Abstract: Fungi have been assured to be one of the wealthiest pools of bio-metabolites with remarkable potential for discovering new drugs. The pathogenic fungi, *Fusarium oxysporum* affects many valuable trees and crops all over the world, producing wilt. This fungus is a source of different enzymes that have variable industrial and biotechnological applications. Additionally, it is widely employed for the synthesis of different types of metal nanoparticles with various biotechnological, pharmaceutical, industrial, and medicinal applications. Moreover, it possesses a mysterious capacity to produce a wide array of metabolites with a broad spectrum of bioactivities such as alkaloids, jasmonates, anthranilates, cyclic peptides, cyclic depsipeptides, xanthones, quinones, and terpenoids. Therefore, this review will cover the previously reported data on *F. oxysporum*, especially its metabolites and their bioactivities, as well as industrial relevance in biotechnology and nanotechnology in the period from 1967 to 2021. In this work, 180 metabolites have been listed and 203 references have been cited.

Keywords: *Fusarium oxysporum*; fungi; metabolites; bioactivities; nanotechnology; industrial relevance

1. Introduction

Fungi are eukaryotic microorganisms that settled mostly in all kinds of environments and have fundamental roles in maintaining the environmental balance [1,2]. It has been stated that only about 5% of 2.2 to 3.8 million different fungal species on earth have been taxonomically characterized [3,4]. Fungi have been considered as one of the wealthiest pools of natural metabolites with unique structural features and biodiversity that have a remarkable role in developing new drugs [1–3,5–10]. Some fungal metabolites are also highly toxic such as *Aspergillus* mycotoxin and aflatoxin B1, which affect human health when occurring in food products [8,9,11]. Therefore, it is important to unravel the metabolites of fungal species to prevent health risks, as well as to identify new potential bioactive compounds. *Fusarium* is a genus of filamentous fungi that includes many mycotoxin producers, agronomically important plant pathogens, and opportunistic human pathogens [12]. Its species are a widespread cosmopolitan group of fungi that are found in various habitats such as water, soil, or associated with plants [13,14]. They commonly colonize subterranean and aerial plant parts, either as primary or secondary invaders [15]. Many *Fusarium* species are spread out pathogens on crops in temperate and semi-tropical regions that produce a variety of mycotoxins, causing a reduction in yield and quality of crops, as well as animal...
and human health risks [16]. On the other hand, some species have the potential capacity to produce a great number of metabolites with remarkable chemical diversity and significant bioactivities [11,17–26]. *Fusarium oxysporum* is the most encountered and economically important species of this genus. It includes pathogenic (plant, human, and animal) and non-pathogenic strains that even possess bio-control activity against fungal pests and some insects [27]. It is one of the soil-borne pathogens that causes vascular wilt on many plants, which is characterized by various symptoms, including leaf epinasty, vascular browning, progressive wilting, defoliation, stunting, and plant death [28]. Its species complex consists of several formae specialiae (f. sp.) that collectively infect more than one hundred hosts, leading to serious losses in crops such as tomato, melon, banana, and cotton [29]. In humans, *F. oxysporum* causes invasive infections in immuno-compromised patients and it is commonly found in onychomycosis [30,31]. Many studies revealed that *F. oxysporum* showed a remarkable capacity to yield diverse classes of secondary metabolites such as alkaloids, jasmonates, anthranilates, cyclic peptides, cyclic depsipeptides, xanthones, quinones, and terpenoids with various activities such as phytotoxicity, antimicrobial, cytotoxicity, insecticidal, antioxidant, and antiangiogenic. Additionally, *F. oxysporum* possessed significant industrial and biotechnological values as a wealthy source of diverse enzymes with wide applications such as cutinases, nitrilases, glycoside hydrolases (e.g., fucosidase, \( \alpha \)-galactopyranosidases, and xylanases), fructosyl amino acid oxidase, laccases, lipoxygenase, nitric oxide reductase, decarboxylases, keratinase, phospholipase B, and triosephosphate isomerase [32–42]. Further, *F. oxysporum* is widely employed for the synthesis of different types of metal nanoparticles that could have various biotechnological, pharmaceutical, industrial, and medicinal applications [43–55]. The intensive literature search revealed the lack of review articles that deal with *F. oxysporum* particularly the bright side of this economically valuable fungus. The current review summarized the published data regarding secondary metabolites reported from this fungus and their bioactivities. Additionally, the research progress on *F. oxysporum*, including industrial, biotechnological, and nanotechnological applications has been discussed. The studies that have appeared in literature from 1967 to 2021 are reported. The chemical classes, structures, molecular formulae and weights, hosts, places, and bioactivities of the reported metabolites have been listed (Figures 1–19 and Table 1 and Table 2). Moreover, the reported biosynthetic pathways of some major *F. oxysporum* metabolites have been included (Schemes 1–3). The aim of this work is to focus on the interests of biologists, chemists, and natural product researchers on the area of pharmaceutical drug leads development of the reported metabolites. Besides, the covered data of industrial relevance in biotechnology and nanotechnology have been discussed. The literature search for this work was performed through a computer search of data on Web of Knowledge, ScienceDirect, SCOPUS, Taylor & Francis, Wiley Online Library, Springer, PubMed, JACS, and Google Scholar.
| Compound Name               | Mol. Wt. | Mol. Formula | Fungal Source                | Host (Part, Family)               | Place                | Ref. |
|----------------------------|----------|--------------|------------------------------|-----------------------------------|----------------------|------|
| Anthranilic Acid Derivatives |          |              |                              |                                   |                      |      |
| Dianthramide (1)           | 283      | C_{16}H_{13}NO_{4} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Dianthramide B (2)         | 241      | C_{14}H_{11}NO_{3} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthramide B (3)  | 257      | C_{14}H_{11}NO_{4} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthramide M (4)  | 303      | C_{15}H_{15}NO_{6} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthramide S (5)  | 273      | C_{14}H_{11}NO_{5} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthramide R (6)  | 289      | C_{14}H_{11}NO_{6} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Methoxydianthramide M (7)  | 317      | C_{16}H_{13}NO_{6} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Methoxydianthramide B (8)  | 271      | C_{15}H_{13}NO_{4} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Methoxydianthramide S (9)  | 287      | C_{15}H_{13}NO_{5} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Methoxydianthramide R (10) | 303      | C_{15}H_{13}NO_{6} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Methoxydianthramide A (11) | 301      | C_{16}H_{15}NO_{5} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthramide S ethyl ester (12) | 301 | C_{16}H_{15}NO_{5} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthramide S methyl ester (13) | 287 | C_{15}H_{13}NO_{5} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Methoxydianthramide A methyl ester (14) | 315 | C_{15}H_{13}NO_{5} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxyanilide B (15)      | 213      | C_{13}H_{11}NO_{2} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxyanilide S (16)      | 229      | C_{13}H_{13}NO_{3} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxyanilide R (17)      | 245      | C_{15}H_{15}NO_{5} | *F. oxysporum* f. sp. dianthi | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Compound Name | Mol. Wt. | Mol. Formula | Fungal Source | Host (Part, Family) | Place | Ref. |
|---------------|----------|--------------|---------------|---------------------|-------|------|
| **Anthranilic Acid Derivatives** | | | | | |
| Dianthalexin B (18) | 223 | C\(_{14}\)H\(_{9}\)NO\(_2\) | *F. oxysporum* f. sp. *dianthi* | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthalexin B (19) = Dianthalexin | 239 | C\(_{14}\)H\(_{9}\)NO\(_3\) | *F. oxysporum* f. sp. *dianthi* | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Hydroxydianthalexin S (20) | 255 | C\(_{14}\)H\(_{9}\)NO\(_4\) | *F. oxysporum* f. sp. *dianthi* | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| Methoxydianthalexin S (21) | 269 | C\(_{15}\)H\(_{11}\)NO\(_4\) | *F. oxysporum* f. sp. *dianthi* | *Dianthus caryophyllus*, stem (Caryophyllaceae) | The Netherlands | [56] |
| **Fumonisins** | | | | | | |
| Fumonisin B\(_1\) (22) | 721 | C\(_{34}\)H\(_{59}\)NO\(_{15}\) | *F. oxysporum* | *Asparagus officinalis* (Asparagaceae) | Western Poland | [57] |
| Hydroxylated fumonisin C\(_1\) (23) | 723 | C\(_{33}\)H\(_{57}\)NO\(_{16}\) | *F. oxysporum* CAR | *Dianthus caryophyllus* (Caryophyllaceae) | Taejon, Korea | [58,59] |
| Fumonisin C\(_1\) (24) | 707 | C\(_{33}\)H\(_{57}\)NO\(_{15}\) | *F. oxysporum* CAR | *Dianthus caryophyllus* (Caryophyllaceae) | Taejon, Korea | [58,59] |
| Fumonisin C\(_3\) (25) | 691 | C\(_{33}\)H\(_{57}\)NO\(_{14}\) | *F. oxysporum* CAR | *Dianthus caryophyllus* (Caryophyllaceae) | Taejon, Korea | [58,59] |
| Fumonisin C\(_4\) (26) | 675 | C\(_{33}\)H\(_{57}\)NO\(_{13}\) | *F. oxysporum* CAR | *Dianthus caryophyllus* (Caryophyllaceae) | Taejon, Korea | [58,59] |
| Iso-Fumonisin C\(_1\) (27) | 707 | C\(_{33}\)H\(_{57}\)NO\(_{15}\) | *F. oxysporum* KCTC 16654 | *Asparagus officinalis* (Asparagaceae) | Taejon, Korea | [60] |
| N-Acetylated OH-fumonisin C\(_1\) (28) | 765 | C\(_{35}\)H\(_{59}\)NO\(_{17}\) | *F. oxysporum* KCTC 16654 | *Asparagus officinalis* (Asparagaceae) | Taejon, Korea | [60] |
| N-Acetylated fumonisin C\(_1\) (29) | 749 | C\(_{35}\)H\(_{59}\)NO\(_{16}\) | *F. oxysporum* KCTC 16654 | *Asparagus officinalis* (Asparagaceae) | Taejon, Korea | [60] |
| N-Acetylated *iso*-fumonisin C\(_1\) (30) | 749 | C\(_{35}\)H\(_{59}\)NO\(_{16}\) | *F. oxysporum* KCTC 16654 | *Asparagus officinalis* (Asparagaceae) | Taejon, Korea | [60] |
| **Jasmonates derivatives** | | | | | | |
| (−)-Jasmonic acid (31) | 210 | C\(_{12}\)H\(_{18}\)O\(_3\) | *F. oxysporum* f. sp. *matthiolae* | Cultured | The Netherlands | [61] |
| (−)-7-Isos-jasmonic acid (32) | 210 | C\(_{12}\)H\(_{18}\)O\(_3\) | *F. oxysporum* f. sp. *matthiolae* | Cultured | The Netherlands | [61] |
| (1S,2R)-3-Oxo-2-(2Z-pentenyl)cyclopentane-1-butryc acid (33) | 238 | C\(_{14}\)H\(_{22}\)O\(_3\) | *F. oxysporum* f. sp. *matthiolae* | Cultured | The Netherlands | [61] |
Table 1. Cont.

| Compound Name                                                                 | Mol. Wt. | Mol. Formula | Fungal Source                  | Host (Part, Family)           | Place          | Ref.   |
|-------------------------------------------------------------------------------|----------|--------------|--------------------------------|-------------------------------|----------------|--------|
| Jasmonates derivatives                                                       |          |              |                                |                               |                |        |
| (1S,2S)-3-(1S,2S)-3-Oxo-2-(2Z-pentenyl)cyclopentane-1-butryic acid (34)      | 238      | C_{14}H_{22}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2R)-3-Oxo-2-(2Z-pentenyl)cyclopentane-1-hexanoic acid (35)              | 266      | C_{16}H_{26}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2S)-3-Oxo-2-(2Z-pentenyl)cyclopentane-1-hexanoic acid (36)              | 266      | C_{16}H_{26}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2R)-3-Oxo-2-(2Z-pentenyl)cyclopentane-1-octanoic acid (37)              | 294      | C_{18}H_{30}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2S)-3-Oxo-2-(2Z-pentenyl)cyclopentane-1-octanoic acid (38)              | 294      | C_{18}H_{30}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| 9,10-Dihydrojasmonic acid (39)                                               | 212      | C_{12}H_{20}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| 9,10-Dihydro-7-iso-jasmonic acid (40)                                        | 212      | C_{12}H_{20}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2R)-3-Oxo-2-pentylcyclopentane-1-butryic acid (41)                      | 240      | C_{14}H_{24}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2S)-3-Oxo-2-pentylcyclopentane-1-butryic acid (42)                      | 240      | C_{14}H_{24}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2R)-3-Oxo-2-pentylcyclopentane-1-hexanoic acid (43)                     | 268      | C_{16}H_{28}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2S)-3-Oxo-2-pentylcyclopentane-1-hexanoic acid (44)                     | 268      | C_{16}H_{28}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2R)-3-Oxo-2-pentylcyclopentane-1-octanoic acid (45)                     | 296      | C_{18}H_{32}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| (1S,2S)-3-Oxo-2-pentylcyclopentane-1-octanoic acid (46)                     | 296      | C_{18}H_{32}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| 7-Iso-cucurbitic acid (47)                                                   | 212      | C_{12}H_{20}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| Cucurbitic acid (48)                                                        | 212      | C_{12}H_{20}O_{3} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| N-(−)-Jasmonoyl-(S)-isoleucine (49)                                          | 323      | C_{18}H_{26}NO_{4} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| N-(+)-7-Iso-jasmonoyl-(S)-isoleucine (50)                                    | 323      | C_{18}H_{26}NO_{4} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| N-(9,10-Dihydrojasmonoyl)-(S)-isoleucine (51)                                | 325      | C_{18}H_{31}NO_{4} | *F. oxysporum* f. sp. *matthiolae* | Cultured                     | The Netherlands | [61]   |
| Compound Name                                      | Mol. Wt. | Mol. Formula   | Fungal Source                      | Host (Part, Family)                  | Place                      | Ref.  |
|---------------------------------------------------|----------|---------------|-----------------------------------|--------------------------------------|----------------------------|-------|
| **Alkaloids**                                      |          |               |                                   |                                      |                            |       |
| N-(9,10-Dihydro-7-iso-jasmonoyl)-(S)-isoleucine   | 325      | C_{18}H_{31}NO_{4} | *F. oxysporum* f. sp. matthiolae  | Cultured                            | The Netherlands            | [61]  |
| Oxysporidinone                                    | 489      | C_{28}H_{43}NO_{6} | *F. oxysporum* CBS 330.95         | Plant                               | Sweden                     | [62]  |
| (-)-Oxysporidinone                                | 489      | C_{28}H_{43}NO_{6} | *F. oxysporum* N17B              | Cultured                            | Mississippi, USA           | [63]  |
| (-)-4'-Hydroxyl oxysporidinone                    | 491      | C_{28}H_{45}NO_{6} | *F. oxysporum*                    | *Ephedra fasciculata*, root (Ephedraceae)  | Sonoran Desert, USA         | [64]  |
| (-)-6-Deoxyoxysporidinone                         | 473      | C_{28}H_{43}NO_{5} | *F. oxysporum* EPH2RAA           | *Cinnamomum kanehirae*, bark (Lauraceae)  | Jiaoban Mountain, Taiwan, China | [65]  |
| (-)-4,6'-Anhydrooxysporidinone                    | 471      | C_{28}H_{41}NO_{5} | *F. oxysporum* EPH2RAA           | *Ephedra fasciculata*, root (Ephedraceae)  | Sonoran Desert, USA         | [64]  |
| (−)-Sambutoxin                                    | 453      | C_{28}H_{39}NO_{5} | *F. oxysporum* N17B              | Cultured                            | Mississippi, USA           | [63]  |
| 6-Epi-oxysporidinone                              | 489      | C_{28}H_{43}NO_{6} | *F. oxysporum* N17B              | Cultured                            | Mississippi, USA           | [63]  |
| Dimethyl ketal of oxysporidinone                   | 535      | C_{30}H_{46}NO_{7} | *F. oxysporum* N17B              | Cultured                            | Mississippi, USA           | [63]  |
| N-Demethylsambutoxin                              | 439      | C_{27}H_{37}NO_{4} | *F. oxysporum* N17B              | Cultured                            | Mississippi, USA           | [63]  |
| 2-Phenylpropionyl-2-piperidine-3-(R)-yl ester     | 247      | C_{14}H_{17}NO_{3} | *F. oxysporum*                    |                                      |                             |       |
| Fusaric acid                                      | 179      | C_{10}H_{12}NO_{2} | *F. oxysporum* EF119            |                                      | *Capsicum annuum*, root (Solanaceae)  | Taejon, Korea | [66] |
| 9,10-Dehydrofusaric acid                          | 177      | C_{10}H_{11}NO_{2} | *F. oxysporum* f. sp. pisi, F42 and F69 | Cultured                            | Firenze, Italy             | [67]  |
| Fusaricate A                                      | 253      | C_{13}H_{16}NO_{4} | *F. oxysporum*                   |                                      | *Drepanocarpus lunatus*, fruit (Fabaceae)  | Douala, Cameroon | [69] |
| Fusaricate B                                      | 269      | C_{13}H_{16}NO_{5} | *F. oxysporum*                   |                                      | *Drepanocarpus lunatus*, fruit (Fabaceae)  | Douala, Cameroon | [69] |
| Fusaricate C                                      | 283      | C_{14}H_{15}NO_{5} | *F. oxysporum*                   |                                      | *Drepanocarpus lunatus*, fruit (Fabaceae)  | Douala, Cameroon | [69] |
| Fusaricate D                                      | 313      | C_{15}H_{20}NO_{6} | *F. oxysporum*                   |                                      | *Drepanocarpus lunatus*, fruit (Fabaceae)  | Douala, Cameroon | [69] |
Table 1. Cont.

| Compound Name                                      | Mol. Wt. | Mol. Formula    | Fungal Source               | Host (Part, Family)                        | Place                   | Ref.  |
|----------------------------------------------------|----------|----------------|----------------------------|-------------------------------------------|-------------------------|-------|
| **Alkaloids**                                       |          |                |                            |                                           |                         |       |
| Fusaricate E (69)                                   | 313      | C₁₅H₂₃NO₆      | *F. oxysporum*              | *Drepanocarpus lunatus,* fruit (Fabaceae) | Douala, Cameroon         | [69]  |
| Fusaricate F (70)                                   | 311      | C₁₅H₂₁NO₆      | *F. oxysporum*              | *Drepanocarpus lunatus,* fruit (Fabaceae) | Douala, Cameroon         | [69]  |
| Fusaricate G (71)                                   | 311      | C₁₅H₂₁NO₆      | *F. oxysporum*              | *Drepanocarpus lunatus,* fruit (Fabaceae) | Douala, Cameroon         | [69]  |
| 10-Hydroxy-11-chlorofusaric acid (72)               | 215      | C₉H₁₀ClNO₃     | *F. oxysporum*              |                                           | Douala, Cameroon         | [69]  |
| Oxysporizoline (73)                                 | 446      | C₂₈H₂₅N₄O₂     | *F. oxysporum*              | Marine mudflat                           | Suncheon Bay, Korea     | [70]  |
| 1H-Indol-3-butanamide (74)                          | 202      | C₁₂H₁₄N₂O     | *F. oxysporum*              | Marine mudflat                           | Suncheon Bay, Korea     | [70]  |
| Butenolide (75)                                     | 141      | C₇H₇NO₃       | *F. oxysporum*              | Marine mudflat                           | Suncheon Bay, Korea     | [70]  |
| Cyclo-(L-prolyl-L-glycine) (76)                     | 154      | C₇H₁₀N₂O₂      | *F. oxysporum*              | UDLAP 21-92                              | Mexico                  | [71]  |
| Cyclo-(L-prolyl-L-valine) (77)                      | 196      | C₁₀H₁₈N₂O₂     | *F. oxysporum*              | UDLAP 21-92                              | Mexico                  | [71]  |
| Cyclo-(L-leucyl-L-proline) (78)                     | 210      | C₁₁H₁₈N₂O₂     | *F. oxysporum*              | UDLAP 21-92                              | Mexico                  | [71]  |
| (S,E)-Methyl-2-(2,4-dimethylhex-2-enamido)acetate (79) | 213      | C₁₁H₁₉NO₃     | *F. oxysporum R1 and*       | *Aspergillus fumigatus*         |                          |       |
|                                                   |          |                | D co-culture               |                                           |                         |       |
| 2-Oxo-8-azatricyclo [9.3.1.137]-hexadeca-1(15),3(16),4,6,11,13-hexaen-10-one (80) | 225      | C₁₄H₁₁NO₂     | *F. oxysporum*              | *YP9B*                                   |                         |       |
| Fusarioxazin (81)                                   | 337      | C₂₀H₁₉NO₄     | *F. oxysporum*              |                                           |                         |       |
| Epi-trichosetin (82)                                | 359      | C₂₁H₂₀NO₄     | *F. oxysporum FKI-4553      |                                           |                         |       |
| Trichosetin (83)                                    | 359      | C₂₁H₂₀NO₄     | *F. oxysporum FKI-4553      |                                           |                         |       |
| N-(2-Phenylethyl)acetamide (84)                     | 177      | C₁₁H₁₅NO     | *F. oxysporum*              | *Aspergillus fumigatus*         |                          |       |
|                                                   |          |                | D co-culture               |                                           |                         |       |
| Siderophore (85)                                    | 344      | C₁₆H₁₆N₂O₇    | *F. oxysporum*              |                                           |                         |       |
| Vinblastine (86)                                    | 810      | C₄₆H₅₈N₄O₉    | *F. oxysporum*              |                                           |                         |       |
|                                                   |          |                |                            |                                           |                         |       |
| Compound Name                        | Mol. Wt. | Mol. Formula | Fungal Source                  | Host (Part, Family)                  | Place                | Ref. |
|-------------------------------------|----------|--------------|--------------------------------|--------------------------------------|----------------------|------|
| **Alkaloids**                       |          |              |                                |                                      |                      |      |
| Vincristine (87)                    | 824      | C_{46}H_{58}N_{4}O_{10} | *F. oxysporum*                  | *Catharanthus roseus*, leaf (Apocynaceae) | India                | [76] |
| Taxol (88)                          | 853      | C_{47}H_{51}NO_{14}     | *F. oxysporum*                  | *Rhizophora annamalayana*, leaf (Rhizophoraceae) | Vellar Estuary, Tamil Nadu | [77] |
| Flavin adenine dinucleotide (89)    | 785      | C_{27}H_{33}N_{9}O_{15}P_{2} | *F. oxysporum*                  | Cultured                            | USA                  | [78] |
| Flavin adenine dinucleotide-N(5)-Nitrobutane (90) | 888 | C_{31}H_{42}N_{10}O_{17}P_{2} | *F. oxysporum* ATCC 695         | Cultured                            | USA                  | [78] |
|                                     |          |              |                                | *F. oxysporum* ATCC 695              |                      | [79] |
| **Cyclic depsipeptides**            |          |              |                                |                                      |                      |      |
| Enniatin A (91)                     | 681      | C_{36}H_{63}N_{9}O_{9}  | *F. oxysporum* f. sp. *pisi*     | Cultured                            | Germany              | [80] |
| Enniatin A1 (92)                    | 667      | C_{35}H_{60}N_{9}O_{9}  | *F. oxysporum* f. sp. *melonis*  | *Cucumis melo* (Cucurbitaceae)       | Rome, Italy          | [81] |
| Enniatin B (93)                     | 639      | C_{33}H_{57}N_{9}O_{9}  | *F. oxysporum* f. sp. *pisi*     | *Cucumis melo* (Cucurbitaceae)       | Mississipi, USA      | [63] |
| Enniatin B1 (94)                    | 653      | C_{34}H_{59}N_{9}O_{9}  | *F. oxysporum* f. sp. *melonis*  | *Cucumis melo* (Cucurbitaceae)       | Rome, Italy          | [81] |
| Enniatin C (95)                     | 681      | C_{36}H_{63}N_{9}O_{9}  | *F. oxysporum* f. sp. *pisi*     | Cultured                            | Germany              | [80] |
| Enniatin H (96)                     | 653      | C_{34}H_{59}N_{9}O_{9}  | *F. oxysporum* FB1501 (KFCC 11363P) | Soil                                | Korea                | [82] |
| Enniatin I (97)                     | 667      | C_{35}H_{61}N_{9}O_{9}  | *F. oxysporum* FB1501 (KFCC 11363P) | Soil                                | Korea                | [82] |
| Enniatin MK 1688 (98)               | 681      | C_{36}H_{63}N_{9}O_{9}  | *F. oxysporum* FB1501 (KFCC 11363P) | Soil                                | Korea                | [82] |
| Beauvericin (99)                    | 783      | C_{45}H_{57}N_{9}O_{9}  | *F. oxysporum* f. sp. *melonis*  | *Cucumis melo* (Cucurbitaceae)       | Rome, Italy          | [81] |
Table 1. Cont.

| Compound Name                  | Mol. Wt. | Mol. Formula         | Fungal Source                  | Host (Part, Family)                        | Place                  | Ref.    |
|--------------------------------|----------|----------------------|--------------------------------|--------------------------------------------|------------------------|---------|
| **Cyclic depsipeptides**       |          |                      |                                |                                            |                        |         |
| Cyclic peptides                |          |                      |                                |                                            |                        |         |
| Cyclosporine A (100)           | 1201     | C_{62}H_{111}N_{11}O_{12} | F. oxysporum S6               | Soil                                       | Salto, Buenos Aires, Argentina | [86]    |
| Fusaroside (101)               | 751      | C_{43}H_{77}NO_9     | F. oxysporum                  | Cinnamomum kanehirae, bark (Lauraceae)     | Jiaoban Mountain, Taiwan, China | [65]    |
| N-2′-Hydroxyoctadecanoic-1-β-D-glucopyranosyl-9-methyl-4,8-sphingadienine (103) | 771 | C_{43}H_{81}NO_{10} | F. oxysporum IOC 4247         | Cultured                                 | Brazil                         | [87]    |
| N-2′-Hydroxyeicosanoyl-1-β-D-glucopyranosyl-9-methyl-4,8-sphingadienine (104) | 783 | C_{45}H_{85}NO_{9} | F. oxysporum IOC 4247         | Cultured                                 | Brazil                         | [87]    |
| Anhydrofusarubin (105)         | 288      | C_{15}H_{12}O_{6}   | F. oxysporum SS46 and SS50    | Smalanthus sonchifolius, root (Asteraceae) | Brazil                         | [84]    |
| 8-O-Methylbostrycoidin (106)   | 299      | C_{16}H_{13}NO_{5}  | F. oxysporum                  | Citrus sinensis, root (Rutaceae)           | Florida, USA                  | [89]    |
| **Glucosylceramides**          |          |                      |                                |                                            |                        |         |
| Glucosylceramides              |          |                      |                                |                                            |                        |         |
Table 1. Cont.

| Compound Name                          | Mol. Wt. | Mol. Formula          | Fungal Source                        | Host (Part, Family)       | Place            | Ref.   |
|----------------------------------------|----------|-----------------------|--------------------------------------|----------------------------|------------------|--------|
| **Naphthoquinone derivatives**         |          |                       |                                      |                            |                  |        |
| Fusarubin (107)                         | 306      | C₁₅H₁₄O₇              | *F. oxysporum* f. sp. *ciceris*       | Cultured                   | India            | [88]   |
| 9-O-Methylfusarubin (108) = 8-O-Methylfusarubin | 320      | C₁₆H₁₆O₇              | *F. oxysporum*                       | *Citrus sinensis*, root    | Florida, USA     | [89]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
|                                        |          |                       |                                      | *Citrus sinensis*, root    | Florida, USA     | [90]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| 3-O-Methyl-9-O-methylfusarubin (109) = 3-O-Methyl-8-O-methylfusarubin | 334      | C₁₇H₁₈O₇              | *F. oxysporum*                       | Cultured                   | India            | [88]   |
|                                        |          |                       |                                      | *Citrus sinensis*, root    | Florida, USA     | [89]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| 9-O-Methylandrofusarubin (110)         | 302      | C₁₆H₁₄O₆              | *F. oxysporum*                       | *Citrus sinensis*, root    | Florida, USA     | [89]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| 8-O-Methyljavanicin (111)              | 304      | C₁₆H₁₆O₆              | *F. oxysporum*                       | *Citrus sinensis*, root    | Florida, USA     | [89]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| 8-O-Methylsolaniol (112)               | 306      | C₁₆H₁₈O₆              | *F. oxysporum*                       | *Citrus sinensis*, root    | Florida, USA     | [89]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| 8-O-Methyl-2-hydroxyjavanicin (113)    | 306      | C₁₅H₁₄O₇              | *F. oxysporum*                       | *Citrus sinensis*, root    | Florida, USA     | [89]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| Nectriafurone (114)                    | 304      | C₁₅H₁₂O₇              | *F. oxysporum*                       | *Citrus sinensis*, root    | Florida, USA     | [91]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| Nectriafurone-8-methy ether (115)      | 318      | C₁₆H₁₄O₇              | *F. oxysporum*                       | *Citrus sinensis*, root    | Florida, USA     | [91]   |
|                                        |          |                       |                                      | (Rutaceae)                 |                  |        |
| Rhodolamprometrin (116)                | 314      | C₁₆H₁₀O₇              | *F. oxysporum*                       | *Ephedra fasciculate*, root| Sonoran Desert, USA| [64]   |
### Table 1. Cont.

| Compound Name                                | Mol. Wt. | Mol. Formula | Fungal Source | Host (Part, Family) | Place                  | Ref. |
|----------------------------------------------|----------|--------------|---------------|---------------------|------------------------|------|
| **Anthraquinone derivatives**                |          |              |               |                     |                        |      |
| 2-Acetyl-3,8-dihydroxy-6-methoxy-anthraquinone (117) | 312      | C_{17}H_{12}O_{6} | *F. oxysporum* | Citrus sinensis, root (Rutaceae) | Florida, USA [92]       |      |
| 2-(1-Hydroxyethyl)-3,8-dihydroxy-6-methoxy-anthraquinone (118) | 314      | C_{17}H_{14}O_{6} | *F. oxysporum* | Citrus sinensis, root (Rutaceae) | Florida, USA [92]       |      |
| **Xanthone derivatives**                     |          |              |               |                     |                        |      |
| Bikaverin (119)                              | 382      | C_{20}H_{14}O_{8} | *F. oxysporum* | Cultured            | USA                    | [93] |
| Norbikaverin (120)                           | 352      | C_{18}H_{12}O_{7} | *F. oxysporum LCP 531 | Soil               | France [85,96]         |      |
| Oxo-Pre-bikaverin (121)                      | 338      | C_{18}H_{10}O_{7} | *F. oxysporum LCP 531 | Soil               | France [85,96]         |      |
| Me-oxo-pre-bikaverin (122)                   | 352      | C_{18}H_{12}O_{7} | *F. oxysporum LCP 531 | Soil               | France [85]            |      |
| Dinor-bikaverin (123)                        | 354      | C_{18}H_{10}O_{8} | *F. oxysporum LCP 531 | Soil               | France [85]            |      |
| Pre-bikaverin (124)                          | 324      | C_{18}H_{12}O_{8} | *F. oxysporum LCP 531 | Soil               | France [85]            |      |
| 6-Deoxybikaverin (125)                       | 366      | C_{20}H_{14}O_{7} | *F. oxysporum* | Cultured            | India [88]             |      |
| **Terpenoids**                               |          |              |               | Ephedra fasciculata, root (Ephedraceae) | Sonoran Desert, USA [64] |      |
| Ergosterol (126)                             | 396      | C_{28}H_{44}O | *Fusarium oxysporum CM 192679 | Cultured | Kew, England [97] |      |
| Ergosterol peroxide (127)                    | 428      | C_{28}H_{44}O_{3} | *F. oxysporum CM 192679 | Cultured | Kew, England [97] |      |
| Cerevisterol (128)                           | 430      | C_{28}H_{46}O_{3} | *F. oxysporum CM 192679 | Cultured | Kew, England [97] |      |
|                                              |          |              |               | Cinnamomum kanehirae, bark (Lauraceae) | Jiaoban Mountain, Taiwan, China [65] |      |
| Compound Name | Mol. Wt. | Mol. Formula | Fungal Source | Host (Part, Family) | Place | Ref. |
|---------------|----------|--------------|---------------|---------------------|-------|------|
| **Terpenoids** |          |              |               |                     |       |      |
| Wortmannin (129) | 428     | C_{23}H_{24}O_{8} | *F. oxysporum* | *Vicia faba*, root (Fabaceae) | Assiut, Egypt | [18] |
| H1-A = Ergosta-5,8 (14),22-trien-7-one, 3-hydroxy-(3β,22E) (130) | 410 | C_{28}H_{42}O_{2} | *F. oxysporum* N17B | Soil sample | Grassy field near the city of Lakselv in the Arctic region of Norway | [98] |
| (22E,24R)-Stigmasta-5,7,22-trien-3-β-ol (131) | 410 | C_{29}H_{46}O | *F. oxysporum* | *Vicia faba*, root (Fabaceae) | Assiut, Egypt | [18] |
| Stigmasta-4,6,8(14),22-tetraen-3-one (132) | 406 | C_{29}H_{42}O | *F. oxysporum* | *Vicia faba*, root (Fabaceae) | Assiut, Egypt | [18] |
| Isoverrucarol (133) | 266 | C_{15}H_{32}O_{4} | *F. oxysporum* f. sp. radicis-lycopersici | *Lycopersicon esculentum*, root (Solanaceae) | Putuo Island, Zhoushan, China | [102] |
| FCRR-toxin (134) | 346 | C_{20}H_{26}O_{5} | *F. oxysporum* ZZP-R1 | *Rumex madaio* (Polygonaceae) | Putuo Island, Zhoushan, China | [102] |
| Fusarium C (135) | 332 | C_{21}H_{32}O_{3} | *F. oxysporum* ZZP-R1 | *Rumex madaio* (Polygonaceae) | Putuo Island, Zhoushan, China | [102] |
| Fusarium D (136) | 264 | C_{16}H_{24}O_{3} | *F. oxysporum* ZZP-R1 | *Dahlia variabilis*, tuber (Asteraceae) | Padang Luar, West Sumatra, Indonesia | [103] |
| (1R,2S,3R)-3-((S)-2-Hydroxy-6-methylhept-5-en-2-yl)-1,2-dimethylcyclopentanol (137) | 240 | C_{15}H_{28}O_{2} | *F. oxysporum* LBKURCC41 | Soil | Dinghu Mountain Biosphere Reserve, Guangdong, China | [27] |
| Cosmosporasides F (138) | 536 | C_{26}H_{48}O_{11} | *F. oxysporum* SC0002 | Soil | Dinghu Mountain Biosphere Reserve, Guangdong, China | [27] |
| Cosmosporasides G (139) | 532 | C_{27}H_{48}O_{10} | *F. oxysporum* SC0002 | Soil | Dinghu Mountain Biosphere Reserve, Guangdong, China | [27] |
| Cosmosporasides H (140) | 546 | C_{28}H_{50}O_{10} | *F. oxysporum* SC0002 | Soil | Dinghu Mountain Biosphere Reserve, Guangdong, China | [27] |
| Ginkgolide B (141) | 424 | C_{26}H_{44}O_{10} | *F. oxysporum* SYP0056 | *Ginkgo biloba*, root bark (Ginkgoaceae) | Forest site, Changbai Mountain, China | [104] |
| Trichothecenes T-2 toxin (142) | 466 | C_{24}H_{34}O_{9} | *F. oxysporum* 598 | Baccharis spp. (Asteraceae) | Brazil | [105] |
| Trichothecenes HT-2 toxin (143) | 424 | C_{22}H_{32}O_{8} | *F. oxysporum* 598 | Baccharis spp. (Asteraceae) | Brazil | [105] |
Table 1. Cont.

| Compound Name                  | Mol. Wt. | Mol. Formula | Fungal Source                  | Host (Part, Family)            | Place         | Ref.  |
|-------------------------------|----------|--------------|--------------------------------|--------------------------------|---------------|-------|
| **Terpenoids**                |          |              |                                |                                |               |       |
| 3′-OH T-2 toxin (144)         | 482      | C\(_{24}\)H\(_{34}\)O\(_{10}\) | F. oxysporum 598               | Baccharis spp. (Asteraceae)    | Brazil        | [105] |
| Diacetoxyscirpenol (145)      | 366      | C\(_{16}\)H\(_{26}\)O\(_{7}\)  | F. oxysporum 598               | Baccharis spp. (Asteraceae)    | Brazil        | [105] |
| Phenolic and aromatics compounds |        |              |                                |                                |               |       |
| 6-Hydroxymaackiainisoflavan (146) | 300      | C\(_{16}\)H\(_{12}\)O\(_{6}\)  | F. oxysporum f. sp. pisi      | Cultured                       | The Netherlands | [106] |
| Pestalotiollide A (148)       | 386      | C\(_{21}\)H\(_{22}\)O\(_{7}\)  | F. oxysporum                  |                                |               |       |
| Pestalotiollide B (149)       | 386      | C\(_{21}\)H\(_{22}\)O\(_{7}\)  | F. oxysporum                  |                                |               |       |
| Dehydroisopenicillide (150)   | 370      | C\(_{21}\)H\(_{22}\)O\(_{6}\)  | F. oxysporum                  |                                |               |       |
| Podophyllotoxin (151)         | 414      | C\(_{22}\)H\(_{22}\)O\(_{8}\)  | F. oxysporum                  |                                |               |       |
| 1-Benzyl-2-methoxy-2-oxoethyl-2-hydroxy-3-methylbutanoate (153) | 152| C\(_{8}\)H\(_{8}\)O\(_{3}\)    | F. oxysporum                  |                                |               |       |
| Styrene (154)                 | 104      | C\(_{8}\)H\(_{8}\)             | F. oxysporum 13-8             | Prunus dulcis, hull (Rosaceae) | California, USA | [109] |
| 1-Ethyl-4-methoxybenzene (155) | 136      | C\(_{9}\)H\(_{12}\)O             | F. oxysporum 13-8             | Prunus dulcis, hull (Rosaceae) | California, USA | [109] |
| Phenylacetic acid (156)       | 136      | C\(_{6}\)H\(_{8}\)O\(_{2}\)    | F. oxysporum                  | Cultured                       | Hungary       | [108] |
| (+)-Fusarinolic acid (157)    | 194      | C\(_{11}\)H\(_{14}\)O\(_{3}\)  | F. oxysporum                  | Cinnamomum kanehira, bark (Lauraceae) | Jiaoban Mountain, Taiwan, China | [65] |
| Pyran and furan derivatives   |          |              |                                |                                |               |       |
| Chlamydosporol (158)          | 226      | C\(_{11}\)H\(_{14}\)O\(_{5}\)  | F. oxysporum                  | Marine mudflat                 | Suncheon Bay, Korea | [70] |
| Gibepyrone D (159)            | 194      | C\(_{10}\)H\(_{10}\)O\(_{4}\)  | F. oxysporum                  | Cinnamomum kanehira, bark (Lauraceae) - Runex madaio (Polygonaceae) | Jiaoban Mountain, Taiwan, China | [65] |
| Neovasinin (160)              | 308      | C\(_{17}\)H\(_{24}\)O\(_{5}\)  | F. oxysporum R1 and Aspergillus fumigatus D co-culture | - Edgeworthia chrysanth (Thymelaeaceae) | China | [72] |
| Compound Name                        | Mol. Wt. | Mol. Formula | Fungal Source                          | Host (Part, Family)                              | Place                  | Ref.  |
|-------------------------------------|----------|--------------|----------------------------------------|------------------------------------------------|------------------------|-------|
| **Pyran and furan derivatives**     |          |              |                                        |                                                 |                        |       |
| Oxysporone (161)                    | 156      | C₂H₄O₄      | Fusarium oxysporum                     | Cultured Prunus dulcis, hull (Rosaceae)          | England                | [110] |
| Dihydrofuran-2(3H)-one (162)        | 86       | C₄H₆O₂      | F. oxysporum 13-8                      | Prunus dulcis, hull (Rosaceae)                   | California, USA        | [109] |
| Neovasifuranone B (163)             | 282      | C₁₆H₂₆O₄    | F. oxysporum R1 and Aspergillus fumigatus D co-culture | -Edgeworthia chrysantha (Thymelaeaceae)          | China                  | [72]  |
| 2-Pentylfuran (164)                 | 138      | C₉H₁₄O      | F. oxysporum 13-8                      | Prunus dulcis, hull (Rosaceae)                   | California, USA        | [109] |
| **Aliphatic acids**                 |          |              |                                        |                                                 |                        |       |
| 2,3-Dihydroxypropanoic hexadecanoic anhydride (165) | 344 | C₁₉H₃₆O₅ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| 2,3-Dihydroxypropanoic (9Z)-octadecenoic anhydride (Δ⁹;Z) (166) | 370 | C₂₁H₃₈O₅ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| 2,3-Dihydroxypropanoic (9Z,12Z)-octadecadienoic anhydride (Δ⁹,12;Z) (167) | 368 | C₂₁H₃₆O₅ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| 2,3-Dihydroxypropanoic (11Z)-octadecenoic anhydride (Δ¹¹;Z) (168) | 370 | C₂₁H₃₈O₅ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| 2,3-Dihydroxypropanoic (9E,12E)-octadecadienoic anhydride (Δ⁹,12;E) (169) | 368 | C₂₁H₃₆O₅ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| 3-Hydroxy-1,2,6,10-tetramethylundecyl hexadecanoate (170) | 482 | C₁₉H₄₂O₃ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| 3-Hydroxy-1,2,6,10-tetramethylundecyl -octadecanoate (Δ⁹;E) (171) | 508 | C₁₉H₄₄O₃ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| 3-Hydroxy-1,2,6,10-tetramethylundecyl octadecanoate (172) | 510 | C₁₉H₄₆O₃ | F. oxysporum YP9B                      | Solanum lycopersicum, root (Solanaceae)         | Pazar-Rize, Turkey     | [73]  |
| α-Linolenic acid (173)               | 278      | C₁₈H₃₀O₂    | F. oxysporum R1 and Aspergillus fumigatus D co-culture | -Edgeworthia chrysantha (Thymelaeaceae)          | -Edgeworthia chrysantha (Thymelaeaceae)          | China | [72]  |
| α-Elaeostearic acid (174)            | 278      | C₁₈H₃₀O₂    | F. oxysporum R1 and Aspergillus fumigatus D co-culture | -Edgeworthia chrysantha (Thymelaeaceae)          | -Edgeworthia chrysantha (Thymelaeaceae)          | China | [72]  |
Table 1. Cont.

| Compound Name                        | Mol. Wt. | Mol. Formula | Fungal Source                  | Host (Part, Family)                  | Place          | Ref.   |
|--------------------------------------|----------|--------------|--------------------------------|-------------------------------------|----------------|--------|
| **Aliphatic acids**                  |          |              |                                |                                     |                |        |
| Palmitoleic acid (175)               | 254      | C_{16}H_{30}O_{2} | *F. oxysporum* R1 and *Aspergillus fumigatus* D co-culture | -Rumex madaio (Polygonaceae) -Edgeworthia chrysantha (Thymelaeaceae) | China          | [72]   |
| **Sugar derivatives**                |          |              |                                |                                     |                |        |
| α-D-Mannopyranosyl-(1→2)-α-D-glucopyranosyl (176) | 342      | C_{12}H_{22}O_{11} | *F. oxysporum* L. | Cultured | France | [111] |
| α-D-Mannopyranosyl-(1→2)-β-D-glucopyranosyl (177) | 342      | C_{12}H_{22}O_{11} | *F. oxysporum* L. | Cultured | France | [111] |
| α-D-Mannopyranosyl-(1→X)-inositol (178) | 342      | C_{12}H_{22}O_{11} | *F. oxysporum* L. | Cultured | France | [111] |
| **Miscellaneous**                    |          |              |                                |                                     |                |        |
| Moniliformin (179)                   | 97       | C_{4}H_{10}NaO_{3}  | *F. oxysporum* 598           | *Baccharis* spp. (Asteraceae)       | Brazil         | [105]  |
| 7-Methyl-1,3,5-cyclooctatriene (MCOT) (180) | 120      | C_{9}H_{12}     | *F. oxysporum* 13-8          | *Asparagus officinalis* (Asparagaceae) | Western Poland | [57]   |
2. Nanotechnological Applications

Nanotechnology holds promise in the medicine, agriculture, and pharmaceutical industries [112]. Natural nanostructures have gained more attention due to the wide spectrum of bioactivities and fewer animals, humans, and environmental toxicity. The microbial synthesis of nanoparticles is an approach of green chemistry that combines both nanotechnology and microbial biotechnology [113]. Metals nanoparticles are increasingly used in various biotechnological, pharmaceutical, and medicinal applications, including drug delivery, gene transfer, insect-pests management in agriculture, and bioelectronics devices fabrication, as well as antibacterial agents towards many pathogenic bacteria, including the MDR (multidrug-resistant) strains [114–116].

2.1. Metal Nanoparticles

Several studies reported the synthesis and characterization of metal nanoparticles (NPs) using *F. oxysporum*, as well as their bioactivities. Additionally, some studies dealt with optimizing the conditions for the synthesis of NPs by *F. oxysporum*, including temperature, media, pH, salt concentration, light intensity, the volume of filtrate, and biomass quantity [44,47,50,51,54,55]. Marcato et al., synthesized AgNPs (silver nanoparticles) using *F. oxysporum*. The incorporation of these NPs in cotton cloth was found to exhibit a bactericidal effect towards *S. aureus*, leading to its sterilization [50]. Ishida et al., synthesized AgNPs using *F. oxysporum* aqueous extract that showed significant antifungal potential towards *Cryptococcus* and *Candida* (MIC values ≤ 1.68 µg/mL) [51]. Moreover, it was found that the biosynthesized AgNPs by two *F. oxysporum* isolates exhibited higher antibacterial potential towards human-pathogenic bacteria; *E. coli*, *Proteus vulgaris*, *S. aureus*, and *K. pneumonia* than the used antibiotics. These AgNPs could be favorable antibacterial agents, especially towards MDR bacteria [44]. Ahmed et al., synthesized AgNPs using *F. oxysporum*, which inhibited some MDR species of *Staphylococcus* and *Enterobacteriaceae* (conc. 50% v/v), as well as *Candida krusei* and *C. albicans*, suggesting that they might be potential alternatives to antibiotics [46]. The in-silico and in-vitro studies demonstrated the immense antibacterial potential of *F. oxysporum*’s AgNPs against *P. aeruginosa* and *E. coli* [45]. The AgNPs synthesized using nitrate reductase purified from *F. oxysporum* IRAN-31C showed potent antimicrobial potential towards a wide array of human pathogenic bacteria and fungi in the disk diffusion method [117]. A study by Ballottin et al., revealed that the cotton fibers impregnated with biogenic AgNPs synthesized from *F. oxysporum* filtrate solution possessed potent antimicrobial potential even after repeated mechanical washing cycles. This might highlight the potential use of biogenic AgNPs as an antiseptic in textiles for medical applications [118].

Moreover, a study by Hamedi et al., revealed that the existence of ammonium lowered the productivity of AgNPs using *F. oxysporum* cell-free filtrate and prohibited the nitrate reductase enzyme secretion [119]. Longhi et al., reported that the combination of AgNPs synthesized using *F. oxysporum* with FLC (fluconazole) reduced the MIC of FLC around 16 to 64 times towards planktonic cells of *C. albicans* and induced a significant dose-dependent inhibition of both initial and mature biofilms of FLC-resistant *C. albicans*. Therefore, these AgNPs could represent a new strategy for treating FLC-resistant *C. albicans* infections [49]. Additionally, the combination of simvastatin with these AgNPs demonstrated antibacterial activity towards *E. coli*-producing ESBL (extended-spectrum β-lactamase) and MRSA (methicillin-resistant *S. aureus*). This could be a great future alternative in bacterial infection control, where smaller doses of these AgNPs are required with the same antibacterial activity [120]. Besides, its combination with polymyxin B showed a 16-fold reduction of the MIC of polymyxin B and decreased carbapenem-resistant *Acinetobacter baumannii* viability with additive and synergic effects, as well as significantly reduced cytotoxicity towards mammalian Vero cells, indicating its pharmacological safety [121]. The AgNPs synthesized with *F. oxysporum* f.sp. pisi were found to have moderate adulticidal potential on *Culex quinquefasciatus* (vector of filariasis) (LC50 0.4, LC90 4.8, and LC90 4 µL/cm²).
after 24 h exposure [122]. The synthesized AgNPs using F. oxysporum aqueous extract had anticancer potential towards MCF7 (IC\textsubscript{50} 14 µg/mL) that was characterized using CLSM (confocal laser scanning microscopic) technique [123]. Bawskar et al. stated that the biosynthesized AgNPs using F. oxysporum possessed more potent antibacterial potential towards E. coli and S. aureus than chemo-synthesized AgNPs that may be due to the protein capping and their mode of entry into the bacterial cell, which encouraged biosynthetic method over the chemosynthetic one in AgNPs synthesis [124]. Two types of AgNPs, phyto-synthesized and myco-synthesized NPs were biosynthesized by AgNO\textsubscript{3} reduction with Azadirachta indica extract and F. oxysporum cell filtrate, respectively that possessed lower cytotoxic potential on C26 and HaCaT cell lines as compared with citrate coated AgNPs [125]. Santos et al. proved that F. oxysporum-biosynthesized AgNPs without pluronic F68 (stabilizing agent) had high antibacterial potential towards E. coli, P. aeruginosa, and S. aureus. On the contrary, chemo-synthesized AgNPs exhibited synergism in antibacterial activity in the presence of pluronic F68 [126]. Streptococcus agalactiae is an important cause of invasive diseases, mainly in newborns, pregnant women, and elderly individuals [127]. The combination of F. oxysporum-produced AgNPs (AgNPbio) and eugenol led to a remarkable synergistic effect and significant reduction of the MIC values of both eugenol and AgNPbio towards planktonic cells of S. agalactiae [127]. Thakker et al., reported the synthesis of GNP (gold nanoparticles) using F. oxysporum f. sp. cubense JT1 that showed antibacterial potential versus Pseudomonas sp. [128]. Moreover, the conjugated GNP with tetracycline demonstrated powerful antibacterial activity against Gram-negative and -positive bacteria in comparison to tetracycline and free GNPs. Therefore, tetracycline conjugation with these GNPs enhanced the antibacterial potential, which may have significant therapeutic applications [129]. Yahyaei and Pourali studied the conjugation of GNPs with chemotherapeutic agents such as paclitaxel, tamoxifen, and capecitabine. Moreover, the cytotoxic effect of conjugated GNPs was assessed towards MCF7 and AGS cell lines, using MTT assay. Unlike the paclitaxel conjugated GNPs, the tamoxifen and capecitabine conjugated GNPs revealed no toxic effects due to their low half-lives and deactivation [130]. Further, Syed and Ahmad reported the synthesis of stable extracellular platinum nanoparticles, using F. oxysporum [131]. CdSe (cadmium/selenium) quantum dots are often used in industry as fluorescent materials. Kumar et al., and Yamaguchi et al., reported the synthesis of highly luminescent CdSe quantum dots by F. oxysporum [132,133]. In 2013, Syed and Ahmad synthesized highly fluorescent CdTe quantum dots using F. oxysporum at ambient conditions by the reaction with a mixture of TeCl\textsubscript{4} and CdCl\textsubscript{2}. These nanoparticles exhibited antibacterial potential towards Gram-negative and -positive bacteria [53]. Riddin et al., analyzed the biosynthesized platinum (Pt) nanoparticles by F. oxysporum f. sp. lycopersici at both intercellular and extracellular levels. It was found that only the extracellular nanoparticle production was proved to be statistically significant with a yield of 4.85 mg/L [134].

2.2. Metal Sulfide Nanoparticles

In addition, Q-state CdS NPs were biosynthesized by the reaction of aqueous CdSO\textsubscript{4} solution with F. oxysporum [135]. The chemically-synthesized CdSQDs inhibited E. coli cell proliferation in a dose-dependent manner, unlike the biogenic CdSQDs synthesized by F. oxysporum f. sp. lycopersici, which showed an antibacterial potential only at high concentration. Additionally, only the biogenic CdSQDs showed no inhibition on seed germination after incubation of biogenic and chemical CdSQDs with Lactuca sativa seeds [43]. Bi\textsubscript{2}S\textsubscript{3} (bismuth sulfide) NPs have significantly varied applications, including photodiode arrays, photovoltaic materials, and bio-imaging. Uddin et al., synthesized a highly fluorescent, natural protein capped Bi\textsubscript{2}S\textsubscript{3} NPs by subjecting F. oxysporum to bismuth nitrate penta-hydrate, along with sodium sulfite under ambient conditions of pressure, temperature, and pH. It was found that they were fundamentally much more fluorescent than fluorophores (toxic fluorescent chemical compounds), which are largely utilized in immunohistochemistry, imaging, and biochemistry [48].
2.3. Metal Oxide Nanoparticles

It was reported that *F. oxysporum* might have vast commercial implications in low-cost, room-temperature, ecofriendly syntheses of technologically significant oxide nanomaterials from available potentially cheap naturally raw materials [136]. *F. oxysporum* rapidly bio-transformed the naturally occurring amorphous biosilica in rice husk into crystalline silica NPs. This could lead to an economically viable and energy-conserving green approach toward the large-scale synthesis of oxide nanomaterials [136]. Moreover, the mesophilic *F. oxysporum* bioleached Fly-ash at ambient conditions produced highly stable, crystalline, fluorescent, water-soluble, and protein-capped silica nanoparticles [52]. It was found that *F. oxysporum* enriched zirconia in zircon sand by a process of selective extracellular bioleaching of silica nanoparticles. It was proposed that the fungal enzymes specifically hydrolyzed the silicates in the sand to form silicic acid, which on condensation by certain other fungal enzymes resulted in silica nanoparticles synthesis at room temperature [136]. A water dispersible and thermo-stable Ag/Ag$_2$O NPs were produced from silver oxide micro-powder using *F. oxysporum*. These Ag/Ag$_2$O NPs may become a potential candidate for enzyme-free glucose determination and exhibited catalytic potency for MB (methylene blue) degradation in presence of NaBH$_4$ (reducing agent). Additionally, they showed an excellent antimicrobial potential against *A. niger* and *B. subtilis* [137].

3. Biotechnological and Industrial Relevance of *F. oxysporum*

*F. oxysporum* is a wealthy source of enzymes with significant biotechnological and industrial potential. In various studies, *F. oxysporum* demonstrated a remarkably high enzymatic performance and the ability to degrade different biomasses. Herein, the reported enzymes from *F. oxysporum* and their industrial and biotechnological applications are highlighted.

3.1. *F. oxysporum* Enzymes and Their Applications

3.1.1. Glycoside Hydrolases

Cellulases are accountable for cellulose hydrolysis, including β-1,4-endoglucanase, cellobiohydrolase, and β-glucosidases (BGL), which catalyze the hydrolysis of aryl- and alkyl-β-glucosides, as well as oligosaccharides and diglucosides [1,3,5]. Cellulases’ preparations have been added to the ruminant animals’ diets to stimulate feed processing and fiber digestion to increase the extent and rate of digestion [138]. Zhao et al., purified extracellular BGL from *F. oxysporum* that had high acid stability (pH 3) and cellobiose hydrolytic activity relative to Celluclast® (commercial cellulase). Its supplementation also released more reducing sugars (330 mg/g substrate) from cellulose, in comparison to Novozymes (commercial BGL, 267 mg/g substrate) under simulated gastric conditions. Thus, it could be a good source for a new commercial BGL for improving the feed and food quality in the animal feed industry and could be used in combination with Celluclast for industrial applications that required degradation of cellulose at acidic pH [37].

Fucose is a low abundant deoxy-hexose sugar, usually attached to the non-reducing ends of oligolipids, oligosaccharides, and other glycoconjugates (e.g., immunoglobulins, glycoproteins, blood group substances, and mucins). Besides, it is a component of marine algal polysaccharides, human milk oligosaccharides, and plant gums [139]. FUC (α-L-fucosidase) a glycoside hydrolase, catalyzes the breakdown of the terminal α-L-fucosidic bonds. It has remarkable roles in various bioprocesses, and it is used as a marker for hepatocellular carcinoma detection and structural analyses of complex natural products [140]. *F. oxysporum* produced FUC in large amounts through induction by L-fucose. This enzyme hydrolyzed p-nitrophenyl α-L-fucoside (synthetic substrate) like marine gastropod and mammalian enzymes, thus it could replace these enzymes. It had beneficial use as an analytical tool for the structural elucidation of complex carbohydrates and oligosaccharides [41]. Additionally, Yano et al., purified a novel FUC from *F. oxysporum* culture broth. Besides nitrophenyl compounds, this enzyme had a novel substrate specificity. It could hydrolyze porcine mucin and blood group substances [42].
α-D-Galactopyranosidase (GPase) is a glycoside hydrolase that hydrolyzes the α-galactopyranosyl linkages at non-reducing ends of sugar chains. They are utilized for various applications, including eliminating non-digestible oligosaccharides such as stachyose in legume products and soybean, improving the digestibility of animal feed, and increasing the yield and quality of sucrose in sugar refineries [141]. FoAP1 and FoAP2 are two bifunctional enzymes that were isolated and characterized from the culture supernatant of *F. oxysporum* 12S, possessing GPase (α-D-galactopyranosidase)/APase (β-L-arabinopyranosidase) activities in a ratio 1.7 and 0.2, respectively using PNP-α-D-Galp (para-nitrophenyl α-D-galactopyranoside) and PNP-β-L-Arap (para-nitrophenyl α-L-arabinopyranoside) as substrates [38]. A novel GPase, FoGP1 was purified from *F. oxysporum*, exhibiting degrading activity with terminal α-1,3-galactosyl linkages in gum Arabic side chains. Therefore, it might be used for improving gum Arabic physical properties, which is an industrially important polysaccharide used as a coating agent and an emulsion stabilizer [34].

Xylan is one of the most abundant carbohydrates on earth. Its complete degradation is accomplished by the action of various enzymes such as β-D-xylosidases and endo-β-1,4-xylanases. Alconada and Martinez characterized extracellular β-xylosidase and endo-1,4-β-xylanase from *F. oxysporum* f. sp. *melonis*, growing in a medium containing oat spelt xylan. The latter had a high affinity towards oat spelt xylan [142]. Additionally, FoXyn10a, new GH10 xylanase was purified and structurally characterized from *F. oxysporum* [143].

### 3.1.2. Nitrilases

Microbial nitrilases are biocatalysts of remarkable organic importance in terms of nitrile conversion. Nitrile compounds include aromatic and simple aliphatic metabolites, cyano-lipids, and cyano-glucosides which serve as key intermediates and compounds in various biochemical pathways [148]. Processes involving enzymatic conversion of nitrile substrates to higher value amides and carboxylic acid groups are preferred over the chemical synthesis for their production of fewer harmful reaction by-products and greater reaction specificity [149]. Industrial application of nitrile-converting enzymes includes acrylamide and nicotinamide production [35]. The newly isolated nitrilase from *F. oxysporum* f. sp. *lycopersici* ED-3 strain had a wide substrate specificity toward ortho-substituted heterocyclic, aliphatic, and aromatic nitriles and had optimal activity at temperature 50 °C and pH 7.0 [35].

### 3.1.3. Nitric Oxide Reductases

Denitrification is a substantial process in the nitrogen cycle, which involves the reduction of NO⁻² and/or NO³⁻ to either N₂O or N₂. This process can be performed by many bacteria, as well as fungi through a series of consecutive metallo-enzyme-catalyzed chemical reactions [150]. It is a reversible process of nitrogen fixation, where it carries back the fixed N₂ to the atmosphere. It was found that the main source of global N₂O
emissions is the microbial activities of denitrification and nitrification [151]. Therefore, controlling microbial denitrification is most important for N$_2$O emission reduction [152]. It was reported that _F. oxysporum_ exhibited a distinct denitrifying potential that resulted in the anaerobic evolution of N$_2$O from NO$^{-2}$ and NO$^{3-}$ [153]. Further, a nitric oxide reductase (NOR), cytochrome P450nor, belonging to P450 superfamily was purified from _F. oxysporum_, which exhibited remarkable NO reduction potential [36,150,152]. It showed a unique bio-function compared with other usual P450s. While the usual P450s are involved in metabolizing various biological substances through mono-oxygenation reaction using O$_2$, P450nor catalyzed the NO reduction but not the mono-oxygenation [150,154]. Shoun and Tanimoto described a heme-thiolate protein or P450 from _F. oxysporum_ that was involved in the NO (nitrogen monoxide) reduction to N$_2$O (dinitrogen oxide) [153]. In contrast to other bacterial cytochrome bc-containing NO reductases, it did not need a flavoprotein for electron transfer from NADH to the heme, but it utilized NADH directly for the reduction process [155]. Additionally, Daiber et al., identified P450nor (cytochrome P450 NADH-NO), a heme-thiolate protein that catalyzed the reduction of two NO molecules to N$_2$O. P450nor was observed to have a remarkable role in protecting the fungus from NO inhibition of mitochondria [156].

### 3.1.4. Cutinases

Esters having a chain of fewer than 10 carbon atoms are used as flavor compounds in the pharmaceutical, cosmetic, and food industries [157]. Natural synthesis of flavor compounds takes place either by enzymatic bioconversion or by microorganisms, the former path was found to be an easier and more suitable method [157]. The high demand of various industries for fatty acid ester leads to possible growth of the market to $2.44 billion by 2022, from $1.83 billion in 2014 [33,158]. Enzyme immobilization increases their stability and allows their easy separation from the reaction and reuse to overcome the drawbacks of utilizing enzymes such as low operational or storage stability, and/or heat and organic solvent sensitivity [159]. The imFocut5a a CLEAs (cross-linked enzyme aggregates) was produced from a crude _F. oxysporum_ cutinase preparation. This immobilized cutinase possessed a remarkable thermo-stability and was able to synthesize butyl butyrate (pineapple flavor) at a high yield of bioconversion (99%) through the trans-esterification of vinyl butyrate with butanol. This bioconversion presented an eco-friendly and sustainable production of natural flavor compounds, underpinning its industrial potential for use in food bioprocesses [33]. FoCut5a, a cutinase was purified from _F. oxysporum_ and expressed either in the periplasm or cytoplasm of _E. coli_ BL21. It could hydrolyze PET (polyethylene terephthalate) and synthetic polymers. Therefore, it could be used in industrial applications as a biocatalyst for the eco-friendly treatment of synthetic polymers [160].

### 3.1.5. Fructosyl Amino Acid Oxidases

Glycation is the non-enzymatic glycosylation of proteins due to the condensation of reducing sugars such as glucose with the proteins (α- or ε-amino groups) to form a Schiff’s base [161]. Glycation leads to browning of foods during long-term storage, which represents a problem in the food industry [39]. Glycation of hemoglobin, blood proteins, and albumin was found to be enhanced in diabetic patients. Glycated proteins, particularly glycated hemoglobin A1c, are important markers for assessing the effectiveness of anti-diabetic agents. Fructosyl amino acid oxidase (FAOD) based assays have become an attractive alternative to conventional detection methods for measuring glycated proteins [161]. Sakai et al., purified FLO (fructosyl lysine oxidase) from _F. oxysporum_ S-IIF4 that acted against fructosyl poly L-lysine. FLOD could be used for measuring glycated proteins such as glycated albumin in the serum [39].

### 3.1.6. Lipoxygenase

Lipoxygenase (LOX) is a dioxygenase that catalyzes the hydro-peroxidation of polyunsaturated fatty acids such as arachidonic and linoleic acids [162]. It is expressed in epithelial,
tumor, and immune cells that have various physiological functions such as skin disorders, inflammation, and tumorigenesis [163]. Bisakowski et al., extracted and purified LOX from *F. oxysporum* that shared many of the characteristics with LOXs reported from other sources such as substrate specificity, pH, enzyme inhibition, activation, and other kinetic studies [40].

3.1.7. Laccases

Laccases are belonging to oxidoreductases that catalyze the O₂ reduction to H₂O with simultaneous organic substrates oxidation. They oxidize phenolic substrates but are also able to oxidize bigger or non-phenolic substrates by LMS (laccase-mediator system), where a small phenolic compound acts as a mediator [164]. Additionally, they have been reported as potential lignin-degrading enzymes and as solubilizing agents [165,166]. They have attracted great interest because of their wide applications in diverse biotechnological and industrial fields such as textile dye decolorization, pulp bleaching, organic synthesis, bioremediation, and detoxification of environmental pollutants, delignification, or biofuel production [1,3,5].

Kwiatos et al., expressed *F. oxysporum* Gr2 laccase in *Saccharomyces cerevisiae* and engineered it for getting higher effect against 2,6-dimethoxyphenol and higher expression levels. The resulted laccase had a promising potential for different industrial uses such as solubilization of brown coal, which is a clean coal technology, aiming at converting lignite to its cleaner form [164]. In 2018, Kwiatos et al., reported that *F. oxysporum* LOCK-1134 isolated from brown coal, efficiently bio-solubilized lignite, producing liquefied products that had over 99% less Hg and 50% less sulfur than the crude coal. Additionally, its laccase was expressed in *Pichia pastoris*. The resulted novel laccase improved the biodegradation process in presence of LMS. It released fulvic and humic acids from liquefied coal. The latter are environmentally friendly fertilizers that possessed a stimulating influence on crop growth [165].

3.1.8. Aromatic Carboxylic Acid Decarboxylases

The non-oxidative aromatic carboxylic acid decarboxylases catalyze the reversible decarboxylation of phenolic carboxylic acids. Therefore, they are useful biocatalysts for preparing high-value phenolic compounds by the decarboxylation of phenolic carboxylic acids derived from lignin, which opens up a new prospect for high-value utilization of the world second most abundant organic substance [167,168]. Song et al., characterized 2,3-DHBD_Fo, a 2,3-dihydroxybenzoic acid decarboxylase from *F. oxysporum* that possessed a relatively high catalytic decarboxylation efficiency for DHBA (2,3-dihydroxybenzoic acid) and catechol, hence it had a different substrate spectrum from other benzoic acid decarboxylases [167].

3.1.9. Keratinases

Keratins are complex proteins that formed of β-sheets and α-helix structures. They are commonly found in agro-industrial residues such as swine hair and chicken feathers. Keratinous wastes are treated in non-eco-friendly ways, including landfills and incinerators [169,170]. *F. oxysporum* isolated from chicken feathers showed potential for keratinase production that had the highest degradation percentage (59.20% w/w) in swine hair [169].

3.1.10. Phospholipase B

Phospholipase B (PLB) hydrolyzes the phospholipid acyl groups to produce fatty acids and phosphoglycerates [171]. PLB is utilized to produce beneficial phospholipid derivatives, reduce food’s cholesterol content, and refine vegetable oils, especially in terms of crude oil degumming [172]. Su et al., characterized a putative lipase from *F. oxysporum* NCBI-EGU84973.1 that was expressed in *P. pastoris* and classified as a PLB. It had phospholipids hydrolyzing potential greater than its lipase capacity where it hydrolyzed the fatty acyl ester bond at the sn-1 and -2 positions of the phospholipids and reduced
the oil phosphorus contents. This proved the potential industrial use of this PLB in oil degumming applications [172].

3.1.11. Triosephosphate Isomerase

TPI (triosephosphate isomerase) is a glycolysis enzyme that catalyzes the reversible isomerization between DHAP (dihydroxyacetone-3-phosphate) and GAP (glyceraldehyde-3-phosphate) [173]. Therefore, TPI is essential for pathogenic organisms to get the energy needed for survival and infection. Hernández-Ochoa et al., isolated, cloned, and overexpressed Tpi gene from F. oxysporum isolated from a wild species collected from a bean crop. They purified FoxTPI recombinant protein that had the TPIs classical topology conserved in other organisms [14].

3.2. Applications of F. oxysporum

Biodiesel (biofuel) is obtained from renewable sources such as animal fat or vegetable oil by trans-esterification of triglycerides to give fatty acid alkyl esters [174]. It is used as a full or partial substitute for petrol diesel in combustion engines [175]. Its production attracts attention worldwide due to the environmental benefits such as biodegradation that reduced the emission of sulfur and aromatic hydrocarbons during fuel combustion and decreased emission of CO₂, CO, and particulate materials. The accumulated lipids in microorganisms such as algae, fungi, and bacteria are mainly triacylglycerols (TAG) that are utilized as metabolites for biodiesel production [32]. F. oxysporum NRC2017 isolated from Egyptian soil had remarkable lipid producing capacity (55.2%). It showed the highest lipid accumulation 98.3 mg/g in the presence of bagasse and its fatty acids were found to be suitable for biodiesel production based on GC analysis [32].

On earth, the most abundant source of biomass is lignocellulosic material that includes agricultural residues, grasses, wood, or any non-food-plant sources. Its microbial fermentation produces ethanol and other solvents that represent an alternative path for wastes treatment and production of fuel additives and chemical feedstocks. F. oxysporum was found to have the potential for converting D-xylose, as well as cellulose to ethanol in a one-step process, indicating its capacity for ethanol production [176].

Bioethanol production is a harsh operational process that needs potent biocatalysts. CBP (consolidated bioprocessing) is an economical and efficient method of manufacturing bioethanol from lignocellulose. CBP integrates the fermentation and hydrolysis steps into a single process, leading to a significant reduction in the steps of the biorefining process. Ali et al., reported that F. oxysporum had a high potential for CBP of lignocellulose to bioethanol and it could be a commercially competitive CBP agent [177]. It was observed a significant inter-strain divergence regarding the capacity of different F. oxysporum strains to produce alcohol from wheat straw [178]. Nait M’Barek et al., assessed the potential of F. oxysporum for bioethanol production from non-valorized OMW (olive mill waste) using CBP. It showed maximum bioethanol yield and production of 0.84 g/g and 2.47 g/L, respectively, indicating its importance as a bio-agent for single-pot local bio-refinery [179]. Moreover, F. oxysporum BN converted imidazolium-based ionic liquid (IL)-pretreated rice straw to bioethanol via CBP with 64.2% of the theoretical yield of 0.125 g ethanol/g rice straw [164]. It secreted a novel IL-tolerant cellulase that can direct the conversion of IL-pretreated lignocellulose residue to ethanol, which had a significant potential to bring a breakthrough in commercial ethanol production by the reduction of the overall cost [180].
4. Secondary Metabolites from *F. oxysporum* and Their Bioactivities

4.1. Anthranilates

Anthranilates are derivatives of anthranilic acid that constitute an important part of several bio-metabolites and serve as a scaffold for developing remarkable pharmaceuticals for the management of the pathogenesis and pathophysiology of diverse disorders. They possessed impressive bioactivates such as antiviral, antimicrobial, insecticidal, anti-inflammatory, anti-diabetic, and anticancer [181]. Compounds 1–21 are anthranilic acid derivatives that had been purified and characterized only from *F. oxysporum* f. sp. *dianthi* extracts using HPLC-, pyrolysis-, and HR-MS [56]. It was reported that the anthranilic acid derivatives are originated from 2 that is formed from benzoate and anthranilate [182]. Subsequently, it undergoes hydroxylation at C-2′ to produce dianthalexin, hydroxylation at C-4 to yield 3 or 5, and methylation to 9 or 8. Moreover, 20 and 19 are produced from 5 and 3 [56,183] (Scheme 1, Figure 1).

**Scheme 1.** Possible biosynthetic pathway for the formation of anthranilic acid derivatives [56,182,183].
4.2. Fumonisins

Fumonisins are mycotoxins, belonging to fungal polyketides. They have two propane-1,2,3-tricarboxylic acid chains esterified to an aminopolyol skeleton [184]. They inhibit a ceramide synthase, the key enzyme in the biosynthetic pathway of sphingolipids, leading to serious mycotoxicoses [57,185]. Fumonisin derivatives 22–30 were isolated from *F. oxysporum* associated with *Asparagus officinalis* and *Dianthus caryophyllus*. They were characterized by FABMS, ES-LCMS, and NMR techniques [57–60] (Figure 2).

4.3. Jasmonates

Jasmonates are lipid-based metabolites, possessing jasmonic acid (3-oxo-2-(pent-2′-enyl)cyclopentane acetic acid) framework that are found in fungi, bacteria, and plants [186,187]. In plants, they function as growth regulators and play major roles in the defense of plants against insects and diseases [187]. In addition, hydroxylated jasmonic acids, unsaturated or saturated, and cis- or trans-configured elongated side-chain derivatives were reported from fungi. They can also form conjugates with amino acids such as isoleucine. In a study by Miersch et al., jasmonates derivatives 31–52 were purified from

![Figure 1. Structures of anthranilic acid derivatives (1–21) isolated from *F. oxysporum*.](image-url)
*F. oxysporum* f. sp. *matthiolae* using RP-18 Lichrolut, DEAE-Sephadex-A25, and 100-C18 Eurospher and characterized by GC-MS and HPLC [61] (Figures 3 and 4).

**Figure 2.** Structures of fumonisins 22–30 isolated from *F. oxysporum*.
Figure 3. Structures of jasmonates derivatives (31–42) isolated from *F. oxysporum*. 

- (-)-Jasmonic acid (31)
- (+)-7-iso-jasmonic acid (32)
- (1S,2S)-3-(1S,2S)-3-Oxo-2-(2Z-penteny) cyclopentane-1-butryc acid (33)
- (1S,2R)-3-Oxo-2-(2Z-penteny)cyclopentane-1-hexanoic acid (34)
- (1S,2R)-3-Oxo-2-(2Z-penteny)cyclopentane-1-hexanoic acid (35)
- (1S,2S)-3-Oxo-2-(2Z-penteny)cyclopentane-1-hexanoic acid (36)
- (1S,2R)-3-Oxo-2-(2Z-penteny)cyclopentane-1-octanoic acid (37)
- (1S,2S)-3-Oxo-2-(2Z-penteny)cyclopentane-1-octanoic acid (38)
- 9,10-Dihydrojasmonic acid (39)
- (1S,2R)-3-Oxo-2-pentylcyclopentane-1-butryc acid (40)
- 9,10-Dihydro-7-iso-jasmonic acid (41)
- (1S,2S)-3-Oxo-2-pentylcyclopentane-1-butryc acid (42)
4.4. Alkaloids

The reported studies revealed the isolation of diverse classes of alkaloids from *F. oxysporum*. Oxysporidinone (53), a novel 3,5-disubstituted N-methyl-4-hydroxy-2-pyridone was purified from *F. oxysporum* (CBS 330.95) culture by counter-current and SiO$_2$ CC and characterized by UV, NMR, IR, and MS tools. It had growth inhibitory potential towards phyto-pathogenic fungi; *Aspergillus niger*, *Botrytis cinerea*, *Alternaria alternata*, and *Venturia inequalis* (MICs 10, 1, 50, and 10 µg/mL, respectively) (Table 2). It showed no observable activity towards *B. subtilis*, *P. aeruginosa*, *C. albicans*, and *S. cervisiae* (conc.
Bioassay-guided separation of *F. oxysporum* (N17B) extract gave three new N-methyl-4-hydroxy-2-pyridinone derivatives; 6-epi-oxysporidinone (59), dimethyl ketal of oxysporidinone (60), and N-demethylsambutoxin (61), along with (−)-oxysporidinone (54) and (−)-sambutoxin (58) that were identified by NMR and MS techniques [63] (Figure 5). Compound 54 was identical to 53 but with the opposite sign of optical rotation. Compound 59 was a 6′-hydroxy epimer of 53, however, 61 was similar to 58 with the lack of N-CH$_3$ group. Compound 58 was isolated previously as a hemorrhagic mycotoxin from *F. sambucinum* [188]. Interestingly, 54 (IC$_{50}$ 2.0 µg/mL) had a powerful fungistatic potential towards *A. fumigatus*, whereas its epimer 59 (IC$_{50}$ 35.0 µg/mL) showed a marginal effect, compared with amphotericin B (IC$_{50}$ 0.91 µg/mL) in the MABA (microplate Alamar blue assay). Whilst other compounds were inactive [63]. (−)-4,6′-Anhydrooxysporidinone (57) isolated from EtOAc extract of a solid endophytic fungus *F. oxysporum*, had moderate anti-BS (*Bacillus subtilis*) activity (MIC 25.0 µg/mL) and weak anti-MRSA potential (MIC 100 µg/mL) [65]. On the other side, (−)-oxysporidinone (54), (−)-6-deoxyoxysporidinone (56), and (−)-4,6′-anhydrooxysporidinone (57) isolated from *F. oxysporum* EPH2R$_{AA}$ harboring *Ephedra fasciculata* had no cytotoxic activities towards NCI-H460, MIA Pa Ca-2, MCF-7, and SF-268 [64]. Fusaric acid (63) was identified as antioomycete metabolite from *F. oxysporum* EF119 by MS and NMR analyses. It possessed in vivo and in vitro antioomycete potential against *P. capsici* (causative agent of wheat leaf rust) and *P. infestans* (causative agent of tomato late blight) with IC$_{50}$ values < 1 µg/mL. It also completely suppressed the growth of various bacteria (IC$_{50}$ values ranged from 0.2 to 12 µg/mL, Conc. < 100 µg/mL). Thus, it could be used as a biocontrol agent towards tomato late blight produced by *P. infestans* [66]. Moreover, 63 was identified from *F. oxysporum* isolated from an infected grapevine. It induced extensive necrosis formation on tobacco in the leaf-puncture assay at 0.5 mg/mL. Fusaric acid is a nonspecific toxin produced by many *Fusarium* species, and usually is the main phytotoxin [67]. The new fusaric acid derivatives, fusaricates A-G (65–71) and 10-hydroxy-11-chlorofusaric acid (72) purified from *F. oxysporum* isolated from *Drepanocarpus lunatus* fruits had fusaric acid linked to a polyalcohol moiety through an ester bond (Figure 6). Their structures were elucidated by NMR and MS data and the absolute configuration was established using chiral GC-MS. Only 72 had weak cytotoxicity against L5178Y (IC$_{50}$ 37.7 µM), compared to kahalalide F (IC$_{50}$ 4.3 µM).
| Compound Name | Biological Activity | Assay, Organism, or Cell Line | Biological Results | Positive Control | Ref. |
|---------------|---------------------|-------------------------------|-------------------|-----------------|-----|
| Oxysporidinone (53) | Antifungal | Agar diffusion/Aspergillus niger | 10 µg/mL (MIC) | - | [62] |
| | | Agar diffusion/Botrytis cinerea | 1 µg/mL (MIC) | - | [62] |
| | | Agar diffusion/Alternaria alternata | 50 µg/mL (MIC) | - | [62] |
| | | Agar diffusion/Venturia inaequalis | 10 µg/mL (MIC) | - | [62] |
| (−)-Oxysporidinone (54) | Antifungal | MABA/Cryptococcus neoformans | 35.0 µg/mL (IC<sub>50</sub>) | Amphotericin B 0.45 µg/mL (IC<sub>50</sub>) | [63] |
| | | MABA/Aspergillus fumigatus | 2.0 µg/mL (IC<sub>50</sub>) | Amphotericin B 0.91 µg/mL (IC<sub>50</sub>) | [63] |
| (−)-4,6′-Anhydrooxysporidinone (57) | Antibacterial | Microtiter plate/B. subtilis | 25.0 µg/mL (MIC) | - | [65] |
| | | Microtiter plate/MRSA | 100.0 µg/mL (MIC) | - | [65] |
| 6-Epi-oxysporidinone (59) | Antifungal | MABA/Aspergillus fumigatus | 35.0 µg/mL (IC<sub>50</sub>) | Amphotericin B 0.91 µg/mL (IC<sub>50</sub>) | [63] |
| Fusaric acid (63) | Antimicrobial | Microtiter plate/Colletotrichum coccodes | 81.0 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Magnaporthe grisea | 50.0 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Phytophthora capsici | 0.36 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Phytophthora infestans | 1.0 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Rhizoctonia solani | 11.0 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Phytophthora sojae | 0.2 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Agrobacterium tumefaciens | 3.0 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Burkholderia glumae | 1.7 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Pectobacterium carotovora ssp. carotovora | 12.0 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Pseudomonas syringae pv. lachrymans | 11.0 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| | | Microtiter plate/Xanthomonas euvesicatoria | 0.2 µg/mL (IC<sub>50</sub>) | DMSO 1% | [66] |
| Fusaricate B (66) | Cytotoxicity | MTT/L5178Y | 37.7 µM (IC<sub>50</sub>) | Kahalalide F 4.3 µM (IC<sub>50</sub>) | [69] |
| Oxysporizoline (73) | Antioxidant | DPPH | 10 µM (IC<sub>50</sub>) | Ascorbic acid 20 µM (IC<sub>50</sub>) | [70] |
| Butenolide (75) | Antioxidant | DPPH | 12 µM (IC<sub>50</sub>) | Ascorbic acid 20 µM (IC<sub>50</sub>) | [70] |
| 2-Oxo-8-azatricyclo[9.3.1.1<sup>3,7</sup>]-hexadeca-1(15),3(16),4,6,11,13-hexaen-10-one (80) | Antimicrobial | Double microdilution/Escherichia coli ATCC25922 | 1.6 µg/mL (MIC) | Ampicillin 10 µg/mL (MIC) | [73] |
| | | Double microdilution/Versinia pseudotuberculosis ATCC911 | 1.6 µg/mL (MIC) | Ampicillin 18 µg/mL (MIC) | [73] |
| | | Double microdilution/Klebsiella pneumonia subsp. pneumonia ATCC13883 | 1.6 µg/mL (MIC) | Ampicillin 18 µg/mL (MIC) | [73] |
| | | Double microdilution/Pseudomonas aeruginosa ATCC27853 | 1.6 µg/mL (MIC) | Ampicillin >128 µg/mL (MIC) | [73] |
| | | Double microdilution/Staphylococcus aureus ATCC29233 | 1.6 µg/mL (MIC) | Ampicillin 10 µg/mL (MIC) | [73] |
| | | Double microdilution/Enterococcus faecalis ATCC29212 | 1.6 µg/mL (MIC) | Ampicillin 35 µg/mL (MIC) | [73] |
| Compound Name                                      | Biological Activity | Assay, Organism, or Cell Line | Biological Results | Positive Control | Ref. |
|---------------------------------------------------|---------------------|-------------------------------|--------------------|------------------|------|
| Double microdilution / Streptococcus mutans       |                     |                               | 6.3 µg/mL (MIC)    |                  | [73] |
| RSK07038                                          |                     |                               |                    |                  |      |
| Double microdilution / Lactobacillus casei        |                     |                               | 12.5 µg/mL (MIC)   |                  | [73] |
| RSK591                                            |                     |                               |                    |                  |      |
| Double microdilution / Bacillus cereus 702 Roma   |                     |                               | 0.8 µg/mL (MIC)    | Ampicillin 15 µg/mL (MIC) | [73] |
| Double microdilution / Mycobacterium smegmatis ATCC 607 |                     |                               | 3.1 µg/mL (MIC)    | Streptomycin 4 µg/mL (MIC) | [73] |
| Double microdilution / Candida albicans ATCC60193 |                     |                               | 3.1 µg/mL (MIC)    | Fluconazole < 8 µg/mL (MIC) | [73] |
| Double microdilution / C. tropicalis ATCC 13803   |                     |                               | 3.1 µg/mL (MIC)    | Fluconazole < 8 µg/mL (MIC) | [73] |
| Double microdilution / Saccharomyces cerevisiae RSK251 |                     |                               | 6.3 µg/mL (MIC)    | Fluconazole < 8 µg/mL (MIC) | [73] |
| Fusarioxazin (81)                                 | Cytotoxicity        | MTT/MCF-7                      | 2.1 µM (IC_{50})   | Doxorubicin 0.68 µM (IC_{50}) | [18] |
|                                                   |                     | MTT/HCT116                     | 4.7 µM (IC_{50})   | Doxorubicin 1.34 µM (IC_{50}) | [18] |
|                                                   |                     | MTT/AS49                       | 3.2 µM (IC_{50})   | Doxorubicin 0.39 µM (IC_{50}) | [18] |
|                                                   | Antimicrobial       | Disc diffusion / S. aureus     | 5.3 µg/mL (MIC)    | Ciprofloxacin 3.9 µg/mL (MIC) | [18] |
|                                                   |                     | Disc diffusion / B. cereus     | 3.7 µg/mL (MIC)    | Ciprofloxacin 2.3 µg/mL (MIC) | [18] |
|                                                   |                     | Disc diffusion / E. coli       | 15.9 µg/mL (MIC)   | Ciprofloxacin 4.1 µg/mL (MIC) | [18] |
|                                                   |                     | Disc diffusion / C. albicans   | 18.2 µg/mL (MIC)   | Clotrimazole 3.5 µg/mL (MIC) | [18] |
| Epi-trichosetin (82)                              | Inhibition of UPP synthase | Enzyme-coupled fluorescent / S. aureus | 83.0 µM (IC_{50})  |                  | [74] |
|                                                   | Antimicrobial       | Disc diffusion / S. aureus ATCC 658P (MSSA) | 18.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / S. aureus K24 (MRSA) | 16.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Bacillus subtilis PCI 219 | 18.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Micrococcus luteus PCI 9341 | 17.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Mycobacterium smegmatis ATCC 607 | 9.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Escherichia coli NIH | 10.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Xanthomonas campestris KB 88 | 9.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Bacteroides fragilis ATCC 23745 | 11.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Acholeplasma laidlawii KB 174 | 12.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Pseudomonas oryzae KF 180 | 14.0 mm (IZD)     |                  | [74] |
|                                                   |                     | Disc diffusion / Macromucor IFO 4581 | 7.0 mm (IZD)     |                  | [74] |

| Trichosetin (83)                                  | Inhibition of UPP synthase | Enzyme-coupled fluorescent / S. aureus | 30.0 µM (IC_{50})  |                  | [74] |
|                                                   | Antimicrobial             | Disc diffusion / S. aureus ATCC 658P (MSSA) | 15.0 mm (IZD)     |                  | [74] |
|                                                   |                      | Disc diffusion / S. aureus K24 (MRSA) | 14.0 mm (IZD)     |                  | [74] |
|                                                   |                      | Disc diffusion / Bacillus subtilis PCI 219 | 16.0 mm (IZD)     |                  | [74] |
|                                                   |                      | Disc diffusion / Micrococcus luteus PCI 9341 | 15.0 mm (IZD)     |                  | [74] |
|                                                   |                      | Disc diffusion / Mycobacterium smegmatis ATCC 607 | 8.0 mm (IZD)     |                  | [74] |
|                                                   |                      | Disc diffusion / Escherichia coli NIH | 10.0 mm (IZD)     |                  | [74] |
|                                                   |                      | Disc diffusion / Xanthomonas campestris KB 88 | 7.0 mm (IZD)     |                  | [74] |
|                                                   |                      | Disc diffusion / Bacteroides fragilis ATCC 23745 | 11.0 mm (IZD)     |                  | [74] |
| Compound Name       | Biological Activity | Assay, Organism, or Cell Line | Biological Results | Positive Control          | Ref. |
|---------------------|---------------------|-------------------------------|--------------------|----------------------------|------|
|                     |                     | Disc diffusion / Acholoplasma laidlavii KB 174 | 9.0 mm (IZD)       | -                          | [74] |
|                     |                     | Disc diffusion / Pyricularia oryzae EF 180 | 11.0 mm (IZD)      | -                          | [74] |
|                     |                     | Disc diffusion / Mucor racemosus FIO 4581 | 7.0 mm (IZD)       | -                          | [74] |
| Enniatin A (91)     | Antifungal          | MABA / Candida albicans       | 2.0 µg/mL (IC₅₀)   | Amphotericin B 0.35 µg/mL (IC₅₀) | [63] |
|                     |                     | MABA / Cryptococcus neoformans | 3.5 µg/mL (IC₅₀)   | Amphotericin B 0.45 µg/mL (IC₅₀) | [63] |
|                     |                     | MABA / Mycobacterium intracellular | 3.0 µg/mL (IC₅₀)   | Ciprofloxacin 0.3 µg/mL (IC₅₀) | [63] |
| Enniatin A1 (92)    | Antifungal          | MABA / Candida albicans       | 2.0 µg/mL (IC₅₀)   | Amphotericin B 0.35 µg/mL (IC₅₀) | [63] |
|                     |                     | MABA / Cryptococcus neoformans | 4.5 µg/mL (IC₅₀)   | Amphotericin B 0.45 µg/mL (IC₅₀) | [63] |
|                     |                     | MABA / Mycobacterium intracellular | 9.0 µg/mL (IC₅₀)   | Ciprofloxacin 0.3 µg/mL (IC₅₀) | [63] |
| Enniatin B1 (93)    | Antifungal          | MABA / Candida albicans       | 2.0 µg/mL (IC₅₀)   | Amphotericin B 0.35 µg/mL (IC₅₀) | [63] |
|                     |                     | MABA / Cryptococcus neoformans | 9.0 µg/mL (IC₅₀)   | Amphotericin B 0.45 µg/mL (IC₅₀) | [63] |
|                     |                     | MABA / Mycobacterium intracellular | 15.0 µg/mL (IC₅₀)  | Ciprofloxacin 0.3 µg/mL (IC₅₀) | [63] |
| Enniatin H (96)     | Cytotoxicity        | SRB / A549                    | 1.84 µM (EC₅₀)     | Doxorubicin 0.03 µM (EC₅₀)   | [83] |
|                     |                     | SRB / SK-OV-3                | 1.71 µM (EC₅₀)     | Doxorubicin 0.06 µM (EC₅₀)   | [83] |
|                     |                     | SRB / SK-MEL-2               | 1.77 µM (EC₅₀)     | Doxorubicin 0.04 µM (EC₅₀)   | [83] |
|                     |                     | SRB / HCT15                  | 2.45 µM (EC₅₀)     | Doxorubicin 0.2 µM (EC₅₀)    | [83] |
| Enniatin I (97)     | Cytotoxicity        | SRB / A549                    | 0.50 µM (EC₅₀)     | Doxorubicin 0.03 µM (EC₅₀)   | [83] |
|                     |                     | SRB / SK-OV-3                | 0.49 µM (EC₅₀)     | Doxorubicin 0.06 µM (EC₅₀)   | [83] |
|                     |                     | SRB / SK-MEL-2               | 0.53 µM (EC₅₀)     | Doxorubicin 0.04 µM (EC₅₀)   | [83] |
|                     |                     | SRB / HCT15                  | 0.53 µM (EC₅₀)     | Doxorubicin 0.2 µM (EC₅₀)    | [83] |
| Enniatin MK1688 (98)| Cytotoxicity        | SRB / A549                    | 0.45 µM (EC₅₀)     | Doxorubicin 0.03 µM (EC₅₀)   | [83] |
|                     |                     | SRB / SK-OV-3                | 0.45 µM (EC₅₀)     | Doxorubicin 0.06 µM (EC₅₀)   | [83] |
|                     |                     | SRB / SK-MEL-2               | 0.63 µM (EC₅₀)     | Doxorubicin 0.04 µM (EC₅₀)   | [83] |
|                     |                     | SRB / HCT15                  | 0.53 µM (EC₅₀)     | Doxorubicin 0.2 µM (EC₅₀)    | [83] |
| Beauvericin (99)    | Cytotoxicity        | MTT / MIA Pa Ca-2             | 0.26 µM (IC₅₀)     | Doxorubicin 0.01 µM (IC₅₀)   | [64] |
|                     |                     | MTT / MCF-7                  | 0.42 µM (IC₅₀)     | Doxorubicin 0.05 µM (IC₅₀)   | [64] |
|                     |                     | MTT / SF-268                 | 0.38 µM (IC₅₀)     | Doxorubicin 0.07 µM (IC₅₀)   | [64] |
|                     |                     | SRB / A549                   | 1.43 µM (EC₅₀)     | Doxorubicin 0.04 µM (IC₅₀)   | [64] |
|                     |                     | SRB / SK-OV-3                | 1.39 µM (EC₅₀)     | Doxorubicin 0.03 µM (EC₅₀)   | [83] |
|                     |                     | SRB / SK-MEL-2               | 1.47 µM (EC₅₀)     | Doxorubicin 0.06 µM (EC₅₀)   | [83] |
|                     |                     | SRB / HCT15                  | 1.86 µM (EC₅₀)     | Doxorubicin 0.04 µM (EC₅₀)   | [83] |
|                     |                     | MTT / PC-3                   | 49.5 µM (IC₅₀)     | Doxorubicin 0.2 µM (EC₅₀)    | [83] |
|                     |                     | MTT / PAN-1                  | 47.2 µM (IC₅₀)     | Cisplatin 26.8 µM (IC₅₀)     | [65] |
|                     |                     | MTT / AS49                   | 10.4 µM (IC₅₀)     | Cisplatin 26.2 µM (IC₅₀)     | [65] |
|                     |                     | MTT / HCT-8                  | 3.02 µg/mL (IC₅₀)  | Doxorubicin 0.04 µg/mL (IC₅₀) | [84] |
|                     |                     | MTT / MDA-MB435              | 3.17 µg/mL (IC₅₀)  | Doxorubicin 0.2 µg/mL (IC₅₀) | [84] |
|                     |                     | MTT / SF295                  | 2.39 µg/mL (IC₅₀)  | Doxorubicin 0.04 µg/mL (IC₅₀) | [84] |
|                     | Antibacterial       | Microtiter plate / MRSA      | 3.125 µg/mL (MIC)  | -                          | [65] |
|                     |                     | Microtiter plate / B. subtilis | 3.125 µg/mL (MIC)  | -                          | [65] |
| Compound Name                  | Biological Activity          | Assay, Organism, or Cell Line                           | Biological Results       | Positive Control              | Ref.  |
|-------------------------------|------------------------------|---------------------------------------------------------|--------------------------|-----------------------------|-------|
|                               |                              | MTT (anti-promastigote)/L. Cell Line                     |                          |                             |       |
| Anhydrofusarubin (105)        | Cytotoxicity                 | MTT/HCT-8                                               | 9.85 µg/mL (IC₅₀)        | Doxorubicin 0.04 µg/mL (IC₅₀) | [84]  |
|                               |                              | MTT/MDA-MB435                                           | 6.23 µg/mL (IC₅₀)        | Doxorubicin 0.2 µg/mL (IC₅₀)  | [84]  |
|                               |                              | MTT/SF295                                               | 6.32 µg/mL (IC₅₀)        | Doxorubicin 0.04 µg/mL (IC₅₀) | [84]  |
|                               |                              | Antinemic/M. incognita                                  | 257.6 µg/mL (LC₅₀)       | Carbofuran 54.2 µg/mL (LC₅₀) | [88]  |
|                               |                              | Antinemic/R. reniformis                                 | 285.3 µg/mL (LC₅₀)       | Carbofuran 37.6 µg/mL (LC₅₀) | [88]  |
| Fusarubin (107)               | Plant nematicidal            | Antinemic/M. incognita                                  | 248.9 µg/mL (LC₅₀)       | Carbofuran 54.2 µg/mL (LC₅₀) | [88]  |
|                               |                              | Antinemic/R. reniformis                                 | 301.6 µg/mL (LC₅₀)       | Carbofuran 37.6 µg/mL (LC₅₀) | [88]  |
| 8-O-methylfusarubin (108)     | Plant nematicidal            | Antinemic/M. incognita                                  | 376.4 µg/mL (LC₅₀)       | Carbofuran 54.2 µg/mL (LC₅₀) | [88]  |
| 9-O-Methylfusarubin (108)     |                              | Antinemic/R. reniformis                                 | 518.4 µg/mL (LC₅₀)       | Carbofuran 37.6 µg/mL (LC₅₀) | [88]  |
| 3-O-Methyl-8-O-methylfusarubin| Plant nematicidal            | Antinemic/M. incognita                                  | 478.5 µg/mL (LC₅₀)       | Carbofuran 54.2 µg/mL (LC₅₀) | [88]  |
| 3-O-Methyl-9-O-methylfusarubin|                              | Antinemic/R. reniformis                                 | 465.2 µg/mL (LC₅₀)       | Carbofuran 37.6 µg/mL (LC₅₀) | [88]  |
| 8-O-Methyljavanicin (111)     | Antibacterial                | Microdilution/S. aureus                                 | 4 µg/mL (MIC)            | -                           | [90]  |
|                              |                              | Microdilution/Streptococcus pyogenes                    | >128 µg/mL (MIC)         | -                           | [90]  |
| 8-O-Methylsolanil (112)       | Antibacterial                | Microdilution/S. aureus                                 | 32.0 µg/mL (MIC)         | -                           | [90]  |
|                              |                              | Microdilution/Streptococcus pyogenes                    | 64.0 µg/mL (MIC)         | -                           | [90]  |
| Nectriafurone (114)           | Antibacterial                | Microdilution/S. aureus                                 | >128 µg/mL (MIC)         | -                           | [90]  |
|                              |                              | Microdilution/Streptococcus pyogenes                    | 128 µg/mL (MIC)          | -                           | [90]  |
| Bikaverin (119)               | Antimicrobial                | Microtitre plate/Colletotrichum coccodes                | 70.0 µg/mL (IC₅₀)        | DMSO 1%                      | [66]  |
|                               |                              | Microtitre plate/Magnaporthe grisea                     | 70.0 µg/mL (IC₅₀)        | DMSO 1%                      | [66]  |
|                               |                              | Microtitre plate/Phytophthora capsici                   | 10.0 µg/mL (IC₅₀)        | DMSO 1%                      | [66]  |
|                               |                              | Microtitre plate/Phytophthora infestans                 | 60.0 µg/mL (IC₅₀)        | DMSO 1%                      | [66]  |
|                               | Cytotoxicity                 | MTT/NCH460                                              | 1.41 µM (IC₅₀)           | Doxorubicin 0.01 µM (IC₅₀)   | [64]  |
|                               |                              | MTT/MIA Pa Ca-2                                          | 1.66 µM (IC₅₀)           | Doxorubicin 0.05             | [64]  |
|                               |                              | MTT/MCF-7                                               | 1.81 µM (IC₅₀)           | Doxorubicin 0.07 µM (IC₅₀)   | [64]  |
|                               |                              | MTT/SF268                                               | 2.29 µM (IC₅₀)           | Doxorubicin 0.04 µM (IC₅₀)   | [64]  |
|                               | Nematicidal                  | Antinemic/M. incognita                                  | 392.9 µg/mL (LC₅₀)       | Carbofuran 54.2 µg/mL (LC₅₀) | [88]  |
|                               |                              | Antinemic/R. reniformis                                 | 618.0 µg/mL (LC₅₀)       | Carbofuran 37.6 µg/mL (LC₅₀) | [88]  |
| Wortmannin (129)              | Antifungal                   | MABA/C. albicans                                        | 0.25 µg/mL (IC₅₀)        | Amphotericin B 0.35 µg/mL (IC₅₀) | [63]  |
| H1-A = Ergosta-5,8-(14,22-trien-one, 3-hydroxy-(3β, 22E) (130) | Anti-hepatitis C virus (HCV) NS3 serine protease | FRET/HCV NS3 protease | 99.7 µM/L (Ki value)         | VX950 3.5 µM/L (Ki value)     | [89]  |
| Compound Name | Biological Activity | Assay, Organism, or Cell Line | Biological Results | Positive Control | Ref. |
|---------------|---------------------|-------------------------------|-------------------|------------------|-----|
| Fusariumins C (135) | Antimicrobial | Microbroth dilution/ S. aureus | 6.25 µM (MIC) | Ampicillinum sodium | [102] |
| Fusariumins D (136) | Antimicrobial | Microbroth dilution/ S. aureus | 25 µM (MIC) | Ampicillinum sodium | [102] |
| (1-Benzyl-2-methoxy-2-oxoethyl)-2-hydroxy-3-methylbutanoate (153) | Cytotoxicity | MTT/MCF-7 | 15.01 µM (IC50) | Doxorubicin 0.053 µM (IC50) | [73] |
|  | Antimicrobial | MTT/PC-3 | 19.13 µM (IC50) | Doxorubicin 0.09 µM (IC50) | [73] |
|  |  | MTT/A549 | 17.06 µM (IC50) | Doxorubicin 17.75 µM (IC50) | [73] |
|  | Double microdilution/Escherichia coli ATCC25922 | 60 µg/mL (MIC) |  | Ampicillin 10 µg/mL (MIC) | [73] |
|  | Double microdilution/Yersinia pseudotuberculosis ATCC911 | 60 µg/mL (MIC) |  | Ampicillin 18 µg/mL (MIC) | [73] |
|  | Double microdilution/Klebsiella pneumonia subsp. pneumonia ATCC13883 | 60 µg/mL (MIC) |  | Ampicillin 18 µg/mL (MIC) | [73] |
|  | Double microdilution/Pseudomonas aeruginosa ATCC27853 | 60 µg/mL (MIC) |  | Ampicillin >128 µg/mL (MIC) | [73] |
|  | Double microdilution/Staphylococcus aureus ATCC25923 | 0.94 µg/mL (MIC) |  | Ampicillin 10 µg/mL (MIC) | [73] |
|  | Double microdilution/Enterococcus faecalis ATCC29212 | 1.8 µg/mL (MIC) |  | Ampicillin 35 µg/mL (MIC) | [73] |
|  | Double microdilution/Streptococcus mutans RSKK07038 | 1.8 µg/mL (MIC) |  |  | [73] |
|  | Double microdilution/Lactobacillus casei RSK591 | 30 µg/mL (MIC) |  |  | [73] |
|  | Double microdilution/Bacillus cereus 702 Roma | 0.94 µg/mL (MIC) |  | Ampicillin 15 µg/mL (MIC) | [73] |
|  | Double microdilution/Mycobacterium smegmatis ATCC607 | 0.47 µg/mL (MIC) |  | Streptomycin 4 µg/mL (MIC) | [73] |
|  | Double microdilution/Candida albicans ATCC60193 | 60 µg/mL (MIC) |  | Fluconazole < 8 µg/mL (MIC) | [73] |
|  | Double microdilution/C. tropicalis ATCC13805 | 60 µg/mL (MIC) |  | Fluconazole < 8 µg/mL (MIC) | [73] |
|  | Double microdilution/Saccharomyces cerevisiae RSKK251 | 120 µg/mL (MIC) |  | Fluconazole < 8 µg/mL (MIC) | [73] |
| Mixture of 2,3-dihydroxypropanoic (11Z)-octadecenoic anhydride (168) and 2,3-dihydroxypropanoic, (9E,12E)-octadecadienoic anhydride (169) | Antimicrobial | Double microdilution/E. coli ATCC25922 | 7.8 µg/mL (MIC) | Ampicillin 10 µg/mL (MIC) | [73] |
|  | Double microdilution/Yersinia pseudotuberculosis ATCC911 | 7.7 µg/mL (MIC) |  | Ampicillin 18 µg/mL (MIC) | [73] |
|  | Double microdilution/Klebsiella pneumonia subsp. pneumonia ATCC13883 | 7.7 µg/mL (MIC) |  | Ampicillin 18 µg/mL (MIC) | [73] |
|  | Double microdilution/Pseudomonas aeruginosa ATCC27853 | 7.7 µg/mL (MIC) |  | Ampicillin > 128 µg/mL (MIC) | [73] |
Table 2. Cont.

| Compound Name | Biological Activity | Assay, Organism, or Cell Line | Biological Results | Positive Control | Ref. |
|---------------|---------------------|-------------------------------|--------------------|------------------|------|
| Double microdilution/ *Staphylococcus aureus* ATCC25923 | | | 3.8 µg/mL (MIC) | Ampicillin 10 µg/mL (MIC) | [73] |
| Double microdilution/ *Enterococcus faecalis* ATCC29212 | | | 7.7 µg/mL (MIC) | Ampicillin 35 µg/mL (MIC) | [73] |
| Double microdilution/ *Streptococcus mutans* RSKK07038 | | | 30.6 µg/mL (MIC) | - | [73] |
| Double microdilution/ *Lactobacillus casei* RSK9 | | | 61.2 µg/mL (MIC) | - | [73] |
| Double microdilution/ *Bacillus cereus* 702 Roma | | | 7.7 µg/mL (MIC) | Ampicillin 15 µg/mL (MIC) | [73] |
| Double microdilution/ *Mycobacterium smegmatis* ATCC607 | | | 30.6 µg/mL (MIC) | Streptomycin 4 µg/mL (MIC) | [73] |
| Double microdilution/ *C. albicans* ATCC60193 | | | 30.6 µg/mL (MIC) | Fluconazole < 8 µg/mL (MIC) | [73] |
| Double microdilution/ *C. tropicalis* ATCC13803 | | | 30.6 µg/mL (MIC) | Fluconazole < 8 µg/mL (MIC) | [73] |
| Double microdilution/ *Saccharomyces cerevisiae* RSKK251 | | | 30.6 µg/mL (MIC) | Fluconazole < 8 µg/mL (MIC) | [73] |
| Mixture of 3-hydroxy-1,2,6,10-tetramethylundecyl hexadecanoate (170), 3-hydroxy-1,2,6,10-tetramethylundecyl (9E)-octadecaenoate (171), and 3-hydroxy-1,2,6,10-tetramethylundecyl octadecanoate (172) | Cytotoxicity | MTT/MCF-7, MTT/PC-3, MTT/AS49 | 7.75 µM (IC₅₀), 17.75 µM (IC₅₀), 7.51 µM (IC₅₀) | Doxorubicin 0.053 µM (IC₅₀), Doxorubicin 0.09 µM (IC₅₀), Doxorubicin 17.75 µM (IC₅₀) | [73] |
| | | | 4.3 µg/mL (MIC), 4.3 µg/mL (MIC) | Ampicillin 10 µg/mL (MIC), Ampicillin 35 µg/mL (MIC) | [73] |
| | | | 4.3 µg/mL (MIC) | - | [73] |
| | | | 2.1 µg/mL (MIC) | Ampicillin 15 µg/mL (MIC) | [73] |
Figure 5. Structures of pyridinone alkaloids (53–61) isolated from *F. oxysporum*.

Compounds 65, 68, 69, and 72 showed phytotoxicity towards barley leaves using cotyledonary leaf bioassay almost equal to that of fusaric acid, suggesting their promising potential in organic farming. It was suggested that the existence of the C-10-hydroxyl group or C-10 and C-11 double bond led to a decrease in phytotoxicity. Liu et al. postulated the biosynthetic pathway of fusaric acids A-G (65–71). Isotopic 13C and 14C tracer studies revealed that C-2 to C-4 and C-7 of fusaric acid were originated from oxaloacetate, while C-5, C-6, and C-8 to C-11 were derived from three acetate units. The nitrogen atom of pyridine ring is originated mainly from glutamine. The formation of

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Figure 5. Structures of pyridinone alkaloids (53–61) isolated from *F. oxysporum*. 
Figure 6. Structures of alkaloids (62–75) isolated from *F. oxysporum*.

Compounds 65, 68, 69 and 72 showed phytotoxicity towards barley leaves using cotton cotyledonary leaf bioassay almost equal to that of fusaric acid, suggesting their promising potential in organic farming. It was suggested that the existence of the C-10-hydroxyl group or C-10 and C-11 double bond led to a decrease in phytotoxicity [69]. Liu et al., postulated the biosynthetic pathway of fusaricates A-G (65–71). Isotopic $^{13}$C and $^{14}$C tracer studies revealed that C-2 to C-4 and C-7 of fusaric acid were originated from oxaloacetate, while
C-5, C-6, and C-8 to C-11 were derived from three acetate units [189,190]. The nitrogen atom of pyridine ring is originated mainly from glutamine [191]. The formation of ester linkage between polyalcohols and fusaric acid could be catalyzed by lipases [192] (Scheme 2).

Nenkep et al., isolated a polycyclic quinazoline alkaloid, oxysporizoline (73), in addition to 1H-indol-3-butanamide (74) and butenolide (75) from marine-mudflat-derived *F. oxysporum*. Compounds 73 and 75 displayed weak antibacterial activity against MRSA (MIC 6.25 µg/mL). They also exhibited potent DPPH radical scavenging potential (IC₅₀ 10 and 12 µM, respectively) than ascorbic acid (IC₅₀ 20 µM) [70] (Figure 6).

2-Oxo-8-azatricyclo [9.3.1.1³,7] -hexadeca-1(15),3(16),4,6,11,13-hexaen-10-one (80) isolated from *F. oxysporum*, exhibited weak activity towards MCF-7, PC-3, and A549 and potent antimicrobial effect more than controls against various tested microorganisms with MIC values ranging from 0.8–12.5 µg/mL [73] (Figure 7). Fusarioxazin (81) was separated from *F. oxysporum* associated with *Vicia faba* roots. It displayed a significant cytotoxic effect toward HCT-116, MCF-7, and A549 cell lines (IC₅₀ 2.1, 1.8, and 3.2 µM, respectively), in comparison to doxorubicin (IC₅₀ 0.68, 0.54, and 0.39 µM, respectively). Additionally, it possessed antibacterial potential towards *S. aureus* (IZD 14.8 mm and MIC 5.3 mg/mL) and *B. cereus* (MIC 3.7 mg/mL and IZD 18.9 mm), in comparison to ciprofloxacin (IZDs 16.9 and 20.5 mm; MICs 3.9 and 2.3 mg/mL, respectively) [18]. Epi-trichosetin A (82), a new tetramic acid derivative, along with trichosetin (83) were separated by SiO₂ and Rp-HPLC from *F. oxysporum* FKI-4553 broth. Compound 82 was a C-5' epimer of 83. Compounds 82 (IC₅₀ 83 µM) and 83 (IC₅₀ 30 µM) inhibited UPP (undecaprenyl pyrophosphate) synthase activity of *S. aureus*. They had a broad antibacterial effect, in particular potent effect against Gram-positive bacteria, including MSSA (methicillin-sensitive *S. aureus*) and MRSA, where 82 appeared to be more potent than 83 in the paper disk method [74]. Kumar et al. purified vinblastine (86) and vincristine (87) from *F. oxysporum* isolated from *Catharanthus roseus* using preparative TLC and HPLC (Figure 8). They were characterized by UV-Vis, ESIMS, and NMR spectroscopy [76].
HPLC from *F. oxysporum* FKI-4553 broth. Compound 82 was a C-5′ epimer of 83. Compounds 82 (IC\(_{50}\) 83 µM) and 83 (IC\(_{50}\) 30 µM) inhibited UPP (undecaprenyl pyrophosphate) synthase activity of *S. aureus*. They had a broad antibacterial effect, in particular potent effect against Gram-positive bacteria, including MSSA (methicillin-sensitive *S. aureus*) and MRSA, where 82 appeared to be more potent than 83 in the paper disk method [74].

Kumar et al. purified vinblastine (86) and vincristine (87) from *F. oxysporum* isolated from *Catharanthus roseus* using preparative TLC and HPLC (Figure 8). They were characterized by UV-Vis, ESIMS, and NMR spectroscopy [76].

Figure 7. Structures of alkaloids (76–85) isolated from *F. oxysporum*.

### 4.5. Cyclic Peptides and Depsipeptides

*F. oxysporum* yielded bioactive cyclic depsipeptides such as enniatins (ENs) and beauvericin (BEA, 99) (Figures 9 and 10). ENs are characterized by an alternating sequence of three D-\(\alpha\)-hydroxyisovaleric acids and three N-methyl-L-amino acids in their structure. ENs H (96), I (97), and MK1688 (98), and BEA (99) were purified from *F. oxysporum* KFCC-11363P submerged cultures chloroform extracts using HPLC and assessed for cytotoxicity towards A549, SK-OV-3, SK-MEL-2, and HCT15 in the SRB (sulforhodamine B). Compound 97 (EC\(_{50}\) 0.49–0.53 µM) and MK1688 (EC\(_{50}\) 0.45–0.63 µM) exhibited the most potent growth inhibition towards the tested cell lines that were three- to four-fold more than that of 99 and 96. On the other side, 96 and 99 exhibited powerful activity towards SK-OV-3, A549, SK-MEL-2, and HCT15 cells (EC\(_{50}\) 1.71–2.45 µM for 96 and 1.39–1.86 µM for 99) [83]. ENs cytotoxic potential could be attributed to their ionophorous behavior, since altering the ions transport across membranes may lead to disruption of the cationic selectivity of the cell wall and induction of cell death by apoptosis accompanied by DNA fragmentation [83]. ENs A (91), A1 (92), and B1 (93) isolated from *F. oxysporum* N17B exhibited moderate effectiveness towards *C. albicans*, *C. neoformans*, and *M. intracellulare* with IC\(_{50}\) values ranging.

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![Figure 7. Structures of alkaloids (76–85) isolated from *F. oxysporum*.](image-url)
from 2.0 to 50.0 µg/mL in the MABA [63]. Moreover, Wang et al., reported that 99 isolated from F. oxysporum obtained from C. kanehiarai bark exhibited cytotoxic potential towards A549, PC-3, and PANC-1 (IC₅₀s 10.4, 49.5, and 47.2 µM, respectively), in comparison to cisplatin (IC₅₀s 19.8, 26.8, and 26.2 µM, respectively) in the MTT method. It also had strong anti-MRSA and anti-BS potential (MIC 3.125 µg/mL) in the microtiter plate assay [65].

Figure 8. Structures of alkaloids (86–90) isolated from F. oxysporum.

Vinblastine (86)

Vincristine (87)

Taxol (88)

Flavin adenine dinucleotide (89)

Flavin adenine dinucleotide-N(5)-nitrobutane (90)

Figure 8. Structures of alkaloids (86–90) isolated from F. oxysporum.
Furthermore, it prohibited migration of MDA-MB-231 and PC-3M cells (concentrations ranging from 3.0 to 4.0 µM and 2.0 to 2.5, respectively) in the WHA (wound healing assay). NIH ImageJ software and WHA suggested that 99 was able to inhibit PC-3M and MDA-MB-231 migration at sub-lethal concentrations. Moreover, it possessed potent antiangiogenic potential at sub-lethal concentrations, as indicated by complete inhibition of HUVEC network formation at 3.0 µM below IC$_{25}$ (5.0 µM) and IC$_{50}$ (7.5 µM) [64]. Cyclosporine A (100) was isolated from mycelia extract of non-pathogenic F. oxysporum S6 using reversed-phase silica gel and HPLC. It prohibited the growth and suppressed sclerotia formation of the phytopathogenic fungus Sclerotinia sclerotiorum with MIC 0.1 µg/disc that made it suitable to be utilized as a biofungicide. Moreover, a remarkable increase in the number of surviving soybean plants was noted when F. oxysporum and S. sclerotiorum were inoculated together, in comparison to plants inoculated with S. sclerotiorum alone in the greenhouse assay. Hence, F. oxysporum could be a good biocontrol agent for S. sclerotiorum in soybean because of its metabolite 100 that was responsible for the in vitro antiag.

Figure 9. Structures of cyclic depsipeptides (91–96) isolated from F. oxysporum.
It is noteworthy to mention that some *F. oxysporum* strains could repress the growth of *Pythium ultimum* in cucumber [193] and affected *S. sclerotiorum* sclerotia germination [194].

Figure 10. Structures of cyclic depsipeptides (97–99) and cyclic peptide (100) isolated from *F. oxysporum*.

Further, 99 was obtained from the EtOAc extracts of *F. oxysporum* SS46 and SS50 associated with *Smallanthus sonchifolius*. It showed cytotoxicity against MDA-MB435, HCT-8, and SF295 (IC\(_{50}\)s 3.17, 3.02, and 2.39 µg/mL, respectively), compared to doxorubicin (IC\(_{50}\) 0.2, 0.04, and 0.04 µg/mL, respectively) in the MTT assay. Additionally, it had potent in vitro leishmanicidal potential (EC\(_{50}\) 1.86 µM) towards *Leishmania braziliensis*, compared to geneticin (EC\(_{50}\) 0.007 µM) [84]. Zhan et al., revealed that 99 was cytotoxic towards NCI-H460, MIA Pa Ca-2, MCF-7, and SF-268 (IC\(_{50}\)s 1.41–2.29 µM, respectively), compared with doxorubicin (IC\(_{50}\) 0.01–0.07 µM) [64].

Furthermore, it prohibited migration of MDA-MB-231 and PC-3M cells (conc. ranging from 3.0 to 4.0 µM and 2.0 to 2.5, respectively) in the WHA (wound healing assay). NIH ImageJ software and WHA suggested that 99 was able to inhibit PC-3M and MDA-MB-231 migration at sub-lethal concentrations. Moreover, it possessed potent antiangiogenic potential at sub-lethal concentrations, as indicated by complete inhibition of HUVEC-2 network formation at 3.0 µM below IC\(_{25}\) (5.0 µM) and IC\(_{50}\) (7.5 µM) [64]. Cyclosporine A...
(100) was isolated from mycelia extract of non-pathogenic *F. oxysporum* S6 using reversed-phase silica gel and HPLC. It prohibited the growth and suppressed sclerotia formation of the phytopathogenic fungus *Sclerotinia sclerotiorum* with MIC 0.1 µg/disc that made it suitable to be utilized as a bio-fungicide. Moreover, a remarkable increase in the number of surviving soybean plants was noted when *F. oxysporum* and *S. sclerotiorum* were inoculated together, in comparison to plants inoculated with *S. sclerotiorum* alone in the greenhouse assay. Hence, *F. oxysporum* could be a good biocontrol agent for *S. sclerotiorum* in soybean because of its metabolite 100 that was responsible for the in vitro antagonistic activity [86]. It is noteworthy to mention that some *F. oxysporum* strains could repress the growth of *Pythium ultimum* in cucumber [193] and affected *S. sclerotiorum* sclerotia germination [194].

4.6. Glucosylceramides

Glucosylceramides (GCs) are neutral glycosphingolipids, having glucose in 1-O-β-glycosidic linkage with a ceramide [195]. Bernardino et al., isolated and purified the GCs, 102–104 from *F. oxysporum*. These GCs were assessed for their potential in inducing resistance in *Nicotiana tabacum cv Xanthi* plants against TMV (Tobacco mosaic virus) (Figure 11). Spraying tobacco plants with GCs before virus infection reduced the incidence of necrotic lesions caused by TMV. After GCs treatment, the infected plants with the virus exhibited a reduction in HR (hypersensitive response) lesions, indicating GCs antiviral effect. The results revealed that GCs stimulated the early accumulation of H$_2$O$_2$ and superoxide radicals, which act as a plant immunity elicitor to combat diseases influencing the plants [87].

4.7. Quinones

Chromatographic separation of *F. oxysporum* f. sp. *ciceris* ITCC-3636 EtOAc extract afforded anhydrofusarubin (105), fusarubin (107), 8-O-methylfusarubin (108), and 3-O-methyl-8-O-methylfusarubin (109) that were elucidated by LC/ESI-MS and detailed NMR spectra (Figure 12). The EtOAc extract had strong anti-nematic activity towards *Meloidogyne incognita* (LC$_{50}$ 56.2 µg/mL) than n-BuOH fraction (LC$_{50}$ 97.4 µg/mL), while they were moderately active versus *Rotylenchulus reniformis* (LC$_{50}$ 134.5–189.2 µg/mL). All metabolites exhibited high anti-nematic potential towards both nematodes (LC$_{50}$ ranged from 248.9 to 652.3 µg/mL). Among them, 107 showed the highest potential on both nematodes (LC$_{50}$ 248.9 µg/mL for *M. incognita* and LC$_{50}$ 301.6 µg/mL for *R. reniformis*), followed by 105 (LC$_{50}$ 257.6 and 285.3 µg/mL, respectively), compared to carbofuran (LC$_{50}$ 54.2 and 37.6 µg/mL, respectively). Whilst the methyl-substituted derivatives had moderate activity against *M. incognita* (LC$_{50}$ ranging from 478.5 to 376.4 µg/mL) [88]. Moreover, the EtOAc extracts of *F. oxysporum* SS46 and SS50 isolated from *Smallanthus sonchifolius* yielded 105 that showed cytotoxicity against MDA-MB435, HCT-8, and SF295 (IC$_{50}$ 6.23, 9.85, and 6.32 µg/mL, respectively), compared to doxorubicin (IC$_{50}$ 0.2, 0.04, and 0.04 µg/mL, respectively) in the MTT assay [84]. Further, naphthoquinone derivatives, 106–108 and 111–115 were isolated from *F. oxysporum* obtained from citrus trees diseased roots. Compound 111 had strong activity towards *S. aureus* (MIC 4 µg/mL) and weak activity against *Streptococcus pyogenes* (MIC > 128 µg/mL), while 112 was moderately active against the two strains (MICs 32.0 and 64.0 µg/mL, respectively). On the other hand, 106, 108, 113, and 114 showed weak activity towards *S. pyogenes* in the microdilution assay [90].
Figure 11. Structures of glucosylceramides (101–104) isolated from *F. oxysporum*. 

Fusarubin (105)

(2S,2'R,3R,3'E,4E,8E)-1-O-D-Glucopyranosyl-2-N-(2'-hydroxy-3'-octadecenoyl) -3-hydroxy-9-ethyl-4,8-sphingadienine (102)

N-2'-Hydroxyoctadeanoic-1-b-D-glucopyranosyl-9-methyl-4-hydroxy-4,8-sphingadienine (103)

N-2'-Hydroxyeicosanoyl-1-b-D-glucopyranosyl-9-methyl-4,8-sphingadienine (104)

Figure 11. Structures of glucosylceramides (101–104) isolated from *F. oxysporum*. 
Figure 12. Structures of naphthoquinone (105–115) and anthraquinone (116) derivatives isolated from *F. oxysporum*. 
4.8. Xanthone Derivatives

Bikaverin (119), intensively colored pigment was reported firstly from *F. vasinfectum* and *F. lycopersici* [85,96]. It belongs to the NRPKs (non-reducing polyketides) group that is produced by type I PKS [196,197]. By genetic engineering together with HPLC-HRMS and NMR tools, Arndt et al., identified the biosynthetic way for 119 and characterized its intermediates [198] (Scheme 3). Compounds 119 and 125 were isolated from *F. oxysporum* CECIS associated with *Cylindropuntia echinocarpus* (Figure 13). They were assessed for their cytotoxic activity towards a panel of four sentinel cancer cell lines by the MTT assay. Only 119 was cytotoxic towards NCI-H460, MIA Pa Ca-2, MCF-7, and SF-268 (IC\(_{50}\) 0.26–0.43 \(\mu\)M), compared with doxorubicin (IC\(_{50}\) 0.01–0.07 \(\mu\)M). It is noteworthy that 125 that lacks the C-6-OH group did not have cytotoxic activity even at concentrations of 4.0 and 2.0 \(\mu\)g/mL [64]. Further, 119 isolated from *F. oxysporum* f. sp. *lycopersici* as a purple-colored compound, exhibited a protective effect on oxidative stress and attenuated \(\text{H}_2\text{O}_2\)-induced neurotoxicity on human neuroblastoma SH-SY5Y cells. Pretreatment of neurons with 119 attenuated the \(\text{H}_2\text{O}_2\) (100 \(\mu\)M)-induced oxidative stress through improving the cell viability, antioxidant status, mitochondrial membrane integrity, and regulation of gene expression [95]. Therefore, it could be utilized as an alternative to some of the toxic synthetic antioxidants and a preventive agent against neurodegeneration [95]. Carmen et al., reported that bikaverin-contaminated products had no negative effect on human health [199]. Kundu et al., also purified 119 from *F. oxysporum* f. sp. *ciceris* ITCC-3636 EtOAc extract that had a weak anti-nemic potential towards *M. incognita* (LC\(_{50}\) 392.9 \(\mu\)g/mL) [88]. Additionally, Son et al., reported that 119 isolated from *F. oxysporum* EF119 showed antimicrobial activities against various phyto-pathogenic oomycetes and fungi. It suppressed the development of tomato late blight by 71% at conc. 300 \(\mu\)g/mL. Therefore, it may be used as a bio-control agent towards *P. infestans*-caused tomato late blight [66].

![Putative biosynthetic pathway of 119 and its intermediates. The bold arrows represent the preferred pathway and dashed lines represented other possible reaction steps](image-url)

**Scheme 3.** Putative biosynthetic pathway of 119 and its intermediates. The bold arrows represent the preferred pathway and dashed lines represented other possible reaction steps [196–198].
4.9. Terpenoids

Wortmannin (129) a steroidal furan, exhibited potent and selective antifungal activity toward C. albicans (IC$_{50}$ 0.25 µg/mL and MIC 0.78 µg/mL), compared with amphotericin B (IC$_{50}$ 0.35 and MIC 1.25 µg/mL) [63]. Another study revealed that 129 was a hemorrhagic factor reported from F. oxysporum (N17B) that caused different organs hemorrhage and finally death in rats and mice [98,200]. It also showed a powerful inhibitory potential of phosphatidylinositol 3-kinase [201] and had antifungal potential towards Botrytis allii [202]. Ergosta-5,8(14),22-trien-7-one,3-hydroxy-(3β,22E) (130) was characterized from F. oxysporum, which had HCV (hepatitis C virus) NS3 protease inhibitory activity (Ki
99.7 µM/L), compared to VX950 (Ki 3.5 µM/L) in the FRET (fluorescence resonance energy transfer) [99] (Figure 14).

Figure 14. Structures of sterols (126–132) isolated from F. oxysporum.

Isoverrucarol (133), a trichotheccene was isolated from F. oxysporum CJS-12, harboring corn produced toxic effects (dose 10 and 20 mg/kg/b.wt., orally) in rats, including body weakness, loss of appetite, stomach severe mucus, and death. It also caused a definite dermatitis reaction of the epidermis and an edematous-necrotic response of the dermis [100]. FCRR (134) a new phytotoxin, having a labdane framework was purified from F. oxysporum f. sp. radicis-lycopersici (causal agent of Fusarium rot and crown rot of tomato). It (conc. 0.25 µg/mL) induced leaf necrosis for Momotaro (a cultivar of tomato, Lycopersicon esculentum Mill.) [101]. Chen et al., separated and characterized two novel compounds, fusariumins C (135) and D (136) from F. oxysporum ZZP-R1 derived from Rumex madaio. They were assigned as a meroterpene with cyclohexanone unit and a sesquiterpene ester with a conjugated triene and an unusual oxetene ring, respectively based on NMR.
tools and optical rotation analysis. They had a potent inhibitory effect on *S. aureus* (MICs 6.25 and 25 µM, respectively), however, they were weakly active towards *E. coli* and *C. albicans* in the micro-broth dilution method [102].

The sesquiterpenoid, 137 isolated from *F. oxysporum* LBKURCC41 obtained from *Dahlia variabilis* tubers showed antibacterial activity towards *S. aureus* and *E. coli* (IZD 2.1 mm) in the agar disc diffusion assay [103]. Cosmosporasides F–H (138–140), new sugar alcohol conjugated acyclic sesquiterpenes isolated from *F. oxysporum* SC0002, showed weak cytotoxic effect towards A549, HepG2, and HeLa (inhibition rates 13–24%) (Figure 15). They exhibited weak antibacterial potential towards *S. aureus*, *B. cereus*, *E. coli*, *S. typhimurium*, and *S. dysenteriae* (growth inhibition rate of 8–21%, conc. 100 µg/mL) in the Alamar blue assay. They also displayed weak inhibition of LPS-induced NO production in RAW 264.7 macrophages (9–16%, conc. 50 µM) [27].

![Figure 15. Structures of terpenoids (133–141) isolated from *F. oxysporum*.](image-url)
4.10. Phenolic and Aromatic Compounds

Podophyllotoxin (151), an aryltetralin lignan was reported from *F. oxysporum* isolated from *Juniperus recurva* and quantified by HPLC, LC-MS, and LC-MS/MS [106] (Figure 16). Kılıç et al. reported the isolation of 153 from *F. oxysporum YP9B* that displayed potent cytotoxic potential towards MCF-7, PC-3, and A549 (IC₅₀ 15.01, 19.13, and 17.06 µM, respectively), compared to doxorubicin (IC₅₀ 0.053, 0.09, 17.75 µM, respectively). It showed antiviral potential towards the HSV type-1 virus that lysed VERO cells. It produced a partial increase in VERO cell viability (conc. 0.312 µM). Moreover, it had a powerful antibacterial potential (MICs 0.47–1.8 µg/mL) towards *B. cereus*, *S. mutans*, *S. aureus*, *E. faecalis*, and *M. smegmatis* [73].

![Figure 16. Structures of terpenoids (142–145), flavonoids (146 and 147), depsidones (148–150), lignan (151), and phenolic compound (152).](image-url)
4.11. Pyran and Furan Derivatives

Chlamydosporol (158) a pyran lactone derivative was isolated from marine-mudflat-derived *F. oxysporum* and assessed for its antibacterial potential towards MRSA and MDRSA. It displayed weak antibacterial activity against MRSA and MDRSA (MIC 31.5 µg/mL) [70]. The co-culture of *F. oxysporum* R1 and *A. fumigatus* D afforded neovasinin (160) and neovasifuranone B (163) that had a weak antimicrobial activity towards *E. coli, S. aureus*, and *C. albicans* (MICs ≥ 25 µM) [72] (Figure 17).

![Structural formula of Chlamydosporol (158)](image1)

![Structural formula of Neovasinin (160)](image2)

![Structural formula of Neovasifuranone B (163)](image3)

Figure 17. Structures of aromatic compounds (153–157), pyran (158–160) and furan (161–164) derivatives, and aliphatic acids (165–172) isolated from *F. oxysporum.*
4.12. Aliphatic Acids

Mixtures of acid esters: 165–167, 168, and 169, and 170–172 were identified from F. oxysporum YP9B by NMR, UV, FT-IR, and GC-FID- and LC-QTOF-MS [73]. Only 170–172 mixture showed potent cytotoxic activity on MCF-7, PC-3, and A549 (IC\textsubscript{50} 7.75, 17.75, and 7.51 µM, respectively), compared to doxorubicin (IC\textsubscript{50} 0.053, 0.09, and 17.75 µM, respectively), where it was about two folds more active than doxorubicin on A549. Only the mixture of 168 and 169 caused a partial cell viability increase (conc. 1.25 µM) in the antiviral assay towards HSV-I. Moreover, they exhibited strong to weak antimicrobial potential towards various tested microorganisms. On the other hand, the mixture of 170–172 showed potent activity only against S. aureus ATCC25923, E. faecalis ATCC29212, S. mutans RSKK07038, and B. cereus 702 Roma (MIC ranging from 2.1 to 4.3 µg/mL) [73].

Yu et al., purified compounds 173–175 from F. oxysporum R1 and A. fumigatus D co-culture, which displayed weak antimicrobial activity (MICs ≥ 25 µM) towards E. coli, S. aureus, and C. albicans [72] (Figure 18).

Figure 18. Structures of fatty acids (173–175) and sugar derivatives (176–180) isolated from F. oxysporum.
4.13. Volatile Organic Compounds

GCMS analysis of the VOCs (volatile organic compounds) of *F. oxysporum* isolate 21 obtained from coffee plant rhizosphere, *Meloidogyne exigua* eggs and egg masses revealed the existence of 38 VOCs, five of them were above 1% (diocetyl disulfide, 1-(2-hydroxyethoxy) tridecane or 2-propyldecan-1-ol, 4-methyl-2,6-di-tert-butylphenol, caryophyllene, and acordiene). VOCs from *F. oxysporum* displayed nematicidal potential towards *M. incognita*, thus it could be useful for the development of bio-control agent for *Meloidogyne* spp. in coffee fields [203].

Do Nascimento et al., reported that GCMS of n-hexane extract of *F. oxysporum* SS50 isolated from *Smallanthus sonchifolius* revealed twelve compounds; pentadecane, (2E,4E)-decadienal, hexadecane, octadecane, heptadecane, bis(2-methylpropyl) ester, 1,2-benzenedicarboxylic acid, methyl hexadecanoate or methyl palmitate, (9Z,12Z)-octadecadienoic acid methyl ester, clionasterol, dehydroergosterol, (9Z)-octadecenoic acid methyl ester, and stig mast-4-en-3-one, where fatty acid methyl esters and alkanes were predominated (4.70% (9Z)-octadecenoic acid methyl ester, 9.73% methyl hexadecanoate, and 54.45% (9Z,12Z)-octadecadienoic acid methyl ester). The n-hexane extract possessed cytotoxic activity towards HCT-8, MDA-MB435, and SF295 (% growth inhibition ranging from 83.78 to 97.72%, conc. 50 μg/mL) in the MTT assay. This could be attributed to the mixture of three methyl esters [84].

5. Conclusions and Future Research Directions

Currently, more focus has been directed to fungi as they are a wealthy platform for the biosynthesis of a huge number of structural diverse metabolites. *F. oxysporum* is a species with great physiological and morphological variations and its wide-ranging existence in ecological activities worldwide indicates its profoundly diversified and significant role in nature. It can produce various bio-metabolites that may directly and indirectly be utilized as therapeutic agents for various health problems. In this work, 180 metabolites were reported from *F. oxysporum* in the period from 1967 to 2021. Alkaloids, quinones, and jasmonates, and anthranilate derivatives represented the major metabolites that were isolated from this fungus (Figure 19).

![Chemical class](image)

**Figure 19.** Different classes of metabolites reported from *F. oxysporum.*
Although, this big number of reported metabolites, few of them are evaluated for their bioactivities. The assessed activities of these metabolites were antimicrobial, cytotoxicity, nematicidal, antiviral, leishmanicidal, antiviral, and antioxidant. Additionally, there is a lack of pharmacological studies that focus on exploring the possible mechanisms of the active metabolites. In addition, the untested metabolites should be further explored for their possible bioactivities. Co-cultivation experiments should be employed to elicit the production of these metabolites. The discovery of the underlying biosynthetic pathways of these bio-metabolites is needed, which would allow the rational engineering or refactoring of these pathways for industrial purposes. Further, research for identifying the responsible biosynthetic genes for these metabolites may open the opportunity to explore the genetic potential of *F. oxysporum* for discovering novel metabolites by metabolic engineering that could result in more affordable and novel pharmaceutics and food additives. Moreover, studies on the structure-activity relationships and/or derivatization of these fungus metabolites should be carried out.

Although, the reported data revealed that *F. oxysporum* is widely employed for the synthesis of different types of metal nanoparticles that could have various biotechnological, agronomical, pharmaceutical, industrial, and medicinal applications. Many of these biosynthesized NPs possessed favorable antimicrobial potential, especially towards MDR microbes that can be potential alternatives to antibiotics. Further, it was found that the combination of NPs synthesized using *F. oxysporum* with antibiotics produced additive and synergic effects that could represent a new strategy for treating some antibiotics resistant strains and lower the doses of the used antibiotics. *F. oxysporum* might have vast commercial implications in low-cost, room-temperature, ecofriendly syntheses of technologically significant oxide nanomaterials from naturally available potentially cheap raw materials. However, the NPs synthesized from *F. oxysporum* are limited to metals and fewer metal oxides and sulfides. Therefore, future research should focus on developing protocols for implementing the biosynthesis of NPs of other metals, metal oxides, nitrides, and carbides. Research on the toxic effect of these NPs, as well as their effects on animals and human health and accumulation in the environment, is needed.

Additionally, in-vivo studies and clinical trials are needed to elaborate the exact mechanism responsible for their observed bioactivities. There is also a need for evaluating these NPs for their effectiveness towards various diseases, which can open in the future a new avenue in the biomedical field. More research is required for optimizing various reaction conditions to achieve better control over the shape, size, stability, and monodispersity of these NPs. *F. oxysporum* is considered as an efficient enzyme producer. Its enzymes have attracted great interest because of their possible applications in diverse biotechnological and industrial fields such as pharmaceutical, cosmetic, and food industries, organic synthesis, bioremediation, and detoxification of environmental pollutants, delignification, denitrification, or biofuel production. Additionally, they are involved in eco-friendly bioconversion processes of various substrates to highly valuable products that could be preferred more over the chemical synthesis. Research that focuses on engineering enzymes in such a way for maximum stability and activity under appropriate conditions is desirable. Recombinant DNA technology and engineering of proteins are required to improve the industrial production of these enzymes. Additionally, some *F. oxysporum* strains can be utilized as bio-control agents because of their ability to prohibit the growth of several fungal plant pathogens.

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Abbreviations

A549 Human non-small-cell lung cancer cell line
AgNPs Silver nanoparticles; AGS: Gastric adenocarcinoma
APase β-L-Arabino-pyranosidase
BGL β-Glucosidases
Bi2S3 Bismuth sulphide
C26 Murine colon carcinoma
CBP Consolidated bioprocessing
CdSe Cadmium/selenium
CLEAs Cross-linked enzyme aggregates
CLSM Confocal laser scanning microscopic
DHAP Dihydroxyacetone-3-phosphate
DHBA 2,3-Dihydroxybenzoic acid
DPPH 2,2-Diphenyl-1-picrylhydrazyl
EC50 Concentration required inhibiting cell growth in vitro by 50%
ESBL Extended-spectrum beta-lactamase
FAOD Fructosyl amino acid oxidase
FLC Fluconazole
FLO Fructosyl lysine oxidase
FRET Fluorescence resonance energy transfer
FUC α-L-Fucosidase
GAP Glyceraldehyde-3-phosphate
GH-11 Glycosyl hydrolase family 11
GNPs Gold nanoparticles
GPase α-D-Galactopyranosidase
HaCaT Human immortalized keratinocyte cells
HCT116 Human colorectal adenocarcinoma
HCT15 Human colorectal cancer cell line
HCT8 Human colon tumor cell lines
HeLa Human cervix carcinoma cell line
HepG2 Human liver cancer cell line
HUVEC-2 Human umbilical vascular endothelial cells
IC50 Concentration causing 50% growth inhibition
IL Ionic liquid
IZD Inhibition zone diameter
L5178Y Mouse lymphoma cell line
LC Lethal concentration
LDH Lactate dehydrogenase release assay
LMS Laccase mediator system
LOX Lipooxygenase
MABA Microplate Alamar blue assay
MB Methylene blue
MCF-7 Breast cancer cell line
MDA-MB-231 Metastatic breast cancer cell line
MDA-MB435 Human melanoma tumor cell lines
MDR Multidrug-resistant
MIA Pa Ca-2 Pancreati cancer cell line
MIC Minimum inhibitory concentration
MRSA Methicillin-resistant Staphylococcus aureus
MRSa Methicillin-resistant S. aureus
MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide)
N2O Dinitrogenoxide
NCI-H460 Non-small-cell lung
References

1. Ibrahim, S.R.M.; Mohamed, S.G.A.; Sindi, I.A.; Mohamed, G.A. Biologically active secondary metabolites and biotechnological applications of species of the family Chaetomiaceae (Sordariales): An updated review from 2016 to 2021. Mycol. Prog. 2021, 20, 595–639. [CrossRef]

2. Noor, A.O.; Almasri, D.M.; Bagalagel, A.A.; Abdallah, H.M.; Mohamed, S.G.A.; Mohamed, G.A.; Ibrahim, S.R.M. Naturally occurring isocoumarins derivatives from endophytic fungi: Sources, isolation, structural characterization, biosynthesis, and biological activities. Molecules 2020, 25, 395. [CrossRef]

3. Ibrahim, S.R.M.; Altyar, A.E.; Mohamed, S.G.A.; Mohamed, G.A. Genus Thielavia: Phytochemicals, industrial importance and biological relevance. Nat. Prod. Res. 2021, 1–16. [CrossRef]

4. Bräse, S.; Encinas, A.; Keck, J.; Nising, C.F. Chemistry and biology of mycotoxins and related fungal metabolites. Chem. Rev. 2009, 109, 3903–3990. [CrossRef] [PubMed]

5. Ibrahim, S.R.M.; Mohamed, S.G.A.; Altyar, A.E.; Mohamed, G.A. Natural products of the fungal genus Humicola: Diversity, biological activity, and industrial importance. Curr. Microbiol. 2021, 78, 2488–2509. [CrossRef]

6. El-Agamy, D.S.; Ibrahim, S.R.M.; Ahmed, N.; Khoshhal, S.; Abo-Haded, H.M.; Elkablawy, M.A.; Aljuhani, N.; Mohamed, G.A. Aspernolide F, as a new cardioprotective butyrolactone against doxorubicin-induced cardiotoxicity. Int. Immunopharmacol. 2019, 72, 429–436. [CrossRef]

7. Ibrahim, S.R.M.; Mohamed, G.A.; Al Haidari, R.A.; El-Kholy, A.A.; Zayed, M.F.; Khayat, M.T. Biologically active fungal depsidones: Chemistry, biosynthesis, structural characterization, and bioactivities. Fitoterapia 2018, 129, 317–365. [CrossRef]

8. Ibrahim, S.R.M.; Mohamed, G.A.; Al Haidari, R.A.; El-Kholy, A.A.; Zayed, M.F. Potential anti-malarial agents from endophytic fungi: A review. Mini. Rev. Med. Chem. 2018, 18, 1110–1132. [CrossRef]

9. Ibrahim, S.R.M.; Mohamed, G.A.; Khedr, A.I.M. γ-Butyrolactones from Aspergillus species: Structures, biosynthesis, and biological activities. Nat. Prod. Commun. 2017, 12, 791–800. [CrossRef]

10. Elkhayat, E.S.; Ibrahim, S.R.; Mohamed, G.A.; Ross, S.A. Terrenolide S, a new antileishmanial butenolide from the endophytic fungus Aspergillus terreus. Nat. Prod. Res. 2016, 30, 814–820. [CrossRef]

11. Ibrahim, S.R.M.; Abdallah, H.M.; Elkhayat, E.S.; Al Musayeib, N.M.; Asfour, H.Z.; Zayed, M.F.; Mohamed, G.A. Fusaripeptide A: New antifungal and anti-malarial cyclodepsipeptide from the endophytic fungus Fusarium sp. J. Asian Nat. Prod. Res. 2018, 20, 75–85. [CrossRef] [PubMed]

12. Ma, L.J.; Geiser, D.M.; Proctor, R.H.; Rooney, A.P.; O'Donnell, K.; Trail, F.; Gardiner, D.M.; Manners, J.M.; Kazan, K. Fusarium pathogenomics. Annu. Rev. Microbiol. 2013, 67, 399–416. [CrossRef]

13. Wang, C.J.; Thanarat, C.; Sun, P.L.; Chung, W.H. Colonization of human opportunistic Fusarium oxysporum (HOFo) isolates in tomato and cucumber tissues assessed by a specific molecular marker. PLoS ONE 2020, 15, e0234517. [CrossRef]

14. Hernandez-Ochoa, B.; Gómez-Manzo, S.; Alcaraz-Carmona, E.; Serrano-Posada, H.; Centeno-Leija, S.; Arreguin-Espinosa, R.; Cuevas-Cruz, M.; Gonzalez-Valdez, A.; Mendoza-Espinosa, J.A.; Acosta Ramos, M.; et al. Gene cloning, recombinant expression, characterization, and molecular modeling of the glycolytic enzyme triosephosphate isomerase from Fusarium oxysporum. Microorganisms 2020, 8, 40. [CrossRef] [PubMed]
15. El-Kazzaz, M.K.; El-Fadly, G.B.; Hassan, M.A.A.; El-Kot, G.A.N. Identification of some Fusarium spp. using molecular biology techniques. *Egypt J. Phytopathol.* 2008, 36, 57–69.

16. Rojas, E.C.; Sapkota, R.; Jensen, B.; Jørgensen, H.J.L.; Henriksen, T.; Jørgensen, L.N.; Nicolaisen, M.; Collinge, D.B. *Fusarium* head blight modifies fungal endophytic communities during infection of wheat spikes. *Microb. Ecol.* 2020, 79, 397–408. [CrossRef]

17. Al-Rabia, M.W.; Mohamed, G.A.; Ibrahim, S.R.M.; Asfour, H.Z. Anti-inflammatory ergosterol derivatives from the endophytic fungus *Fusarium chlamydosporum*. Nat. Prod. Res. 2020, 1–9. [CrossRef] [PubMed]

18. Mohamed, G.A.; Ibrahim, S.R.M.; Alhakamy, N.A.; Aljohani, O.S. Fusaroxazin, a novel cytotoxic and antimicrobial xanthone derivative from *Fusarium oxysporum*. Nat. Prod. Res. 2020, 1–9. [CrossRef]

19. Khayat, M.T.; Ibrahim, S.R.M.; Mohamed, G.A.; Abdallah, H.M. Anti-inflammatory metabolites from endophytic fungus *Fusarium* sp. *Phytochem. Lett.* 2019, 29, 104–109. [CrossRef]

20. Ibrahim, S.R.M.; Mohamed, G.A.; Al Haidari, R.A.; Zayed, M.F.; El-Kholy, A.A.; Elkhayat, E.S.; Ross, S.A. Fusarithioamide B, a new benzamide derivative from the endophytic fungus *Fusarium chlamydosporum* with potent cytotoxic and antimicrobial activities. *Bioorg. Med. Chem.* 2018, 26, 786–790. [CrossRef] [PubMed]

21. Ibrahim, S.R.M.; Mohamed, G.A.; Al Haidari, R.A.; El-Kholy, A.A.; Asfour, H.Z.; Zayed, M.F. Fusaristerol A: A new cytotoxic and antifungal ergosterol fatty acid ester from the endophytic fungus *Fusarium* sp. associated with *Mentha longifolia* roots. *Phcog. Mag.* 2018, 14, 308–311. [CrossRef]

22. Ibrahim, S.R.M.; Abdallah, H.M.; Mohamed, G.A.; Ross, S.A. Integracides H-J: New tetracyclic triterpenoids from the endophytic fungus *Fusarium* sp. *Fitoterpapia* 2016, 112, 161–167. [CrossRef]

23. Ibrahim, S.R.M.; Mohamed, G.A.; Ross, S.A. Integracides F and G: New tetracyclic triterpenoids from the endophytic fungus *Fusarium* sp. *Phytochem. Lett.* 2016, 15, 125–130. [CrossRef]

24. Ibrahim, S.R.M.; Elkhayat, E.S.; Mohamed, G.A.; Fat’hi, S.M.; Ross, S.A. Fusarithioamide A, a new antimicrobial and cytotoxic benzamide derivative from the endophytic fungus *Fusarium chlamydosporum*. *Biochem. Biophys. Res. Commun.* 2016, 479, 211–216. [CrossRef]

25. Summerell, B.A.; Laurence, M.H.; Liew, E.C.Y.; Leslie, J.F. Biogeography and phylogeography of *Fusarium*: A review. *Fungal Divers.* 2010, 44, 3–13. [CrossRef]

26. Summerell, B.A.; Leslie, J.F. Fifty years of *Fusarium*: How could nine species have ever been enough? *Fungal Divers.* 2011, 50, 135–144. [CrossRef]

27. Fu, Y.; Wu, P.; Xue, J.; Zhang, M.; Wei, X. Cosmosporasides F-H, three new sugar alcohol conjugated acyclic sesquiterpenes from a *Fusarium oxysporum* fungus. *Nat. Prod. Res.* 2020, 1–9. [CrossRef]

28. Gordon, T.R. *Fusarium oxysporum* and the *Fusarium* wilt syndrome. *Annu. Rev. Phytopathol.* 2017, 55, 23–39. [CrossRef]

29. Michielse, C.B.; Rep, M. Pathogen profile update: *Fusarium oxysporum*. *Mol. Plant Pathol.* 2009, 10, 311–324. [CrossRef]

30. Nucci, M.; Anaisie, E. *Fusarium* infections in immunocompromised patients. *Clin. Microbio. Rev.* 2007, 20, 695–704. [CrossRef]

31. Dean, R.; Van Kan, J.A.; Pretorius, Z.A.; Hammond-Kosack, K.E.; Di Pietro, A.; Spanu, P.D.; Rudd, J.J.; Dickman, M.; Kahmann, R.; Ellis, J.; et al. The Top 10 fungal pathogens in molecular plant pathology. *Mol. Plant. Pathol.* 2012, 13, 414–430. [CrossRef] [PubMed]

32. Abdelhamid, S.A.; Asker, M.S.; El Sayed, O.H.; Hussein, A.A.; Mohamed, S.S. Biodiesel production from Egyptian isolate *Fusarium oxysporum* NRC2017. Bull. Natl. Res. Cent. 2019, 43, 210. [CrossRef]

33. Nikolaiwits, E.; Makris, G.; Topakas, E. Immobilization of a cutinase from *Fusarium oxysporum* and application in pineapple flavor synthesis. *J. Agric. Food Chem.* 2017, 65, 3505–3511. [CrossRef] [PubMed]

34. Maruta, A.; Yamane, M.; Matsubara, M.; Suzuki, S.; Nakazawa, M.; Ueda, M.; Sakamoto, T. A novel α-galactosidase from *Fusarium oxysporum* and its application in determining the structure of the gum arabic side chain. *Enzyme Microb. Technol.* 2017, 103, 25–33. [CrossRef] [PubMed]

35. Bura Gohain, M.; Talukdar, S.; Talukdar, M.; Yadav, A.; Gogoi, B.K.; Bora, T.C.; Kiran, S.; Gulati, A. Effect of physicochemical parameters on nitrile-hydrolyzing potentials of newly isolated nitrilase of *Fusarium oxysporum* f. sp. *lycoperdci* ED-3. *Biotechnol. Appl. Biochem.* 2015, 62, 226–236. [CrossRef] [PubMed]

36. McQuarters, A.B.; Wirgau, N.E.; Lehner, N. Model complexes of key intermediates in fungal cytochrome P450 nitric oxide reductase (P450nor). *Curr. Opin. Chem. Biol.* 2014, 19, 82–89. [CrossRef]

37. Zhao, Z.; Ramachandran, P.; Kim, T.S.; Chen, Z.; Jeya, M.; Lee, J.K. Characterization of an acid-tolerant β-1,4-glucosidase from *Fusarium oxysporum* and its potential as an animal feed additive. *Appl. Microbiol. Biotechnol.* 2013, 97, 10003–10011. [CrossRef]

38. Sakamoto, T.; Tsujitani, Y.; Fukamachi, K.; Taniguchi, Y.; Ibara, H. Identification of two GH27 bifunctional proteins with β-L-arabinopyranosidase/α-D-galactopyranosidase activities from *Fusarium oxysporum*. *Appl. Microbiol. Biotechnol.* 2010, 86, 1115–1124. [CrossRef]

39. Sakai, Y.; Yoshida, N.; Isogai, A.; Tani, Y.; Kato, N. Purification and properties of fructosyl lysine oxidase from *Fusarium oxysporum* S-1F4. *Biosci. Biotechnol. Biochem.* 1995, 59, 487–491. [CrossRef]

40. Bisakowski, B.; Kermasha, S.; Klopfenstein, M. Partial purified lipoygenase from *Fusarium oxysporum* characterization and kinetic studies. *Process Biochem.* 1995, 30, 261–268. [CrossRef]

41. Yamamoto, K.; Tsui, Y.; Kumagai, H.; Tochikura, T. Induction and purification of α-Yamfucosidase from *Fusarium oxysporum*. *Agric. Biol. Chem.* 1986, 50, 1689–1695.
42. Yano, T.; Yamamoto, K.; Kumagai, H.; Tochikura, T.; Yokoyama, T.; Seno, T.; Yamaguchi, H. Purification and characterization of a novel α-L-fucosidase from Fusarium oxysporum grown on sludge. Agr. Biol. Chem. 1985, 49, 3179–3187. [CrossRef]

43. Calvo-Olvera, A.; De Donato-Capote, M.; Pool, H.; Rojas-Avelizapa, N.G. In vitro toxicity assessment of fungal-synthesized cadmium sulphide quantum dots using bacteria and seed germination models. J. Environ. Sci. Health. A Tox. Hazard Subst. Environ. Eng. 2021, 56, 713–722. [CrossRef] [PubMed]

44. Shati, A.A.; Elsaid, F.G. Biosynthesized silver nanoparticles and their genotoxicity. J. Biochem. Mol. Toxicol. 2020, 34, e22418. [CrossRef] [PubMed]

45. Srivastava, S.; Bhargava, A.; Pathak, N.; Srivastava, P. Production, characterization and antibacterial activity of silver nanoparticles produced by Fusarium oxysporum and monitoring of protein-ligand interaction through in-silico approaches. Microb. Pathog. 2019, 129, 136–145. [CrossRef] [PubMed]

46. Ahmed, A.A.; Hamzah, H.; Maarof, M. Analyzing formation of silver nanoparticles from the filamentous fungus Fusarium oxysporum under different processing conditions. Bioprocess Biosyst. Eng. 2017, 40, 1291–1303. [CrossRef]

47. Almeida, E.S.; de Oliveira, D.; Hotza, D. Characterization of silver nanoparticles produced by biosynthesis mediated by Fusarium oxysporum and their antimicrobial activity. Turk. J. Biol. 2018, 42, 54–62. [CrossRef] [PubMed]

48. Uddin, I.; Ahmad, A.; Siddiqui, E.A.; Rahaman, S.H.; Gambhir, S. Biosynthesis of fluorescent Bi2S3 nanoparticles and their application as dual-function SPECT-CT probe for animal imaging. Curr. Top. Med. Chem. 2016, 16, 2019–2025. [CrossRef]

49. Longhi, C.; Santos, J.P.; Morey, A.T.; Marcato, P.D.; Durán, N.; Pinge-Filho, P.; Nakazato, G.; Yamada-Ogatta, S.F.; Yamachi, L.M. Combination of fluconazole with silver nanoparticles produced by Fusarium oxysporum improves antifungal effect against planktonic cells and biofilm of drug-resistant Candida albicans. Med. Mycol. 2016, 54, 428–432. [CrossRef]

50. Marcato, P.D.; De Souza, G.I.H.; Alves, O.L.; Esposito, E.; Durán, N. Antibacterial activity of silver nanoparticles synthesized by the fungus Fusarium oxysporum strain. In Proceedings of the 2nd Mercosur Congress on Chemical Engineering, 4th Mercosur Congress on Process Systems Engineering, Rio de Janeiro, Brazil, 14–18 August 2014; pp. 1–5.

51. Ishida, K.; Cipriano, T.F.; Rocha, G.M.; Weissmsller, G.; Gomes, F.; Miranda, K.; Rozenal, S. Silver nanoparticle production by the fungus Fusarium oxysporum: Nanoparticle characterisation and analysis of antifungal activity against pathogenic yeasts. Mem. Inst. Oswaldo Cruz. 2014, 109, 220–228. [CrossRef]

52. Khan, S.A.; Uddin, I.; Moez, S.; Ahmad, A. Fungus-mediated preferential bioleaching of waste material such as fly—Ash as a means of producing extracellular, protein capped, fluorescent and water soluble silica nanoparticles. PLoS ONE 2014, 9, e107597. [CrossRef] [PubMed]

53. Syed, A.; Ahmad, A. Extracellular biosynthesis of CdTe quantum dots by the fungus Fusarium oxysporum and their anti-bacterial activity. Spectrochim. Acta A Mol. Biomol. Spectrosc. 2013, 106, 41–47. [CrossRef] [PubMed]

54. Birla, S.S.; Gaikwad, S.C.; Gade, A.K.; Rai, M.K. Rapid synthesis of silver nanoparticles from Fusarium oxysporum by optimizing physicochemical conditions. Sci. World J. 2013, 2013, 796018. [CrossRef] [PubMed]

55. Korbekandi, H.; Ashari, Z.; Iravani, S.; Abbasi, S. Optimization of Biological Synthesis of Silver Nanoparticles using Fusarium oxysporum. Iran J. Pharm. Res. 2013, 12, 289–298. [PubMed]

56. Niemann, G.J.; Liem, J.; Hoof, A.V.D.K.; Niessen, W.M.A. Phytoalexins, benzoxazinones, N-aroylanthranilates and N-aroylanilines, from Fusarium-infected carnation stems. Phytochemistry 1992, 31, 3761–3767. [CrossRef]

57. Irzykowski, L.; Bocianski, J.; Waśkiewicz, A.; Weber, Z.; Karolewski, Z.; Goliński, P.; Kostecki, M.; Irzykowski, W. Genetic variation of Fusarium oxysporum isolates forming fumonisin B1 and moniliformin. J. Appl. Genet. 2012, 53, 237–247. [CrossRef]

58. Seo, J.A.; Kim, J.C.; Lee, Y.W. Isolation and characterization of two new type C fumonisins produced by Fusarium oxysporum. J. Nat. Prod. 1996, 59, 1003–1005. [CrossRef]

59. Sewram, V.; Mshicileli, N.; Shephard, G.S.; Vismser, H.F.; Rheedee, J.P.; Lee, Y.W.; Leslie, J.F.; Marasas, W.F. Production of fumonisin B and C analogues by several fusarium species. J. Agric. Food Chem. 2005, 53, 4861–4866. [CrossRef] [PubMed]

60. Seo, J.A.; Kim, J.C.; Lee, Y.W. N-Acetyl derivatives of type C fumonisins produced by Fusarium oxysporum. J. Nat. Prod. 1999, 62, 355–357. [CrossRef]

61. Miersch, O.; Bohlmann, H.; Wasternack, C. Jasmonates and related compounds from Fusarium oxysporum. Phytochemistry 1999, 50, 517–523. [CrossRef]

62. Breinhold, J.; Ludvigsen, S.; Rassing, B.R.; Rosendahl, C.N.; Nielsen, S.E.; Olsen, C.E. Oxysporidionone: A novel, antifungal N-methyl-4-hydroxy-2-pyridinone from Fusarium oxysporum. J. Nat. Prod. 1997, 60, 33–35. [CrossRef] [PubMed]

63. Jayasinghe, L.; Abbas, H.K.; Jacob, M.R.; Herath, W.H.; Nanayakkara, N.P. N-Methyl-4-hydroxy-2-pyridinone analogues from Fusarium oxysporum. J. Nat. Prod. 2006, 69, 439–442. [CrossRef]

64. Zhan, J.; Burns, A.M.; Liu, M.X.; Faeth, S.H.; Gunatilaka, A.A. 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] [PubMed]

65. 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 fungus Fusarium oxysporum. Fitoterapia 2011, 82, 777–781. [CrossRef]

66. Son, S.W.; Kim, H.Y.; Choi, G.J.; Lim, H.K.; Jung, K.S.; Lee, S.O.; Lee, S.; Sung, N.D.; Kim, J.C. Bikaverin and fusaric acid from Fusarium oxysporum show antioomycete activity against Phytophthora infestans. J. Appl. Microbiol. 2008, 104, 692–698. [CrossRef]

67. Reveglia, P.; Cinelli, T.; Cimmino, A.; Masi, M.; Evidente, A. The main phytotoxic metabolite produced by a strain of Fusarium oxysporum inducing grapevine plant declining in Italy. Nat. Prod. Res. 2018, 32, 2398–2407. [CrossRef]
95. Nirmaladevi, D.; Venkataramana, M.; Chandranayaka, S.; Ramesha, A.; Jameel, N.M.; Srinivas, C. Neuroprotective effects of bikerin on H2O2-induced oxidative stress mediated neuronal damage in SH-SY5Y cell line. Cell Mol. Neurobiol. 2014, 34, 973–985. [CrossRef] [PubMed]

96. Lebeau, J.; Petit, T.; Clerc, P.; Dufossé, L.; Caro, Y. Isolation of two novel purple naphthoquinone pigments concomitant with the bioactive red bikerin and derivatives thereof produced by Fusarium oxysporum. Biotechnol. Prog. 2019, 35, e2738. [CrossRef] [PubMed]

97. Starratt, A.N.; Madhosingh, C. Sterol and fatty acid components of mycelium of Fusarium oxysporum. Can. J. Microbiol. 1967, 13, 1351–1355. [CrossRef]

98. Abbas, H.K.; Mirocha, C.J. Isolation and purification of a hemorrhagic factor (wortmannin) from Fusarium oxysporum (N17B). Appl. Environ. Microbiol. 1988, 54, 1264–1274. [CrossRef] [PubMed]

99. Hirota, A.; Ando, Y.; Monma, S.; Hirota, H. FCRR-toxin, a novel phytotoxin from Fusarium oxysporum f. sp. radicis-lycopersici. Biosci. Biotech. Biochem. 1994, 58, 1931–1932. [CrossRef]

100. Kim, K.H.; Lee, Y.W.; Mirocha, C.J.; Pawlosky, R.J. Isoverrucarol production by Fusarium oxysporum CJS-12 isolated from corn. Appl. Environ. Microbiol. 1990, 56, 260–263. [CrossRef]

101. Yang, L.Y.; Lin, J.; Zhou, B.; Liu, Y.G.; Zhu, B.Q. H1-A, a compound isolated from Fusarium oxysporum in inhibits hepatitis C virus (HCV) NS3 serine protease. Chin. J. Nat. Med. 2016, 14, 299–302. [CrossRef]

102. Chen, J.; Bai, X.; Hua, Y.; Zhang, H.; Wang, H. Fusarins C and D, two novel antimicrobial agents from Fusarium oxysporum ZZP-R1 symbiotic on Rumex madaio Makino. Fitoterapia 2019, 134, 1–4. [CrossRef]

103. Piska, F.; Teruna, H.Y. Terpenoid as antibacterial produced by endophyte Fusarium oxysporum LBKURCC41 from Dahlia variabilis tuber. J. Phys. Conf. Ser. 2020, 1655, 012034. [CrossRef]

104. Cui, Y.; Yi, D.; Bai, X.; Sun, B.; Zhao, Y.; Zhang, Y. Ginkgolide B produced endophytic fungus (Ginkgo biloba. Fitoterapia 2012, 83, 913–920. [CrossRef]

105. Mirocha, C.J.; Abbas, H.K.; Kommedahl, T.; Jarvis, B.B. Mycotoxin production by Fusarium oxysporum and Fusarium sporotrichioides isolated from Bacillus spp. from Brazil. Appl. Environ. Microbiol. 1989, 55, 254–255. [CrossRef]

106. Kour, A.; Shawl, A.S.; Rehan, S.; Sultan, P.; Qazi, P.H.; Suden, P.; Khajuria, R.K.; Verma, V. Isolation and identification of an endophytic strain of Fusarium oxysporum producing podophyllotoxin from Juniperus recurva. World J. Microbiol. Biotechnol. 2008, 24, 1115–1121. [CrossRef]

107. Kachlicki, P.; Mdryczka, M. Phenylacetic acid and methyl p-hydroxyphenyl acetate-novel phytotoxins of Fusarium oxysporum. In Proceedings of the Fifth European Fusarium Seminar, Szeged, Hungary, 1–5 September 1997; pp. 853–855.

108. Beck, J.J.; Merrill, G.B.; Palumbo, J.D.; O’Keeffe, T.L. Strain of Fusarium oxysporum isolated from almond hulls produces styrene and 7-methyl-1,3,5-cyclooctatriene as the principal volatile components. J. Agric. Food Chem. 2008, 56, 11392–11398. [CrossRef]

109. Fuchs, A.; De Vries, F.W.; Landheer, C.A.; Van Veldhuizen, A. 3-Hydroxymaackiainosilflavon, a pisatin metabolite produced by Fusarium oxysporum f. sp. pisi. Phytochemistry 1990, 29, 917–919. [CrossRef]

110. Adesogan, K.E.; Alo, B.O. Oxysporone, a new metabolite from Fusarium oxysporum. Phytochemistry 1979, 18, 1886–1887. [CrossRef]

111. Nita-Lazar, M.; Heyraud, A.; Gey, C.; Braccini, I.; Lienart, Y. Novel oligosaccharides isolated from Fusarium oxysporum L. rapidly induce PAL activity in Rubus cells. Acta. Biochim. Pol. 2004, 51, 625–647. [CrossRef]

112. Mohanpuria, P.; Rana, N.K.; Yadav, S.K. Biosynthesis of nanoparticles: Technological concepts and future applications. J. Nanopart. Res. 2008, 10, 507–517. [CrossRef]

113. Zhang, X.; Yan, S.; Tyagi, R.D.; Surampalli, R.Y. Synthesis of nanoparticles by microorganisms and their application in enhancing microbiological reaction rates. Chemosphere 2011, 82, 489–494. [CrossRef] [PubMed]

114. Rai, M.K.; Deshmukh, S.D.; Gade, A.K.; Kamel, A.E. Strategic nanoparticle-mediated gene transfer in plants and animals—A novel approach. Curr. Nanosci. 2012, 8, 170–179. [CrossRef]

115. Rai, M.; Ingle, A. Role of nanotechnology in agriculture with special reference to management of insect pests. Appl. Microbiol. Biotechnol. 2012, 94, 287–293. [CrossRef] [PubMed]

116. Ghosh, P.; Han, G.; De, M.; Kim, C.K.; Rotello, V.M. Gold nanoparticles in delivery applications. Adv. Drug Deliv. Rev. 2008, 60, 1307–1315. [CrossRef]

117. Gholami-Shabani, M.; Akbarzadeh, A.; Norouzian, D.; Amini, A.; Gholami-Shabani, Z.; Imani, A.; Chian, M.; Riaz, G.; Shams-Ghahfarokhi, M.; Razzaghi-Abyaneh, M. Antimicrobial activity and physical characterization of silver nanoparticles green synthesized using nitrate reductase from Fusarium oxysporum. Appl. Biochem. Biotechnol. 2014, 172, 4084–4098. [CrossRef]

118. Ballottin, D.; Fulaz, S.; Cabrini, F.; Tsukamoto, J.; Durán, N.; Alves, O.L.; Tasic, L. Antimicrobial textiles: Biogenic silver nanoparticles against Candida and Xanthomonas. Mater. Sci. Eng. C. Mater. Biol. Appl. 2017, 75, 582–589. [CrossRef]

119. Nami, S.; Ghaseminezhad, M.; Shokrollahzadeh, S.; Shojaosadati, S.A. Controlled biosynthesis of silver nanoparticles using nitrate reductase enzyme induction of filamentous fungus and their antibacterial evaluation. Artif. Cells Nanomed. Biotechnol. 2017, 45, 1588–1596. [CrossRef]

120. Figueiredo, E.P.; Ribeiro, J.M.; Nishio, E.K.; Scandoriero, S.; Costa, A.F.; Cardozo, V.F.; Oliveira, A.G.; Durán, N.; Panagio, L.A.; Kobayashi, R.; et al. New approach for simvastatin as an antibacterial: Synergistic effect with bio-synthesized silver nanoparticles against multidrug-resistant bacteria. Int. J. Nanomed. 2019, 14, 7975–7985. [CrossRef] [PubMed]
146. Gómez, S.; Payne, A.M.; Savko, M.; Fox, G.C.; Shepard, W.E.; Fernandez, F.J.; Vega, M.C. Structural and functional characterization of a highly stable endo-β-1,4-xylanase from Fusarium oxysporum and its development as an efficient immobilized biocatalyst. Biotechnol. Biofuels. 2016, 9, 191. [CrossRef]

147. Najjarzadeh, N.; Matsakas, L.; Rova, U.; Christakopoulos, P. Effect of oligosaccharide degree of polymerization on the induction of xylan-degrading enzymes by Fusarium oxysporum f. sp. Lycopersici. Molecules 2020, 25, 5849. [CrossRef] [PubMed]

148. Legras, J.L.; Chuelz, G.; Arnaud, A.; Galzy, P. Natural nitriles and their metabolism. World J. Microbiol. Biotechnol. 1990, 6, 83–108. [CrossRef]

149. Chen, J.; Zheng, R.C.; Zheng, Y.G.; Shen, Y.C. Microbial transformation of nitriles to high-value acids or amides. Adv. Biochem. Eng. Biotechnol. 2009, 113, 33–77.

150. Shiro, Y.; Fujii, M.; Iizuka, T.; Adachi, S.; Tsukamoto, K.; Nakahara, K.; Shoun, H. Spectroscopic and kinetic studies on reaction of cytochrome P450nor with nitric oxide. Implication for its nitric oxide reduction mechanism. J. Biol. Chem. 1995, 270, 1617–1623. [CrossRef]

151. Wang, C.; Amon, B.; Schulz, K.; Mehdi, B. Factors that influence nitrous oxide emissions from agricultural soils as well as their representation in simulation models: A Review. Agronomy 2021, 11, 770. [CrossRef]

152. Shoun, H.; Fushinobu, S.; Jiang, L.; Kim, S.W.; Wakagi, T. Fungal denitrification and nitric oxide reductase cytochrome P450nor. Philos. Trans. R. Soc. Lond B Biol. Sci. 2012, 367, 1186–1194. [CrossRef]

153. Shoun, H.; Tanimoto, T. Denitrification by the fungus Fusarium oxysporum and involvement of cytochrome P-450 in the respiratory nitrite reduction. J. Biol. Chem. 1991, 266, 11078–11082. [CrossRef]

154. Obayashi, E.; Tsukamoto, K.; Adachi, S.; Takahashi, S.; Nomura, M.; Iizuka, T.; Shoun, H.; Shiro, Y. Unique binding of nitric oxide to ferric nitric oxide reductase from Fusarium oxysporum elucidated with infrared, resonance raman, and X-ray absorption spectroscopies. J. Am. Chem. Soc. 1997, 119, 7807–7816. [CrossRef]

155. Zumft, W.G. Cell biology and molecular basis of denitrification. Microbiol. Mol. Biol. Rev. 1997, 61, 533–616. [CrossRef]

156. Daiber, A.; Shoun, H.; Ullrich, V. Nitric oxide reductase (P450nor) from Fusarium oxysporum. J. Inorg. Biochem. 2005, 99, 185–193. [CrossRef] [PubMed]

157. Ben Akacha, N.; Gargouri, M. Microbial and enzymatic technologies used for the production of natural aroma compounds: Synthesis, recovery modeling, and bioprocesess. Food Bioprod. Process 2015, 94, 675–706. [CrossRef]

158. Grand View Research Inc. Report on Fatty Acid Ester Market; Grand View Research, Inc.: San Francisco, CA, USA, 2016.

159. Sheldon, R.A. Characteristic features and biotechnological applications of cross-linked enzyme aggregates (CLEAs). Appl. Microbiol. Biotechnol. 2011, 92, 467–477. [CrossRef] [PubMed]

160. Dimarogona, M.; Nikolaivits, E.; Kanelli, M.; Christakopoulos, P.; Sandgren, M.; Topakas, E. Structural and functional studies of a Fusarium oxysporum cutinase with polyethylene terephthalate modification potential. Biochim. Biophys. Acta. 2015, 1850, 2308–2317. [CrossRef] [PubMed]

161. Ben Akacha, N.; Gargouri, M. Microbial and enzymatic technologies used for the production of natural aroma compounds: Synthesis, recovery modeling, and bioprocesess. Food Bioprod. Process 2015, 94, 675–706. [CrossRef]

162. Ibrahim, S.R.M.; Mohamed, G.A.; Alshali, K.Z.; Al Haidari, R.A.; El-Kholy, A.A.; Zayed, M.F. Lipoxygenase inhibitors flavonoids from Cyperus rotundus aerial parts. Rev. Bras. Farmacogn. 2018, 28, 320–324. [CrossRef]

163. Mashima, R.; Okuyama, T. The role of lipoxygenase in pathophysiology; new insights and future perspectives. Adv. Environ. Sci. Technol. 2020, 14, 1157–1168. [CrossRef]

164. Liu, Y.; Li, M.; Huang, L.; Gui, S.; Jia, L.; Zheng, D.; Fu, Y.; Zhang, Y.; Rui, J.; Lu, F. Cloning, expression and characterisation of phospholipase B from Saccharomyces cerevisiae and its application in the synthesis of L-alpha-glycerophosphorylcholine and peanut oil degumming. Biotech. Biotechnol. Equip. 2018, 32, 968–973. [CrossRef]
Su, L.; Ji, D.; Tao, X.; Yu, L.; Wu, J.; Xia, Y. Recombinant expression, characterization, and application of a phospholipase B from Fusarium oxysporum. *J. Biotechnol.* 2017, 242, 92–100. [CrossRef]

Wierenga, R.K.; Kapetanionu, E.G.; Venkatesan, R. Triosephosphate isomerase: A highly evolved biocatalyst. *Cell Mol. Life Sci.* 2010, 67, 3961–3982. [CrossRef]

Rottig, A.; Wenning, L.; Broker, D.; Steinbuckel, A. Fatty acid alkyl esters: Perspectives for production of alternative biofuels. *Appl. Microbiol. Biotechnol.* 2010, 44, 1713–1733. [CrossRef]

Gavrilutescu, M.; Chisti, Y. A sustainable alternative for chemical industry. *Biotechnol. Adv.* 2005, 23, 471–499. [CrossRef] [PubMed]

Singh, A.; Kumar, P.K. Fusarium oxysporum: Status in bioethanol production. *Crit. Rev. Biotechnol.* 1991, 11, 129–147. [CrossRef]

Ali, S.S.; Nugent, B.; Mullins, E.; Doohan, F.M. Fungal-mediated consolidated bioprocessing: The potential of *Fusarium oxysporum* for the lignocellulosic ethanol industry. *AMB Express* 2016, 6, 13. [CrossRef]

Ali, S.S.; Khan, M.; Fagan, B.; Mullins, E.; Doohan, F.M. Exploiting the inter-strain divergence of *Fusarium oxysporum* for microbial bioprocessing of lignocellulose to bioethanol. *AMB Express* 2012, 2, 16. [CrossRef] [PubMed]

Nait M’Barek, H.; Arif, S.; Taidi, B.; Hajjaj, H. Consolidated bioethanol production from olive mill waste: Wood-decay fungi from central Morocco as promising decomposition and fermentation biocatalysts. *Biotechnol. Rep.* 2020, 28, e00541. [CrossRef]

Xu, J.; Wang, X.; Hu, L.; Xia, J.; Wu, Z.; Xu, N.; Dai, B.; Wu, B. A novel ionic liquid-tolerant Fusarium oxysporum BN secreting ionic liquid-stable cellulase: Consolidated bioprocessing of pretreated lignocellulose containing residual ionic liquid. *Bioreour. Technol.* 2015, 181, 18–25. [CrossRef]

Prasher, P.; Sharma, M. Medicinal chemistry of antranilic acid derivatives: A mini review. *Drug Dev. Res.* 2021. [CrossRef]

Reinhard, K.; Matern, U. The biosynthesis of phytoalexins in *Dianthus Caryophyllus* L. cell cultures: Induction of benzoyl-CoA antranilic N-benzoyltransferase activity. *Arch. Biochem. Biophys.* 1989, 275, 295–301. [CrossRef]

Reinhard, K.; Matern, U. Different types of microsomal enzymes catalyze ortho- or para-hydroxylation in the biosynthesis of caryophyllene oxyphtoalexins. *FEBS Lett.* 1991, 294, 67–72. [CrossRef]

Braun, M.S.; Wink, M. Exposure, occurrence, and structure of fumonisins and their Cryptic derivatives. *Compr. Rev. Food Sci. Food Saf.* 2018, 17, 769–791. [CrossRef] [PubMed]

Voss, K.A.; Smith, G.W.; Haschek, W.M. Fumonisins: Toxicokinetics, mechanism of action and toxicity. *Anim. Feed Sci. Technol.* 2007, 137, 299–325. [CrossRef]

Saniewski, M. *The Role of Jasmonates in Ethylene Biosynthesis in Biology and Biotechnology of the Plant Hormone Ethylene; NATO ASI Series*; Kanellis, A.K., Chang, C., Kende, H., Grierson, D., Eds.; Springer: Dordrecht, The Netherlands, 1997; pp. 39–45.

Jarocka-Karpowicz, I.; Markowska, A. Therapeutic potential of jasmonic acid and its derivatives. *Int. J. Mol. Sci.* 2021, 22, 8437. [CrossRef]

Kim, J.C.; Lee, Y.W.; Tamura, H.; Yoshizawa, T. Sambutoxin: A new mycotoxin isolated from Fusarium sambucinum. *Tetrahedron Lett.* 1995, 36, 1047–1050. [CrossRef]

Desaty, D.; McInnes, A.G.; Smith, D.G.; Vining, L.C. Use of 13C in biosynthetic studies. Incorporation of isotopically labeled acetate and aspartate into fusaric acid. *Can. J. Biochem.* 1968, 46, 1293–1300. [CrossRef] [PubMed]

Dobson, T.A.; Desaty, D.; Brewer, D.; Vining, L.C. Biosynthesis of fusaric acid in cultures of *Fusarium oxysporum* Schlecht. *Can. J. Biochem.* 1967, 45, 809–823. [CrossRef]

Stepanovic, R.D.; Wheeler, M.H.; Puckhaber, L.S.; Liu, J.; Bell, A.A.; Williams, H.J. Nuclear magnetic resonance (NMR) studies on the biosynthesis of fusaric acid from *Fusarium oxysporum f. sp. vasinfectum*. *J. Agric. Food Chem.* 2011, 59, 5351–5356. [CrossRef]

Croitoru, R.; Fitigáu, F.; van den Broek, L.A.M.; Friessen, A.E.; Davidescu, C.M.; Boeriu, C.G.; Peter, F. Biocatalytic acylation of sugar alcohols by 3-(4-hydroxyphenyl)propionic acid. *Process Biochem.* 2012, 47, 1894–1902. [CrossRef]

Benhamou, N.; Garand, C.; Goulet, A. Ability of nonpathogenic *Fusarium oxysporum* strain Fo47 to induce resistance against *Pythium ultimum* infection in cucumber. *Appl. Environ. Microbiol.* 2002, 68, 4044–4060. [CrossRef]

Zazzerini, A.; Tosi, L. Antagonistic activity of fungi isolated from sclerotia of *Sclerotinia sclerotiorum*. *Plant Pathol.* 1985, 34, 415–421. [CrossRef]

Elkhayat, E.S.; Mohamed, G.A.; Ibrahim, S.R.M. Activity and structure elucidation of ceramides. *Curr. Bioact. Compd.* 2012, 8, 370–409. [CrossRef]

Schumacher, J.; Gautier, A.; Morgant, G.; Studt, L.; Ducrot, P.H.; Le Péchuer, P.; Azeddine, S.; Fillinger, S.; Leroux, P.; Tudyński, B.; et al. A functional bikaverin biosynthesis gene cluster in rare strains of *Botrytis cinerea* is positively controlled by VELVET. *PLoS ONE* 2013, 8, e53729. [CrossRef] [PubMed]

Ma, S.M.; Zhan, J.; Watanabe, K.; Xie, X.; Zhang, W.; Wang, C.C.; Tang, Y. Enzymatic synthesis of aromatic polyketides using PKS4 from *Gibberella fujikuroi*. *J. Am. Soc. Chem. Biol.* 2007, 129, 10642–10643. [CrossRef]

Arndt, B.; Studt, L.; Wiemann, P.; Osmanov, H.; Kleigrewe, K.; Köhler, J.; Krug, I.; Tudyński, B.; Humpf, H.U. Genetic engineering, high resolution mass spectrometry and nuclear magnetic resonance spectroscopy elucidate the bikaverin biosynthetic pathway in *Fusarium fujikuroi*. *Fungal Genet. Biol.* 2015, 84, 26–36. [CrossRef] [PubMed]

Limón, M.C.; Rodríguez-Ortiz, R.; Avalos, J. Bikaverin production and applications. *Appl. Microbiol. Biotechnol.* 2010, 87, 21–29. [CrossRef] [PubMed]

Abbas, H.K.; Mirocha, C.J.; Gunther, R. Mycotoxins produced by toxic *Fusarium* isolates obtained from agricultural and nonagricultural areas (Arctic) of Norway. *Mycopathologia* 1989, 105, 143–151. [CrossRef] [PubMed]

Croitoru, R.; Fitigáu, F.; van den Broek, L.A.M.; Friessen, A.E.; Davidescu, C.M.; Boeriu, C.G.; Peter, F. Biocatalytic acylation of sugar alcohols by 3-(4-hydroxyphenyl)propionic acid. *Process Biochem.* 2012, 47, 1894–1902. [CrossRef] [PubMed]
201. Woscholski, R.; Kodaki, T.; McKinnon, M.; Waterfield, M.D.; Parker, P.J. A comparison of demethoxyviridin and wortmannin as inhibitors of phosphatidylinositol 3-kinase. FEBS Lett. 1994, 342, 109–114. [CrossRef]

202. MacMillan, J.; Varnstone, A.E.; Yeboah, S.K. The structure of wortmannin, a steroidal fungal metabolite. Chem. Commun. 1968, 613–614. [CrossRef]

203. Freire, E.S.; Campos, V.P.; Pinho, R.S.; Oliveira, D.F.; Faria, M.R.; Pohlit, A.M.; Noberto, N.P.; Rezende, E.L.; Pfenning, L.H.; Silva, J.R. Volatile substances produced by Fusarium oxysporum from Coffee Rhizosphere and other microbes affect Meloidogyne incognita and Arthrobotrys conoides. J. Nematol. 2012, 44, 321–328.