.; Höfert, S.-P.; Knedel, T.-O.; Jiani, C.; Sureechatchaiyan, P.; Kassack, M.U.; Lin, W.; et al. Metabolites from the Endophytic Fungus Cylindrocarpon sp. Isolated from Tropical Plant Sapium Ellipticum. Fitoterapia 2018, 128, 175–179. [CrossRef]

167. Vu, H.-N.T.; Nguyen, D.T.; Nguyen, H.Q.; Chu, H.H.; Chu, S.K.; Chau, M.V.; Phi, Q.-T. Antimicrobial and Cytotoxic Properties of Bioactive Metabolites Produced by Streptomyces Cavaourensis YBQ59 Isolated from Cinnamomum Cassia Prels in Yen Bai Province of Vietnam. Curr. Microbiol. 2018, 75, 1247–1255. [CrossRef]

168. Liu, H.-X.; Tan, H.-B.; Chen, Y.-C.; Li, S.-N.; Li, H.-H.; Zhang, W.-M. Secondary Metabolites from the Colletotrichum Gloeosporioides A12, an Endophytic Fungus Derived from Aquilaria Sinensis. Nat. Prod. Res. 2018, 32, 2360–2365. [CrossRef]

169. Ouyang, J.; Mao, Z.; Guo, H.; Xie, Y.; Cui, Z.; Sun, J.; Wu, H.; Wen, X.; Wang, J.; Shan, T. Mollicellins O–R, Four New Depsidones Isolated from the Endophytic Fungus Chaetomium sp. Eef-10. Molecules 2018, 23, 3218. [CrossRef]

170. Zhou, J.; Li, G.; Deng, Q.; Zheng, D.; Yang, X.; Xu, J. Cytotoxic Constituents from the Mangrove Endophytic Pestalotiopsis sp. Induce G0/G1 Cell Cycle Arrest and Apoptosis in Human Cancer Cells. Nat. Prod. Res. 2018, 32, 2968–2972. [CrossRef]

171. Ariantari, N.P.; Ancheeva, E.; Wang, C.; Märdi, A.; Knedel, T.-O.; Kurtán, T.; Chaidir, C.; Müller, W.E.G.; Kassack, M.U.; Jiani, C.; et al. Indole Diterpenoids from an Endophytic Penicillium sp. J. Nat. Prod. 2019, 82, 1412–1423. [CrossRef]

172. Senthil Kumar, V.; Kumaresan, S.; Tamizh, M.M.; Hairul Islam, M.I.; Thirugnanasambantham, K. Anticancer Potential of NF-κB Targeting Apoptotic Molecule “Flavipir” Isolated from Endophytic Chaetomium Globosum. Phytomedicine 2019, 61, 152830. [CrossRef]

173. Wang, W.-X.; Zheng, M.-J.; Li, J.; Feng, T.; Li, Z.-H.; Huang, R.; Zheng, Y.-S.; Sun, H.; Ai, H.-L.; Liu, J.-K. Cytotoxic Polyketides from Endophytic Fungus Phoma Bellidis Harbored in Trictyris Maculate. Phytochem. Lett. 2019, 29, 41–46. [CrossRef]

174. Harwoko, H.; Daletos, G.; Stuhldreier, F.; Lee, J.; Wesselborg, S.; Feldbrügge, M.; Müller, W.E.G.; Kalscheuer, R.; Ancheeva, E.; Proksch, P. Dithiodiketopiperazine Derivatives from Endophytic Fungi Trichoderma Harzianum and Epicoccum Nigrum. Nat. Prod. Res. 2021, 35, 257–265. [CrossRef]

175. Xin, X.-Q.; Chen, Y.; Zhang, H.; Li, Y.; Yang, M.-H.; Kong, L.Y. Cytotoxic Seco-Cytochalasinfs from an Endophytic Aspergillus sp. Harbored in Pinellia Ternata Tubers. Fitoterapia 2019, 132, 53–59. [CrossRef]

176. Wang, F.; Zhao, W.; Zhang, C.; Chang, S.; Shao, R.; Xing, J.; Chen, M.; Zhang, Y.; Si, S. Cytotoxic Metabolites from the Endophytic Fungus Chaetomium Globosum 7951. RSC Adv. 2019, 9, 16035–16039. [CrossRef]

177. Peng, F.; Hou, S.-Y.; Zhang, T.-Y.; Wu, Y.-Y.; Zhang, M.-Y.; Yan, X.-M.; Xia, M.-Y.; Zhang, Y.-X. Cytotoxic and Antimicrobial Indole Alkaloids from an Endophytic Fungus Chaetomium sp. SYP-F7950 of Panax Notoginseng. RSC Adv. 2019, 9, 28754–28763. [CrossRef]

178. Chen, Y.; Liu, Z.; Huang, Y.; Liu, L.; He, J.; Wang, L.; Yuan, J.; She, Z. Ascomycatacins A–C, Cytotoxic 12- or 13-Membered-Ring Macroyclic Alkaloids Isolated from the Mangrove Endophytic Fungus Didynella sp. CYSK-4, and Structure Revisions of Phomopyrrolidones A and C. J. Nat. Prod. 2019, 82, 1752–1758. [CrossRef]

179. Li, G.; Xu, K.; Chen, W.-Q.; Gao, Z.-H.; Liu, Y.-T.; Qiao, Y.-N.; Sun, Y.; Sun, G.; Peng, X.-P.; Lou, H.-X. Heptaketides from the Endophytic Fungus Pleosporales sp. F46 and Their Antifungal and Cytotoxic Activities. RSC Adv. 2019, 9, 12913–12920. [CrossRef]

180. Kumarihamy, M.; Ferreira, D.; Croom, E.M.; Sahu, R.; Tekwani, B.L.; Duke, S.O.; Khan, S.; Techen, N.; Nanayakkara, N.P.D. Antiplasmodial and Cytotoxic Metabolites from an Endophytic Fungus, Nemania sp. UM10M, Isolated from a Diseased Torreya Taxifolia Leaf. Molecules 2019, 24, 777. [CrossRef]

181. He, W.; Xu, Y.; Fu, P.; Zuo, M.; Liu, W.; Jiang, Y.; Wang, L.; Zhu, W. Cytotoxic Indoly1 Diketopiperazines from the Aspergillus sp. GZWMJZ-258, Endophytic with the Medicinal and Edible Plant Garcinia Multiflora. J. Agric. Food Chem. 2019, 67, 10660–10666. [CrossRef]

182. Wang, W.-X.; Li, Z.-H.; Ai, H.-L.; Li, J.; He, J.; Zheng, Y.-S.; Feng, T.; Liu, J.-K. Cytotoxic 19,20-Epoxytoccalas from Endophytic Fungus Xylaria Cf. Curta. Fitoterapia 2019, 137, 104253. [CrossRef]

183. De Amorim, M.R.; Hilário, F.; Junior, F.M. dos S.; Junior, J.M.B.; Bauab, T.M.; Araújo, A.R.; Carlos, L.Z.; Vilegas, W.; Santos, L.C. dos New Benzaldehydes and Benzepyan Compounds from the Endophytic Fungus Paraphaeosphaeria sp. F03 and Their Antimicrobial and Cytotoxic Activities. Planta Med. 2019, 85, 957–964. [CrossRef]

184. Zhao, T.; Xu, L.-L.; Zhang, Y.; Lin, Z.-H.; Xia, T.; Yang, D.-F.; Chen, Y.-M.; Yang, X.-L. Three New α-Pyrene Derivatives from the Plant Endophytic Fungus Penicillium Ochrochroline and Their Antibacterial, Antifungal, and Cytotoxic Activities. J. Asian Nat. Prod. Res. 2019, 21, 851–858. [CrossRef]

185. Xu, J.; Hu, Y.-W.; Qu, W.; Chen, M.-H.; Zhou, L.-S.; Bi, Q.-R.; Luo, J.-G.; Liu, W.-Y.; Feng, F.; Zhang, J. Cytotoxic and Neuroprotective Activities of Constituents from Alternaria Alternate, a Fungal Endophyte of Psidium Littorale. Bioorg. Chem. 2019, 90, 103046. [CrossRef]

186. Wu, Y.; Chen, S.; Liu, H.; Huang, X.; Liu, Y.; Tao, Y.; She, Z. Cytotoxic Isocoumarin Derivatives from the Mangrove Endophytic Fungus Aspergillus sp. HN15-5D. Arch. Pharm. Res. 2019, 42, 326–331. [CrossRef]

187. Fu, J.; Hu, L.; Shi, Z.; Sun, W.; Yue, D.; Wang, Y.; Ma, X.; Ren, Z.; Zuo, Z.; Peng, G.; et al. Two Metabolites Isolated from Endophytic Fungus Coniochaeta sp. F-8 in Ageratina Adenophora Exhibit Antioxidative Activity and Cytotoxicity. Nat. Prod. Res. 2021, 35, 2840–2848. [CrossRef]
213. Li, X.-Q.; Dong, Q.-J.; Xu, K.; Yuan, X.-L.; Liu, X.-M.; Zhang, P. Cytotoxic Xanthones from the Plant Endophytic Fungus Paecilomyces sp. TE-540. Nat. Prod. Res. 2020, 35, 6134–6140. [CrossRef]
214. Wen, S.; Fan, W.; Guo, H.; Huang, C.; Yan, Z.; Long, Y. Two New Secondary Metabolites from the Mangrove Endophytic Fungus Pleosporales sp. SK7. Nat. Prod. Res. 2020, 34, 2919–2925. [CrossRef]
215. Wang, A.; Yin, R.; Zhou, Z.; Gu, G.; Dai, J.; Lai, D.; Zhou, L. Eremophilane-Type Sesquiterpenoids From the Endophytic Fungus Rhizopus Vagum and Their Antibacterial, Cytotoxic, and Phytotoxic Activities. Front. Chem. 2020, 8, 96889. [CrossRef]
216. Bang, S.; Kwon, H.E.; Baek, J.Y.; Jang, D.S.; Kim, S.; Nam, S.-J.; Lee, D.; Kang, K.S.; Shim, S.H. Colletotrichalactones A-Ca, Unusual 5/6/10-Fused Tricyclic Polyketides Produced by an Endophytic Fungus, Colletotrichum sp. JS-0361. Bioorganic Chem. 2020, 105, 104449. [CrossRef]
217. Liu, H.; Chen, Y.; Li, S.; Zhang, W.; Liu, Z.; Tan, H.; Zhang, W. Trichothecene Macrolides from the Endophytic Fungus Paranarumycetium Roridum and Their Cytotoxic Activity. Fitoterapia 2020, 147, 104768. [CrossRef]
218. Bang, S.; Kwon, H.E.; Baek, J.Y.; Jang, D.S.; Kim, S.; Nam, S.-J.; Lee, D.; Kang, K.S.; Shim, S.H. Colletotrichalactones A-Ca, Unusual 5/6/10-Fused Tricyclic Polyketides Produced by an Endophytic Fungus, Colletotrichum sp. JS-0361. Bioorganic Chem. 2020, 105, 104449. [CrossRef]
219. Riga, R.; Happyana, N.; Quentmeier, A.; Zammarelli, C.; Kayser, O.; Hakim, E.H. Secondary Metabolites from Diaporothe Lithocarpus Isolated from Artocarpus Heterophyllus. Nat. Prod. Res. 2021, 35, 2324–2328. [CrossRef]
220. Yu, S.; Zhu, Y.-X.; Peng, C.; Li, J. Two New Sterol Derivatives Isolated from the Endophytic Fungus Aspergillus Tubingenensis YP-2. Nat. Prod. Res. 2021, 35, 3277–3284. [CrossRef]
221. Chen, L.; Zhang, Q.-Y.; Jia, M.; Ming, Q.-L.; Yue, W.; Rahman, K.; Qin, L.-P.; Han, T. Endophytic Fungi with Antitumor Activities: Their Occurrence and Anticancer Compounds. Crit. Rev. Microbiol. 2014, 42, 454–473. [CrossRef]
222. Newman, D.J.; Cragg, G.M. Natural Products as Sources of New Drugs from 1981 to 2014. J. Nat. Prod. 2016, 79, 629–661. [CrossRef]
223. Cragg, G.M.; Newman, D.J. Plants as a Source of Anti-Cancer Agents. J. Ethnopharmacol. 2005, 100, 72–79. [CrossRef]
224. Ling-hua, M.; Zhi-yong, L.; Pommier, Y. Non-Camptothecin DNA Topoisomerase I Inhibitors in Cancer Therapy. Curr. Top. Med. Chem. 2003, 3, 305–320. [CrossRef]
225. Pommyier, Y. Topoisomerase I Inhibitors: Camptothecins and Beyond. Nat. Rev. Cancer 2006, 6, 789–802. [CrossRef]
226. Haidle, A.M.; Myers, A.G. An Enantioselective, Modular, and General Route to the Cytochalasins: Synthesis of L-696,474 and Anticancer Agents from Natural Products. Nat. Prod. Res. 2022, ISBN 978-0-429-13085-4.
227. Svoboda, G. Alkaloids of Vinca Rosea (Catharanthus Roseus). IX. Extraction and Characterization of Leurosidine and Leurocristine. Subj. Strain Bibliogr. 1961, 24, 173–178.
228. Kawada, M.; Inoue, H.; Ohba, S.-I.; Masuda, T.; Momose, I.; Ikeda, D. Leucinostatin A Inhibits Prostate Cancer Growth through Reduction of Insulin-like Growth Factor-I Expression in Prostate Stromal Cells. Int. J. Cancer 2020, 126, 810–818. [CrossRef]
229. Chowdhury, N.S.; Sohrab, H.; Rana, S.; Hasan, C.M.; Jamshidi, S.; Rahman, K.M. Cytotoxic Naphthoquinone and Azaanthrquinone Derivatives from an Endophytic Fusarium Solani. J. Nat. Prod. 2017, 80, 1173–1177. [CrossRef]
230. Khawwar, R.N.; Mishra, A.; Gond, S.K.; Sierle, A.; Sierle, D. Anticancer Compounds Derived from Fungal Endophytes; Their Importance and Future Challenges. Nat. Prod. Rep. 2011, 28, 1208–1228. [CrossRef]
231. Wani, M.C.; Taylor, H.L.; Wall, M.E.; Coggon, P.; McPhail, A.T. Plant Antitumor Agents. VI. Isolation and Structure of Taxol, a Novel Antileukemic and Antitumor Agent from Taxus Brevifolia. J. Am. Chem. Soc. 1971, 93, 2325–2327. [CrossRef]
232. Cragg, G.M.; Kingston, D.G.I.; Newman, D.J. (Eds.) Anticancer Agents from Natural Products, 2nd ed.; CRC Press: Boca Raton, FL, USA, 2012; ISBN 978-0-429-13085-4.
233. Zhang, P.; Li, X.; Yuan, X.-L.; Du, Y.-M.; Wang, B.-G.; Zhang, Z.-F. Antifungal Prenylated Diphenyl Ethers from Arthrinium Arundinis, an Endophytic Fungus Isolated from the Leaves of Tobacco (Nicotiana Tabacum L.). Molecules 2018, 23, 3179. [CrossRef]
234. Gao, Y.; Stuhlbreiter, F.; Schmitt, L.; Wesselborg, S.; Wang, L.; Müller, W.E.G.; Kalscheuer, R.; Guo, Z.; Zou, K.; Liu, Z.; et al. Sesterterpenes and Macrolide Derivatives From the Endophytic Fungus Aplosporella Javeedii. Fitoterapia 2020, 146, 104652. [CrossRef]