

Review

# Antagonism to Plant Pathogens by *Epichloë* Fungal Endophytes—A Review

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**Abstract:** *Epichloë* is a genus of filamentous fungal endophytes that has co-evolved with cool-season grasses with which they form long-term, symbiotic associations. The most agriculturally important associations for pasture persistence for grazing livestock are those between asexual vertically transmitted *Epichloë* strains and the pasture species, perennial ryegrass, and tall fescue. The fungus confers additional traits to their host grasses including invertebrate pest deterrence and drought tolerance. Selected strains of these mutualistic endophytes have been developed into highly efficacious biocontrol products and are widely utilized within the Americas, Australia, and New Zealand for pasture persistence. Less publicized is the antagonism *Epichloë* endophytes display towards multiple species of saprophytic and pathogenic microbes. This opinion piece will review the current literature on antimicrobial properties exhibited by this genus of endophyte and discuss the reasons why this trait has historically remained a research curiosity rather than a trait of commercial significance.



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## 1. Introduction

Most multicellular life on Earth lives in symbiosis with microorganisms [1]. Plants, for example, whether they are growing within natural or managed ecosystems, are constantly interacting with a myriad of living microorganisms, including archaea, bacteria, fungi, and protists, throughout their lifecycle [2]. This microbial community (the plant microbiota) coupled with the surrounding environment (the entire habitat = the microbiome) has distinct physio-chemical properties and is crucially important for the health and productivity of the host plant. The interactions between hosts and microbes, or symbiosis, are complex ranging from mutualism through commensalism to parasitism in a continuous manner [3,4] and are important ecological determinants of plant biodiversity [5], although some regard parasitism as an unbalanced status of the symbiosis [6]. Furthermore, mutualistic symbioses were likely responsible for early host plant habitat transitions in the late Precambrian era (ca. 600 Ma) with several microbial species implicated in the evolution of photosynthesizing organisms [7–10]. This concept forms the basis for the hologenome theory of evolution [11] and proposes that the holobiont, the plant host plus all of its symbionts, is a unit of selection [12]. Although the first mutualistic symbioses were likely to have been associations between simple monerans and protists that led to the Cambrian explosion [10], present day symbiosis are more diverse. Examples include lichens (associations between algae or cyanobacteria and several fungal species), those between rhizobia and legumes, mycorrhiza (those associations between plants and fungi), and associations between *Epichloë* fungal endophytes and cool-season grasses.

## 2. *Epichloë* Endophytes

*Epichloë* (family Clavicipitaceae) is a monophyletic genus of filamentous fungi that form perpetual symbioses with cool-season grasses (family Poaceae subfamily Pooideae) [13]. These endophytes are regarded as keystone species, being ecologically important constituents of many grassland ecosystems, which cover over 30% of the Earth's land area and are, therefore, one of the largest biomes on the planet [14–16]. *Epichloë* species are naturally restricted to a host genus or closely related grass genera within a tribe as a result of co-evolution over many millennia [17–19]. However, this group of grass symbionts may have originally emerged from an animal pathogen via an interkingdom host jump [20,21]. As with most members of the Ascomycota, the genus *Epichloë* includes both anamorphic (asexual) and teleomorphic (sexual) species, with the former previously classified as *Neotyphodium* [22]. Over 30 species of *Epichloë* have been described [22] with most exhibiting an anamorphic lifecycle.

Obligatory sexual species of *Epichloë* are largely antagonistic to their host plant as the epiphytic stroma that is formed on the developing host inflorescence, essential for horizontal transmission, suppresses plant seed production, thereby impeding the hosts ability to reproduce [23]. In contrast, the asexual species are symptomless within their host plants being exclusively vertically transmitted via the host's seed [24,25]. Many of the plant's progeny inherit chromosomes and cytoplasm from their parents but also their mutualistic symbionts, constituting a form of hereditary endosymbiosis [26]. *Epichloë* have been documented to confer a multitude of beneficial attributes to their host grasses. These attributes differ across the various endophyte–host associations with the most prominent being protection from mammalian and invertebrate herbivory via the production of secondary metabolites, most notably alkaloids [27]. The major metabolites involved in this defensive mutualism include peramine, an insect feeding deterrent; the lolines, a group of saturated *exo*-1-amino pyrrolizidines that exhibit a broad spectrum of insecticidal activity; indole diterpenes and ergot alkaloids that contain classes of compound that exhibit toxicity towards both vertebrates and invertebrates [28]. Additional attributes include tolerance against abiotic stresses (i.e., when the plant is exposed to adverse environmental conditions) such as those caused by drought and/or nutrient deficiencies [29,30].

*Epichloë* endophytes were initially identified as the cause of a serious agriculture issue due to some endophyte-grass associations producing alkaloidal neurotoxins that are detrimental to many animal species, including livestock (i.e., farmed ruminants) [31]. The most potent of these compounds include the lolitrems (indole diterpenes) and ergot alkaloids that result in ryegrass staggers and heat stress/fescue-foot syndromes respectively [32–34]. Research on the *Epichloë* endophyte associations with *Lolium perenne* L. (perennial ryegrass) in New Zealand (NZ) and *Lolium arundinaceum* (Schreb.) S.J. Darbyshire (= *Festuca arundinacea* Schreb.; tall fescue) in the USA, identified asexual *Epichloë* strains that were less toxic to livestock whilst conferring advantageous traits to their host grasses. Since this initial research in the 1980s and 1990s, scientific programmes have been established that center on bioprospecting pipelines to identify, characterize and select agriculturally beneficial endophyte strains (those that confer advantageous traits to their host while producing little or no detrimental effects to grazing livestock) that could be incorporated into elite grass cultivars with increased pasture persistence and productivity [30,31].

AgResearch (a NZ government owned research institute that carries out scientific research for the benefit of NZ; <https://www.agresearch.co.nz>; accessed on 15 September 2021) developed bioprospecting pipelines that (1) identify *Epichloë* endophytes from global collections of germplasm, (2) characterize *Epichloë* isolates with respect to their genetic diversity, secondary metabolite profiles and bioactivity, (3) inoculate agriculturally useful strains with commercial potential into elite grass cultivars, and (4) evaluate populations of novel grass-endophyte associations through specifically designed agronomic and toxicological screens [35,36]. Endophyte strains that are devoid of lolitrems and ergot alkaloids while possessing insect-deterrent compounds (e.g., peramine and/or lolines) generally have commercial potential. This opinion piece will review the current literature on the antimicrobial

properties exhibited by *Epichloë* fungal endophytes and discuss the reasons why this trait has historically remained a research curiosity rather than a trait of commercial significance.

### 3. Interaction of *Epichloë* spp. with Plant Pathogens

Although a great deal of knowledge regarding the bioactivity of *Epichloë*-derived secondary metabolites on invertebrate pests has been gained, little research has been undertaken on the biological control of fungal phytopathogens by *Epichloë*-infected grasses [37,38]. To the best of our knowledge, no published research documents the biological control of bacterial phytopathogens by *Epichloë*, although certain endophyte strains can influence the host plant's bacterial microbiota [39]. Furthermore, no correlation exists between the antifungal bioactivity expressed by these endophytes and their alkaloid profiles [40,41] and although several *Epichloë*-based grass products are marketed across the continents of Australia, North America and South America for their insect deterrent properties [30,31,42], none are marketed for their control of plant diseases. However, *Epichloë* endophytes can inhibit the growth and reproduction of other microorganisms, including economically important fungal phytopathogens [43]. A recent meta-analysis has shown that all species of phytopathogen significantly affected by the presence of *Epichloë* endophyte regardless of their lifestyle (biotrophic vs. necrotrophic), with both laboratory and greenhouse comparisons showing negative effects of *Epichloë* spp. on the growth and infection by phytopathogens [44]. However, many of the published reports describe bioactivity that has been assessed using crudely designed in vitro dual culture bioassays (Table 1), with fewer reports on this phenomenon in planta within a field situation (Table 2).

**Table 1.** In vitro bioactivity exhibited by species of *Epichloë* towards fungal saprophytes or phytopathogens. Bioassays reviewed here are generally dual culture assays using viable fungal colonies, or their filtered crude extracts, undertaken on potato dextrose agar (PDA) or a similar solid agar medium. These in vitro bioassays are restricted to only assessing antibiosis and cannot assess other mechanisms of action (i.e., induced resistance or competition).

Fungal Species <sup>1</sup>	Host Species	Fungal Pathogen <sup>2</sup>	Division	Country	Reference/s
<i>Epichloë amarillans</i>	<i>Achnatherum sibiricum</i>	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	China	[37]
		<i>Cladosporium cucumerium</i>	Ascomycota	China	[37]
		<i>Fusarium oxysporum</i>	Ascomycota	China	[37]
		<i>Phomopsis vexans</i>	Ascomycota	China	[37]
		<i>Rhizoctonia solani</i>	Basidiomycota	China	[37]
	<i>Agrostis</i> sp.	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
<i>Epichloë bromicola</i>	<i>Hordeum brevisubulatum</i>	<i>Alternaria</i> sp.	Ascomycota	China	[46]
<i>Epichloë chisosa</i>	<i>Achnatherum sibiricum</i>	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	China	[37]
		<i>Cladosporium cucumerium</i>	Ascomycota	China	[37]
		<i>Fusarium oxysporum</i>	Ascomycota	China	[37]
		<i>Phomopsis vexans</i>	Ascomycota	China	[37]
		<i>Rhizoctonia solani</i>	Basidiomycota	China	[37]
<i>Epichloë coenophialum</i> (FaTG-1)	<i>Lolium arundinaceum</i>	<i>Alternaria alternata</i>	Ascomycota	USA	[47]
		<i>Ceratobasidium cornigerum</i> (syn. <i>Rhizoctonia cerealis</i> )	Basidiomycota	NZ and USA	[40,48]
		<i>Cladosporium cladosporioides</i>	Ascomycota	USA	[47]
		<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Poland	[49]
		<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	China and Poland	[49,50]
		<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
		<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	NZ and USA	[40]
		<i>Laetisaria roseipellis</i> (syn. <i>Limonomyces roseipellis</i> )	Basidiomycota	NZ and USA	[40]
		<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ and USA	[41,51]
		<i>Gibberella acuminata</i> (syn. <i>Fusarium acuminatum</i> )	Ascomycota	China	[50]
		<i>Rhizoctonia solani</i>	Basidiomycota	Poland	[49]
		<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ and USA	[40]

Table 1. Cont.

Fungal Species <sup>1</sup>	Host Species	Fungal Pathogen <sup>2</sup>	Division	Country	Reference/s	
<i>Epichloë</i> FaTG-2	<i>Lolium arundinaceum</i>	<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[41]	
		<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ	[41]	
<i>Epichloë</i> FaTG-3	<i>Lolium arundinaceum</i>	<i>Ceratobasidium</i> sp.	Basidiomycota	Australia	[52]	
		<i>Drechslera</i> sp.	Ascomycota	Australia	[52]	
		<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[41]	
		<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ	[41]	
<i>Epichloë festucae</i>	<i>Festuca longifolia</i>	<i>Ceratobasidium cornigerum</i> (syn. <i>Rhizoctonia cerealis</i> )	Basidiomycota	NZ and USA	[40]	
		<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	NZ, Japan and USA	[40,53]	
		<i>Laetisaria roseipellis</i> (syn. <i>Limonomyces roseipellis</i> )	Basidiomycota	NZ and USA	[40]	
		<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[41]	
	<i>Festuca pulchella</i>	<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	<i>Botrytis cinerea</i>	Ascomycota	Japan	[54]
			<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Japan	[53]
			<i>Drechslera dictyoides</i>	Ascomycota	Japan	[53]
			<i>Drechslera siccans</i>	Ascomycota	Japan	[53]
			<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	Japan	[53]
			<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	Japan	[53–55]
			<i>Phytophthora infestans</i>	Oomycota	Japan	[54]
			<i>Claviceps homoeocarpa</i> (syn. <i>Sclerotinia homoeocarpa</i> )	Ascomycota	USA	[56]
			<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Poland	[57]
			<i>Ceratobasidium cornigerum</i> (syn. <i>Rhizoctonia cerealis</i> )	Basidiomycota	NZ and USA	[40]
	<i>Festuca rubra</i> <sup>3</sup>	<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
			<i>Drechslera dictyoides</i>	Ascomycota	Poland	[57]
			<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	NZ, Japan and USA	[40,53]
			<i>Laetisaria roseipellis</i> (syn. <i>Limonomyces roseipellis</i> )	Basidiomycota	USA	[40]
			<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[41]
			<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ	[41]
			<i>Botrytis cinerea</i>	Ascomycota	Japan	[54]
			<i>Pyrenophora erythrospila</i>	Ascomycota	Japan	[54]
			<i>Phytophthora infestans</i>	Oomycota	Japan	[54]
			<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	Japan	[53]
	<i>Festuca trachyphylla</i>	<i>Lolium pratense</i>	<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	Japan	[53]
			<i>Ceratobasidium cornigerum</i> (syn. <i>Rhizoctonia cerealis</i> )	Basidiomycota	NZ and USA	[40,47,48]
			<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	NZ and USA	[40,58]
<i>Ceratobasidium</i> sp.			Basidiomycota	Australia	[52]	
<i>Cryphonectria parasitica</i>			Ascomycota	USA	[45]	
<i>Drechslera andersenii</i>			Ascomycota	Germany	[59]	
<i>Drechslera poae</i>			Ascomycota	Germany	[59]	
<i>Drechslera siccans</i>			Ascomycota	Germany	[59]	
<i>Drechslera</i> sp.			Ascomycota	Australia	[52]	
<i>Drechslera teres</i>			Ascomycota	Germany	[59]	
<i>Fusarium</i> sp.	Ascomycota	Australia	[52]			
<i>Epichloë festucae</i> var. <i>lolii</i> (=LpTG-1)	<i>Lolium perenne</i>	<i>Gibberella acuminata</i> ( <i>Fusarium acuminatum</i> )	Ascomycota	China	[50]	
		<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[41]	
		<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ and USA	[40,41]	
		<i>Laetisaria roseipellis</i> (syn. <i>Limonomyces roseipellis</i> )	Basidiomycota	NZ and USA	[40]	

Table 1. Cont.

Fungal Species <sup>1</sup>	Host Species	Fungal Pathogen <sup>2</sup>	Division	Country	Reference/s
<i>Epichloë gansuensis</i>	<i>Achnatherum inebrians</i>	<i>Alternaria alternata</i>	Ascomycota	China	[50]
		<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	China	[50]
		<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	China	[50]
		<i>Gibberella acuminata</i> (syn. <i>Fusarium acuminatum</i> )	Ascomycota	China	[50]
<i>Epichloë hybrida</i> (=LpTG-2)	<i>Lolium perenne</i>	<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[41]
		<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ	[41]
<i>Epichloë</i> LpTG-3	<i>Lolium perenne</i>	<i>Ceratobasidium</i> sp.	Basidiomycota	Australia	[52]
		<i>Drechslera</i> sp.	Ascomycota	Australia	[52]
		<i>Fusarium</i> sp.	Ascomycota	Australia	[52]
<i>Epichloë occultans</i>	<i>Lolium multiflorum</i>	<i>Gibberella acuminata</i> (syn. <i>Fusarium acuminatum</i> )	Ascomycota	Argentina	[60] *
		<i>Rhizoctonia solani</i>	Basidiomycota	Argentina	[60] *
Unknown <i>Epichloë</i> spp.	<i>Festuca simensis</i>	<i>Alternaria alternata</i>	Ascomycota	China	[61]
		<i>Aspergillus niger</i>	Ascomycota	China	[62]
		<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	China	[61,62]
		<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	China	[61,62]
	<i>Festuca versuta</i>	<i>Ceratobasidium cornigerum</i> (syn. <i>Rhizoctonia cerealis</i> )	Basidiomycota	USA	[48]
		<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	NZ	[58]
	<i>Lolium perenne</i>	<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[58]
		<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
	<i>Poa ampla</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
	<i>Poa autumnalis</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
	<i>Poa interior</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
	<i>Poa palustris</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
	<i>Poa rigidifolia</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
<i>Poa sp.</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]	
<i>Poa sylvestris</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]	
<i>Neotyphodium starii</i> <sup>4</sup>	<i>Festuca arizonica</i>	<i>Glomerella graminicola</i> (syn. <i>Colletotrichum graminicola</i> )	Ascomycota	NZ	[40]
		<i>Laetisaria roseipellis</i> (syn. <i>Limonomyces roseipellis</i> )	Basidiomycota	NZ and USA	[40]
	<i>Festuca obtusa</i>	<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ	[40]
		<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ	[40]
<i>Epichloë tembladerae</i>	<i>Festuca argentina</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
	<i>Poa hueca</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
	<i>Poa sp.</i>	<i>Cryphonectria parasitica</i>	Ascomycota	USA	[45]
<i>Epichloë uncinatum</i>	<i>Lolium pratense</i> (syn. <i>Festuca pratensis</i> )	<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Poland	[57]
		<i>Drechslera dictyoides</i>	Ascomycota	Poland	[57]
		<i>Gibberella avenacea</i> ( <i>Fusarium avenaceum</i> )	Ascomycota	Poland	[57]
		<i>Fusarium culmorum</i>	Ascomycota	Germany	[59]
		<i>Fusarium equiseti</i>	Ascomycota	Poland	[57]
		<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	NZ	[41]
		<i>Rhizoctonia solani</i>	Basidiomycota	Poland	[57]
		<i>Typhula ishikariensis</i>	Basidiomycota	Finland	[63]
		<i>Waitea circinata</i> (syn. <i>Rhizoctonia zeae</i> )	Basidiomycota	NZ	[41]

<sup>1</sup> Current scientific name. <sup>2</sup> Current scientific name, or most accepted name, followed by the synonym used within the citing manuscript.

<sup>3</sup> Including subspecies. <sup>4</sup> *Nomen dubium* according to [22]. \* In vitro experiment with axenic cultures of the pathogen and grass seed infected with *Epichloë*.

**Table 2.** In planta bioactivity exhibited by species of *Epichloë* towards fungal saprophytes or phytopathogens. In planta bioassays included all assays that did not work with axenic cultures of *Epichloë* spp. and included detached leaf assays, whole plant assays with plants grown in controlled climate rooms, glasshouses, or field trials. IR = induced resistance.

Fungal Species <sup>1</sup>	Original Host Species	Type of Association	Fungal Pathogen <sup>2</sup>	Division	Disease	Suggested Mechanism	Country	Reference/s
<i>Epichloë bromicola</i>	<i>Leymus chinensis</i>	original	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Curvularia blight	IR	China	[64]
			<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Spot blotch and root rot	IR	China	[64]
		original	<i>Waitea circinate</i> (syn. <i>Rhizoctonia zaeae</i> )	Basidiomycota	Sheath and leaf spot	IR	Poland	[49]
	<i>Secale cereale</i>	novel	<i>Cercosporidium graminis</i>	Ascomycota	Leaf streak	Unknown	NZ	[65]
		novel	<i>Puccinia recondita</i>	Basidiomycota	Leaf rust	Unknown	NZ	[65]
<i>Epichloë coenophialum</i>	<i>Lolium arundinaceum</i>	original	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Curvularia blight	Competition for nutrients	China	[66]
<i>Epichloë festucae</i>	<i>Festuca rubra</i>	original	<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Spot blotch and root rot	Antibiosis	Poland	[57]
		original	<i>Drechslera</i> sp.	Ascomycota	Head blight	Antibiosis	Poland	[57]
		original	<i>Fusarium poae</i>	Ascomycota	Head blight	Antibiosis	Poland	[57]
	<i>Festuca rubra</i> L. subsp. <i>rubra</i>	novel	<i>Laetisaria fuciformis</i>	Basidiomycota	Red thread	Competitive exclusion	USA	[67]
	<i>Lolium perenne</i>	novel	<i>Pyrenophora erythrospila</i> (syn. <i>Drechslera erythrospila</i> )	Ascomycota	Red leaf spot	Antibiosis	Japan	[53]
<i>Epichloë festucae</i> var. <i>lolii</i> (=LpTG-1)	<i>Lolium perenne</i>	original	<i>Alternaria alternata</i>	Ascomycota	Leaf spot	IR	China	[38]
		original	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Curvularia blight	IR	China	[38]
		original	<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Spot blotch and root rot	Antibiosis, competition and/or IR	China	[38,68,69]
		original	<i>Fusarium chlamydosporum</i>	Ascomycota	Wilt	IR	China	[38]
		original	<i>Fusarium oxysporum</i>	Ascomycota	Fusarium wilt	IR	China	[38]
		original	<i>Fusarium poae</i>	Ascomycota	Head blight	IR	Poland	[70]
		original	<i>Fusarium solani</i>	Ascomycota	Soft root rot	IR	China	[38]
		original	<i>Gibberella acuminata</i> (syn. <i>Fusarium acuminatum</i> )	Ascomycota	Root rot	IR	China	[38]
		original	<i>Puccinia coronata</i>	Basidiomycota	Crown rust	Unknown	Australia and China	[71,72]
novel	<i>Pyrenophora semeniperda</i>	Ascomycota	Leaf spots	Antibiosis	Australia	[73]		

Table 2. Cont.

Fungal Species <sup>1</sup>	Original Host Species	Type of Association	Fungal Pathogen <sup>2</sup>	Division	Disease	Suggested Mechanism	Country	Reference/s
<i>Epichloë gansuensis</i>	<i>Achnatherum inebrians</i>	original	<i>Ascochyta leptospora</i>	Ascomycota	Ascochyta leaf blight	Antibiosis	China	[50]
		original	<i>Alternaria alternata</i>	Ascomycota	Leaf spot	Antibiosis	China	[50]
		original	<i>Blumeria graminis</i>	Ascomycota	Powdery mildew	IR	China	[74–77]
		original	<i>Claviceps purpurea</i>	Ascomycota	Ergot	IR	China	[78]
		original	<i>Clonostachys rosea</i>	Ascomycota	Unknown	Antibiosis	China	[50]
		original	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Curvularia blight	Antibiosis	China	[50,79]
		original	<i>Fusarium chlamydosporum</i>	Ascomycota	Wilt	Antibiosis	China	[50]
		original	<i>Fusarium oxysporum</i>	Ascomycota	Fusarium wilt	Antibiosis	China	[50]
		original	<i>Fusarium solani</i>	Ascomycota	Soft root rot	Antibiosis	China	[50]
		original	<i>Gibberella acuminata</i> (syn. <i>Fusarium acuminatum</i> )	Ascomycota	Root rot	Antibiosis	China	[50]
		original	<i>Gibberella avenacea</i> ( <i>Fusarium avenaceum</i> )	Ascomycota	Fusarium head blight	Antibiosis	China	[50]
		original	<i>Fusarium solani</i>	Ascomycota	Soft root rot	Antibiosis	China	[50]
		original	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Curvularia blight	IR	China	[79]
		original	<i>Achnatherum sibiricum</i>	original	<i>Erysiphales</i>	Ascomycota	Powdery mildew	IR
<i>Epichloë occultans</i>	<i>Lolium multiflorum</i>	original	<i>Claviceps purpurea</i>	Ascomycota	Ergot	Vector exclusion	Argentina	[80]
<i>Epichloë sibiricum</i>	<i>Achnatherum sibiricum</i>	original	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Curvularia blight	IR	China	[79]
		original	<i>Erysiphales</i>	Ascomycota	Powdery mildew	IR	China	[79]
<i>Epichloë sinensis</i>	<i>Festuca sinensis</i>	original	<i>Alternaria alternata</i>	Ascomycota	Leaf spot	Unknown	China	[81]
		original	<i>Ustilago bullata</i>	Basidiomycota	Head smut	Unknown	Argentina	[82]
<i>Epichloë sp.</i>	<i>Bromus auleticus</i>	original	<i>Alternaria alternata</i>	Ascomycota	Leaf spot	Antibiosis	China	[61]
		original	<i>Gibberella acuminata</i> (syn. <i>Fusarium acuminatum</i> )	Ascomycota	Root rot	Antibiosis	China	[61]
		original	<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Spot blotch and root rot	Antibiosis	China	[61]
	<i>Festuca sinensis</i>	original	<i>Cochliobolus lunatus</i> (syn. <i>Curvularia lunata</i> )	Ascomycota	Curvularia blight	Antibiosis	China	[61]
		original wild grass and cultivar	<i>Rhynchosporium sp.</i>	Ascomycota	Leaf blotch	Antibiosis, IR and/or improved host fitness	Finland	[83]
		original	<i>Drechslera siccans</i>	Ascomycota	Brown blight	IR	Poland	[84]
<i>Lolium perenne</i>	original	<i>Fusarium spp.</i>	Ascomycota	Fusarium blight	IR	Poland	[84]	

Table 2. Cont.

Fungal Species <sup>1</sup>	Original Host Species	Type of Association	Fungal Pathogen <sup>2</sup>	Division	Disease	Suggested Mechanism	Country	Reference/s
<i>Epichloë typhina</i>	<i>Phleum pratense</i>	original	<i>Cladosporium phlei</i>	Ascomycota	Purple leaf spot	Unknown	Japan	[85,86]
<i>Epichloë uncinatum</i>	<i>Lolium pratense</i> (syn. <i>Festuca pratensis</i> )	original	<i>Cochliobolus sativus</i> (syn. <i>Bipolaris sorokiniana</i> )	Ascomycota	Spot blotch and root rot	Antibiosis	Poland	[57]
		original	<i>Dreschlera</i> sp.	Ascomycota	Head blight	Antibiosis	Poland	[57]
		original	<i>Fusarium poae</i>	Ascomycota	Head blight	Antibiosis	Poland	[57]
		original	<i>Puccinia coronata</i>	Basidiomycota	Crown rust	Unknown	Poland	[87]

<sup>1</sup> Current scientific name. <sup>2</sup> Current scientific name, or most accepted name, followed by the synonym used within the citing manuscript.



Biological control, in its simplest form, can be defined as applied ecology [88] and is an environmentally sound and effective means of reducing or mitigating viral, microbial, nematode, insect, mite, weed, and vertebrate pests in agriculture, aquatic, forest, natural resources, stored products, and urban environments. Many primary screens using artificial nutrient media are severely criticized as they do not closely resemble the final arena where biological control ultimately takes place. Subsequently, these primary screens, which can determine antagonism between an endophyte and a phytopathogen in vitro, are generally poor at predicting protection within live plant tissues [89,90]. For example, in vitro research conducted in Finland showed clear antifungal activity expressed by strains of *Epichloë* towards the speckled snow mold pathogen, *Typhula ishikariensis*, when grown on potato dextrose agar (PDA). However, in the subsequent field experiment, the endophyte-infected grasses were more susceptible to the pathogen than the endophyte-free control plants [63].

This lack of correlation between in vitro and in planta results may be due to multiple reasons: (1) some *Epichloë*-derived secondary metabolites are only produced in planta. For example, the endophyte-derived alkaloids are metabolites only produced by the grass-endophyte association with the exception of two loline alkaloids that can be produced in vitro from axenic endophyte cultures at a relatively low concentration from a defined minimal media [91], (2) concentrations of *Epichloë*-derived secondary metabolites depend on the host plant. These endophytes may not be able to secure the relevant nutrients or amount of nutrients in planta and the secondary metabolite biosynthetic pathways may be down regulated as with some biotrophic phytopathogens [92], and (3) the in vitro bioassays are largely restricted to identifying antibiosis as the sole mechanism of action exhibited by these fungi while other mechanisms exist. In vitro screens can, therefore, be misleading by either overestimating or underestimating the potential of endophyte strains to protect against phytopathogens.

Antibiosis is defined as antagonism mediated by specific or non-specific metabolites of microbial origin, by lytic agents, enzymes, volatile compounds or other toxic substances [88]. However, there are additional mechanisms of biological control proposed for *Epichloë*-plant associations [93], including induced resistance (reduced disease susceptibility of a plant in response to stimulation by a pathogen, insect herbivore, beneficial microbe, or chemical agent [94]) and competition for limiting factors (e.g., physical space, carbohydrates and amino acids) (see Table 2 for examples). The fourth main mechanism of biological control, direct parasitism, exhibited by several fungal antagonists such as *Trichoderma* spp. [95], has not been reported to date for *Epichloë* spp. The endophyte would have to engage in direct contact with the target phytopathogen, and this seems unlikely due to the restriction of these endophytes within the intracellular spaces of their grass hosts and the sometimes-suppressive nature of the regulation that they encounter during their growth and development [96,97].

As mentioned previously, no correlation exists between the antifungal bioactivity expressed by these endophytic fungi and their alkaloid profiles [40,41]. However, several non-alkaloid secondary metabolites have been implicated in the antagonism exhibited by *Epichloë* spp. towards phytopathogens (see antibiosis studies listed in Table 2). These compounds include sesquiterpenes [45,98], phenolic glycerides [99], hydroxyl unsaturated fatty acids [100], aromatic sterols [101], indole derivatives (indole-3-acetic acid (IAA) and indole-3-ethanol), diacetamides [45] and other volatile insect-attractant compounds, such as Chokol K and methyl esters [102]. Chokol K is an interesting compound, hypothesized to of originated as an antimicrobial agent the compound also has the ability to attract *Botanophila* flies, fungal pollinators of the external fruiting structures, the stroma, of sexually reproducing *Epichloë* species [103].

Research conducted on the bioactivity of *Epichloë* endophytes (Card, unpublished) aligns with previous studies in the literature that show that many *Epichloë* species exhibit antifungal activity towards a wide range of saprophytic and pathogenic fungal species, including those with diverse taxonomy (e.g., species from both the Ascomycota and Basidiomycota) and those with different lifestyles (e.g., biotrophs and necrotrophs)

(Tables 1 and 2). This could indicate that several antifungal compounds are produced simultaneously or that a small number of antifungal compounds have broad antifungal activity. Further work showed that no antifungal activity was attributed to guttation fluid collected from perennial ryegrass plants infected with selected *Epichloë* strains (Lambie and Christensen, unpublished) similar to that found with peramine against insects [104]. This may indicate that if antifungal compound/s are solely responsible for biological control within this system then they may have limited mobilization within the plant.

The *Epichloë*-mediated induction of the plant's own defenses has been proposed as another mechanism of resistance against phytopathogens [43,44]. Plant defenses are regulated by hormonal signaling pathways, including salicylic acid (SA) and jasmonic acid (JA) [105]. The dominant model for conceptualizing plant defenses suggests that the SA and JA signaling pathways protect plants against biotrophic and necrotrophic pathogens, respectively [106]. *Epichloë* spp. can activate host plant SA- and JA-signaling pathways [107]. This *Epichloë*-based activation of plant defense hormonal signaling pathways may explain, at least in part, the increased levels of disease resistance exhibited by *Epichloë*-infected plants (see IR studies listed in Table 2). For example, enhanced plant resistance exhibited by endophyte-infected *A. inebrians* plants against the biotrophic pathogen *B. graminis* was related to the activation of SA signaling pathways, increment in SA levels, and the upregulation in the expression of SA-related genes coding for putative plant enzymes with antifungal activities (i.e.,  $\beta$ -1,3-glucanase and callose synthase) [77]. Similarly, the enhanced plant resistance exhibited by *A. sibiricum* plants against the necrotrophic pathogen *C. lunata* by *A. sibiricum* was correlated to increased levels of JA and plant phenolics [79].

Further novel mechanisms have been proposed for specific grass-endophyte combinations, for example niche exclusion has been proposed for *Epichloë* associations with *Bromus setifolius*, *Festuca ovina*, *F. rubra*, and *Poa ampla* [108]. This mechanism results in the exclusion of phytopathogens by a superficial network of endophyte mycelium that develops on the leaf blade surface of grasses. The epiphytic mycelium was hypothesized to be defensive in function to physically exclude the entry of fungal pathogens into the leaves [109]. Pérez et al. [44] further proposed that two classes of mechanism exist with respect to the reduction of plant disease by *Epichloë* spp., (1) direct pathways mediated by antibiosis, competition and IR (described above) and (2) indirect pathways associated with endophyte-generated changes in either the abiotic or the biotic host environment. These authors describe an indirect pathway for the protection of *L. multiflorum* by its fungal endophyte *E. occultans* from the flower-infecting pathogen *Claviceps purpurea*, the causal agent of ergot [44]. The incidence and severity of *C. purpurea* infection was two-fold lower in endophyte-symbiotic plants than in non-symbiotic ones but when insects were prohibited from visiting the flowers this difference disappeared, indicating that endophyte-derived volatile compounds repel insect vectors of *C. purpurea* and indirectly defend their host grasses against plant disease [80].

Antagonism between *Epichloë* spp. and phytopathogens may have evolved many millions of years ago. A recent article describes an ancient cross-kingdom gene transfer (the transfer of genetic material between organisms) from *Epichloë* to tall wheatgrass (*Thinopyrum ponticum*). The article suggests that Fhb7, a major, semidominant resistance gene, was transferred to the wild cereal grass around 5 million years ago after the divergence of *Thinopyrum* from other grasses [110]. Fhb7 encodes a glutathione S-transferase that detoxifies deoxynivalenol (DON), a mycotoxin that renders grain poisonous to humans and other mammals. It is speculated that *Epichloë* may have evolved Fhb7 to compete with *Fusarium* spp. for grass colonization [111]. Furthermore, transcriptomic studies have identified an abundantly expressed fungal gene coding for a small, secreted protein, similar to antifungal proteins found within species of *Penicillium* and *Aspergillus*, in *Epichloë festucae*-infected red fescue plants [112]. The antifungal protein gene is not found within the genomes of many other *Epichloë* spp. and is hypothesized to be a component of the unique disease resistance observed with endophyte-infected red fescue plants to

dollar spot disease caused by the phytopathogen *Clavireedia jacksonii* [113]. It is suggested that once the endophyte lifestyle evolved in *Epichloë*, and the wider Clavicipitaceae endophytes, the alkaloid and other fungal-mediated defensive features adapted from previous functions to serve as plant host defense functions [114].

Recent theoretical modelling studies suggested that in order to predict biocontrol outcomes there is a need to understand not only the main biocontrol mechanisms involved but also the extent of environmental variability, the level of biocontrol activity, and survival of individual biological control agents in relation to external conditions [115]. *Epichloë* fungi, and other mutualistic endophytes, have a distinctive advantage over other biocontrol microorganisms that are inoculated into the phyllosphere or rhizosphere through drenches or sprays. By inhabiting the intracellular spaces of their plant hosts for their entire life-cycle they are buffered from many cyclic and non-cyclic variables, including potentially damaging ultraviolet rays, extremes of temperature, humidity, dew, rain and wind as experienced, for example, on the leaf surface [88]. Endophytic microorganisms are also protected from faster proliferating, more competitive microorganisms as experienced in many phyllosphere and rhizosphere environments. Endophyte survival is firmly tied with that of the plant host and are therefore totally reliant on the plant for substrates (e.g., water, sugars, and oxygen) and a suitable ecological niche free from competing microorganisms, along with the absence of inhibitory or toxic substances. While nutrients may become limiting in the phyllosphere environment, endophytes are supplied with a bountiful array of organic and inorganic nutrients including sugars, sugar alcohols, nitrates, nitrites, amino acids, organic acids, calcium, chloride, phosphorus, potassium, sulfur and soluble proteins [as reviewed by 116] supplied to the apoplasm from the neighboring phloem. Although the concentration and availability of such compounds within the apoplasm may fluctuate, it is largely a copiotrophic environment [116]. Substrates are not only in plentiful supply to support endophyte growth (biomass) but also may support the production of many secondary metabolites, including many anti-mammalian and insect deterrent alkaloidal compounds [28] as well as antimicrobial compounds active against phytopathogens.

The inhibition of phytopathogens by *Epichloë* has, however, largely remained a research curiosity rather than an attribute exploited for commercial disease biocontrol purposes as very few in planta experiments document the control of economically important phytopathogens in the field. These may be due to several reasons:

- (1) Many phytopathogens, particularly foliar fungal pathogens, are notoriously difficult to control (even by conventional synthetic agrichemicals) as they can produce vast numbers of wind-disseminated spores that are spread over large distances over significant periods of time. These phytopathogens can also exhibit a polycyclic nature that can be completed in just a few days, continuously barraging the plant with fresh inoculum.
- (2) Many plant diseases occur due to underlying abiotic disorders (e.g., nutrient imbalance, and/or water stress) that have weakened or stressed the plant and made it susceptible to invasion by a phytopathogen. Additionally, disease in the field is generally brought about by a complex of interacting microorganisms including primary and secondary pathogens making identification of the causal organism difficult.
- (3) Bioprospecting pipelines have to date identified *Epichloë* strains with deterrent traits against economically important invertebrate pests and therefore endophyte strains with high levels of bioactivity towards phytopathogens could have been missed, overlooked, or not prioritised.
- (4) Many in vitro primary screens overestimate the bioactivity of selected endophyte strains and do not screen enough strains to identify those with high potential for commercialisation. Great strain variation exists with respect to antifungal activity [53] and even morphotypes of the same species from the same host grass species can vary in their antifungal activity [37]. Furthermore, host genotype  $\times$  endophyte effects can impact the degree of antifungal activity expressed.

- (5) A lack of understanding concerning the mechanisms of action attributed to selected *Epichloë* strains. These mechanisms need to be understood to develop suitable novel grass-endophyte associations.
- (6) Many end users completely ignore the concept of biological control in favour of agrichemicals while others view it as essentially a compete synthetic chemistry replacement. However, biological control products have been generally less reliable than agrichemicals which has hampered their development, release, and commercial uptake [117]. For example, *Epichloë* strains with antifungal activity will generally only reduce the frequency or size of diseased lesions and, therefore, disease is still present [53].

#### 4. Interaction of *Epichloë* Endophytes with Other Taxa

As well as fungal phytopathogens, *Epichloë*, or their metabolites, can influence the interactions between endophyte-infected plants and other organisms. As discussed, endophyte-derived alkaloids can influence invertebrates and species such as herbivorous mammals and this in turn can affect species diversity and fundamental ecological processes like decomposition, and food web structures [118–122]. In natural ecosystems, *Epichloë* can reduce plant diversity, enhance the dominance of certain grass-endophyte associations [5] and also generate legacy effects which persist after the death of the host [123]. *Epichloë* endophytes may also impact the microbiome (the microbiota and its theatre of activity) of the vegetative host plant effecting microbial community structure in above and below ground habitats [121]. Studies aimed at investigating the rhizosphere communities of tall fescue plants show that *Epichloë*-infected plants showed a higher species richness over endophyte-free rhizospheres and a greater percentage of Firmicutes [124] while the presence of *Epichloë gansuensis* within its host grass *Achnatherum inebrians* significantly decreased root-associated fungal diversity [125]. These findings within the rhizosphere are paralleled within the phyllosphere where some endophyte-infected fescue species select particular epiphytic bacterial microbiota [39] with loline alkaloids implicated as a significant carbon source for certain bacterial genera including *Burkholderia*, *Serratia*, *Pseudomonas* and *Stenotrophomonas* [124]. In the rhizosphere, strains of these bacterial taxa have subsequently been shown to outcompete and suppress the growth of non-loline catabolizing strains [124]. *Epichloë* endophytes can also impact plant reproduction with endophyte-infected seed harbouring higher populations of plant-growth promoting bacteria compared to endophyte-free varieties, with these bacteria possibly playing an important role in the fitness of the subsequent seedlings [126]. Further work is looking at how *Epichloë* endophytes may shape entire ecological communities [15,127].

A substantial amount of research has investigated the interaction between *Epichloë* species and well-known beneficial microorganisms, such as arbuscular mycorrhizal (AM) fungi [128]. AM fungi aid the host by supplying mineral nutrients (mostly phosphorus) improving the nutritional status of colonised plants while also increasing the host's tolerance to certain abiotic and biotic stresses [4,129]. In planta studies investigating the interaction between *Epichloë* endophytes and AM fungi show that the amount by which symbiotic plant roots are colonised by AM fungi depends on the type of grass-*Epichloë* association [130]. For example, agronomic, novel grass-*Epichloë* associations often have lower amounts of mycorrhizal mycelia in roots of symbiotic plants (i.e., artificial symbioses: *L. perenne*-*E. festucae* var. *lolii*, *Lolium multiflorum*-*Epichloë occultans*, and *F. arundinacea*-*E. coenophiala*) while wild grasses infected with their co-evolved *Epichloë* endophytes usually display greater abundances of AM fungi in roots of symbiotic plants (i.e., *Bromus* spp. and *Poa* spp.) [131–140]. Further complexities also exist with regard to species interactions [141,142]. *Epichloë*-derived bioactive compounds, competition for nutrients, and/or changes in the levels of plant resistance to microorganisms have been proposed as mechanisms to explain the interaction between *Epichloë* and AM fungi [137].

Recent research from NZ has also determined that *Epichloë* strains can associate closely with specific bacterial species [143] and may work in synergy to antagonise microorganisms

that threaten the survival and reproduction of the host plant. This has been shown in other tripartite interactions within multiple fungal species [144] with bacterial endosymbionts responsible for mycotoxin and phytohormone production including IAA [145,146]. IAA is the major plant auxin and is also synthesized by certain microorganisms, including phytopathogens, saprophytes and symbionts [147]. IAA stimulates the production of plant biomass, enhances growth rate of roots, and is implicated in the promotion of disease resistance [147,148]. Tripartite associations involving *Epichloë* endophytes are not restricted to bacteria with several articles reporting that *Epichloë* spp. can also be infected with mycoviruses [149–151]. Although these viruses appear to have no effect on the phenotype of their fungal hosts, the fungus, or plant infected by the endophytic fungus and the virus, may obtain selective advantages yet to be discovered.

## 5. Future Perspectives

Climate change, the most important challenge currently facing mankind [152] is predicted to have serious implications for many agricultural systems. The interaction between disease and crops is as old as agriculture itself [153] but with increasing temperatures and changing precipitation patterns, it is expected that plant disease outbreaks may intensify in some production areas due to invasions of new phytopathogens and/or due to increases in the severity of existing phytopathogens [154–156]. Increasing atmospheric CO<sub>2</sub> levels will impact the degree of resistance exhibited by many plant species to pathogen attack while also altering the availability of photosynthates and defensive compounds produced by plant-associated microorganisms, including *Epichloë* [66,157,158]. For example, when CO<sub>2</sub> was artificially elevated, the beneficial effect of *Epichloë* on its tall fescue host was lost with respect to plant growth and pathogen resistance towards *C. lunata* [66]. Other gases involved in climate change, such as tropospheric ozone, have also been shown to have detrimental effects on plant host fitness and the concentration of *Epichloë*-derived defense compounds [159].

Further challenges include improving and/or changing current agricultural practices that are not sustainable as they can expend valuable resources while degrading the environment [160]. Many agrichemicals have negative effects on the environment due to overuse and inefficient application [161] while the control of plant diseases using synthetic pesticides raises serious concerns about food safety, environmental quality and pathogen resistance [162]. Coupled with other pastoral management practices (e.g., tillage), this has also led to a decrease in soil biodiversity [163] in many regions worldwide. Integrating knowledge from both agricultural and natural ecosystems, from single plants and multispecies plant communities, and from below-ground and above-ground multitrophic interactions holds great promise to further improve the sustainability of crop production, including the need for alternative disease management practices [164].

While *Epichloë* endophytes are not naturally found in modern cereal grasses it has been demonstrated that *Epichloë* strains from wild cereal grass relatives [165] can be inoculated into barley (*Hordeum vulgare*), rye (*Secale cereale*) and wheat (*Triticum aestivum*) to create artificial plant-endophyte associations [166–168]. Field trials with *Epichloë*-infected rye have shown reductions in the prevalence of leaf rust (*Puccinia recondita*) and leaf streak (*Cercosporidium graminis*) [65]. The potential for other fungal endophyte taxa to be used as biological control agents against phytopathogens in rice, wheat and maize has been proposed as a worthy research aim [169].

## 6. Concluding Remarks

Microorganisms have been administered as biological control agents for many decades to manage disease and pest pressures on crop plants. However, they still only make up a small percentage of all pest control products. As well as their overall bioactivity and efficacy in the field, many other factors (such as their stability, reliability, storage and application) must be taken into consideration for the development of commercially successful biological control agents [170]. Endophytes can overcome many of the difficulties faced by traditional

biological control agents as they are encapsulated within the host plant and protected from environmental conditions that disrupt their survival and biocontrol efficacy. Additionally, for those biocontrol agents that are seed transmitted, such as *Epichloë* endophytes, there is an extra advantage for commercialisation as there is no need to develop complicated formulations and delivery techniques [171]. Biological control of phytopathogens is often achieved by the artificial introduction of antagonistic microorganisms into a selected environment. These antagonists may exhibit several mechanisms of action that work in synergy to suppress any one phytopathogen at any one time and although *Epichloë*-derived antibiosis may be overrepresented in many in vitro experiments this mechanism may still play a pivotal role in the protection of grass hosts from phytopathogens. Although *Epichloë* endophyte colonization is generally restricted to the host's aboveground tissues, their bioactivity (at least towards invertebrate herbivores, via antibiosis) extends further, as many endophyte-derived alkaloids are mobilized within the plant's vascular system and translocated to plant organs, such as the roots, where fungal colonization is absent [119,172]. Even volatile secondary metabolites derived from *Epichloë* endophytes have been reported in the roots of endophyte-infected plants [173,174].

Therefore, primary in vitro bioassays, aimed at assessing endophytes for their antagonism towards phytopathogens, must be developed to provide more reliable predictions of field performance [175]. The results from these improved bioassays, coupled with a greater understanding of the mechanisms of action attributed to these *Epichloë* endophytes, will likely lead to the development of ecologically sound and commercially viable *Epichloë*-grass associations with pest and disease control abilities.

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## References

- Rodriguez, R.; Redman, R. More than 400 million years of evolution and some plants still can't make it on their own: Plant stress tolerance via fungal symbiosis. *J. Exp. Bot.* **2008**, *59*, 1109–1114. [[CrossRef](#)] [[PubMed](#)]
- Zipfel, C.; Oldroyd, G.E.D. Plant signalling in symbiosis and immunity. *Nature* **2017**, *543*, 328–336. [[CrossRef](#)] [[PubMed](#)]
- Redman, R.S.; Dunigan, D.D.; Rodriguez, R.J. Fungal symbiosis from mutualism to parasitism: Who controls the outcome, host or invader? *New Phytol.* **2001**, *151*, 705–716. [[CrossRef](#)] [[PubMed](#)]
- Partida-Martinez, L.P.P.; Heil, M. The microbe-free plant: Fact or artifact? *Front. Plant Sci.* **2011**, *2*, 100. [[CrossRef](#)]
- Clay, K.; Holah, J. Fungal endophyte symbiosis and plant diversity in successional fields. *Science* **1999**, *285*, 1742–1744. [[CrossRef](#)]
- Kogel, K.-H.; Franken, P.; Hückelhoven, R. Endophyte or parasite—What decides? *Curr. Opin. Plant Biol.* **2006**, *9*, 358–363. [[CrossRef](#)]
- Heckman, D.S.; Geiser, D.M.; Eidell, B.R.; Stauffer, R.L.; Kardos, N.L.; Hedges, S.B. Molecular evidence for the early colonization of land by fungi and plants. *Science* **2001**, *293*, 1129–1133. [[CrossRef](#)]
- Margulis, L. Symbiosis and evolution. *Sci. Am.* **1971**, *225*, 48–61. [[CrossRef](#)]
- Remy, W.; Taylor, T.N.; Hass, H.; Kerp, H. Four hundred-million-year-old vesicular arbuscular mycorrhizae. *Proc. Natl. Acad. Sci. USA* **1994**, *91*, 11841–11843. [[CrossRef](#)] [[PubMed](#)]
- Pirozynski, K.A.; Malloch, D.W. The origin of land plants: A matter of mycotrophism. *Biosystems* **1975**, *6*, 153–164. [[CrossRef](#)]
- Rosenberg, E.; Sharon, G.; Zilber-Rosenberg, I. The hologenome theory of evolution contains Lamarckian aspects within a Darwinian framework. *Environ. Microbiol.* **2009**, *11*, 2959–2962. [[CrossRef](#)]

12. Rosenberg, E.; Sharon, G.; Atad, I.; Zilber-Rosenberg, I. The evolution of animals and plants via symbiosis with microorganisms. *Environ. Microbiol. Rep.* **2010**, *2*, 500–506. [[CrossRef](#)] [[PubMed](#)]
13. Johnson, L.J.; Bastias, D.A.; Caradus, J.R.; Chettria, P.; Forester, N.T.; Mace, W.J.; Miller, T.A.; Moon, C.D.; Voisey, C.R.; Zhang, W.; et al. The dynamic mechanisms underpinning symbiotic *Epichloë*–Grass interactions: Implications for sustainable and resilient agriculture. In *Microbiome Stimulants for Crops: Mechanisms and Applications*; White, J., Kumar, A., Droby, S., Eds.; Woodhead Publishing: Sawston, UK, 2021.
14. Suttie, J.M.; Reynolds, S.G.; Batello, C. *Grasslands of the World*; Food & Agriculture Organization: Rome, Italy, 2005; Volume 34.
15. Nissinen, R.; Helander, M.; Kumar, M.; Saikkonen, K. Heritable *Epichloë* symbiosis shapes fungal but not bacterial communities of plant leaves. *Sci. Rep.* **2019**, *9*, 5253. [[CrossRef](#)]
16. Gibson, D.J. *Grasses and Grassland Ecology*; Oxford University Press: Oxford, UK, 2009.
17. Schardl, C.L. The epichloae, symbionts of the grass subfamily poöideae. *Ann. Mo. Bot. Gard.* **2010**, *97*, 646–665. [[CrossRef](#)]
18. Schardl, C.L.; Leuchtman, A.; Chung, K.-R.; Penny, D.; Siegel, M.R. Coevolution by common descent of fungal symbionts (*Epichloë* spp.) and grass hosts. *Mol. Biol. Evol.* **1997**, *14*, 133–143. [[CrossRef](#)]
19. Schardl, C.L.; Phillips, T.D. Protective grass endophytes: Where are they from and where are they going? *Plant Dis.* **1997**, *81*, 430–438. [[CrossRef](#)] [[PubMed](#)]
20. Spatafora, J.; Sung, G.; Sung, J.; Hywel-Jones, N.; White, J.F., Jr. Phylogenetic evidence for an animal pathogen origin of ergot and the grass endophytes. *Mol. Ecol.* **2007**, *16*, 1701–1711. [[CrossRef](#)]
21. Sung, G.-H.; Poinar, G.O.; Spatafora, J.W. The oldest fossil evidence of animal parasitism by fungi supports a Cretaceous diversification of fungal–arthropod symbioses. *Mol. Phylogenet. Evol.* **2008**, *49*, 495–502. [[CrossRef](#)]
22. Leuchtman, A.; Bacon, C.W.; Schardl, C.L.; White, J.F.; Tadych, M. Nomenclatural realignment of *Neotyphodium* species with genus. *Epic. Mycol.* **2014**, *106*, 202–215. [[CrossRef](#)]
23. Chung, K.-R.; Schardl, C. Sexual cycle and horizontal transmission of the grass symbiont *Epichloë typhina*. *Mycol. Res.* **1997**, *101*, 295–301. [[CrossRef](#)]
24. Zhang, W.; Card, S.D.; Mace, W.J.; Christensen, M.J.; McGill, C.R.; Matthew, C. Defining the pathways of symbiotic *Epichloë* colonization in grass embryos with confocal microscopy. *Mycologia* **2017**, *109*, 153–161. [[CrossRef](#)] [[PubMed](#)]
25. Liu, J.; Nagabhyru, P.; Schardl, C.L. *Epichloë festucae* endophytic growth in florets, seeds, and seedlings of perennial ryegrass (*Lolium perenne*). *Mycologia* **2017**, *109*, 691–700. [[CrossRef](#)] [[PubMed](#)]
26. Wernegreen, J.J. Endosymbiosis. *Curr. Biol.* **2012**, *22*, R555–R561. [[CrossRef](#)]
27. Clay, K. Fungal endophytes of grasses: A defensive mutualism between plants and fungi. *Ecology* **1988**, *69*, 10–16. [[CrossRef](#)]
28. Schardl, C.L.; Young, C.A.; Faulkner, J.R.; Florea, S.; Pan, J. Chemotypic diversity of epichloae, fungal symbionts of grasses. *Fungal Ecol.* **2012**, *5*, 331–344. [[CrossRef](#)]
29. Caradus, J.R.; Johnson, L.J. Improved adaptation of temperate grasses through mutualism with fungal endophytes. In *Endophyte Biotechnology: Potential for Agriculture and Pharmacology*; Schouten, A., Ed.; CABI: Wageningen, The Netherlands, 2019; pp. 85–108.
30. Johnson, L.J.; Caradus, J.R. The science required to deliver *Epichloë* endophytes to commerce. *Endophytes Grow. World* **2019**, 343–370. [[CrossRef](#)]
31. Johnson, L.; de Bonth, A.; Briggs, L.; Caradus, J.; Finch, S.; Fleetwood, D.; Fletcher, L.; Hume, D.; Johnson, R.; Popay, A.J.; et al. The exploitation of epichloae endophytes for agricultural benefit. *Fungal Divers.* **2013**, *60*, 171–188. [[CrossRef](#)]
32. Caradus, J.R.; Card, S.D.; Finch, S.C.; Hume, D.E.; Johnson, L.J.; Mace, W.J.; Popay, A.J. Ergot alkaloids in New Zealand pastures and their impact. *N. Z. J. Agric. Res.* **2020**, *63*, 1–41. [[CrossRef](#)]
33. Gallagher, R.T.; White, E.P.; Mortimer, P.H. Ryegrass staggers: Isolation of potent neurotoxins lolitrem A and lolitrem B from staggers-producing pastures. *N. Z. Vet. J.* **1981**, *29*, 189–190. [[CrossRef](#)]
34. Bacon, C.W.; Porter, J.K.; Robbins, J.D.; Luttrell, E.S. *Epichloë typhina* from toxic tall fescue grasses. *Appl. Environ. Microbiol.* **1977**, *34*, 576–581. [[CrossRef](#)] [[PubMed](#)]
35. Card, S.; Johnson, L.; de Bonth, A.; Tapper, B.; Mace, W.; Faville, M.; Pennell, C.; Caradus, J.; Hume, D. *Epichloë* endophytes from cool season grasses—reaping the rewards from a well-tuned bio-prospecting pipeline. In Proceedings of the 10th International Mycological Congress, Bangkok, Thailand, 3–8 August 2014.
36. De Bonth, A.; Card, S.; Briggs, L.; Faville, M.; Finch, S.; Hong, W.; Johnson, L.; Liu, L.; Mace, W.; Pennell, C. Fungal foray: The pursuit of beneficial endophyte strains for Australasian pastures. In Proceedings of the 9th International Symposium on Fungal Endophytes of Grasses, Melbourne, VIC, Australia, 28 September–1 October 2015.
37. Ren, A.-Z.; Wang, Y.-H.; Gao, Y.-B. Difference in antifungal activity of morphotypes of clavicipitaceous endophytes within and between species. *Acta Ecol. Sin.* **2009**, *29*, 227–231. [[CrossRef](#)]
38. Tian, P.; Nan, Z.; Li, C.; Spangenberg, G. Effect of the endophyte *Neotyphodium lolii* on susceptibility and host physiological response of perennial ryegrass to fungal pathogens. *Eur. J. Plant Pathol.* **2008**, *122*, 593–602. [[CrossRef](#)]
39. Roberts, E.; Lindow, S. Loline alkaloid production by fungal endophytes of *Fescue* species select for particular epiphytic bacterial microflora. *ISME J.* **2014**, *8*, 359–368. [[CrossRef](#)] [[PubMed](#)]
40. Siegel, M.R.; Latch, G.C.M. Expression of antifungal activity in agar culture by isolates of grass endophytes. *Mycologia* **1991**, *83*, 529–537. [[CrossRef](#)]
41. Christensen, M.J. Antifungal activity in grasses infected with *Acremonium* and *Epichloë* endophytes. *Australas. Plant Pathol.* **1996**, *25*, 186–191. [[CrossRef](#)]

42. Caradus, J.R.; Johnson, L.J. *Epichloë* fungal endophytes—From a biological curiosity in wild grasses to an essential component of resilient high performing ryegrass and fescue pastures. *J. Fungi* **2020**, *6*, 322. [[CrossRef](#)]
43. Xia, C.; Li, N.; Zhang, Y.; Li, C.; Zhang, X.; Nan, Z. Role of *Epichloë* endophytes in defense responses of cool-season grasses to pathogens: A review. *Plant Dis.* **2018**, *102*, 2061–2073. [[CrossRef](#)]
44. Pérez, L.I.; Gundel, P.E.; Zabalgoageazcoa, I.; Omacini, M. An ecological framework for understanding the roles of *Epichloë* endophytes on plant defenses against fungal diseases. *Fungal Biol. Rev.* **2020**, *34*, 115–125. [[CrossRef](#)]
45. Yue, Q.; Miller, C.J.; White, J.F., Jr.; Richardson, M.D. Isolation and characterization of fungal inhibitors from *Epichloë festucae*. *J. Agric. Food Chem.* **2000**, *48*, 4687–4692. [[CrossRef](#)]
46. Yawen, J.; Rui, Z.; Xingxu, Z. Antagonistic effect of *Epichloë bromicola* of *Hordeum brevisubulatum* on a pathogenic fungus. In Proceedings of the 10th International Symposium on Fungal Endophytes of Grasses, Salamanca, Spain, 18–21 June 2018.
47. White, J.F., Jr.; Cole, G.T. Endophyte-host associations in forage grasses. III. In vitro inhibition of fungi by *Acremonium Coenophialum*. *Mycologia* **1985**, *77*, 487–489. [[CrossRef](#)]
48. White, J.F., Jr.; Cole, G.T. Endophyte-host associations in forage grasses. IV. The endophyte of *Festuca versuta*. *Mycologia* **1986**, *78*, 102–107. [[CrossRef](#)]
49. Paňka, D.; West, C.; Guerber, C.; Richardson, M. Susceptibility of tall fescue to *Rhizoctonia zae* infection as affected by endophyte symbiosis. *Ann. Appl. Biol.* **2013**, *163*, 257–268. [[CrossRef](#)]
50. Li, C.; Gao, J.; Nan, Z. Interactions of *Neotyphodium gansuense*, *Achnatherum inebrians* and plant pathogenic fungi. *Mycol. Res.* **2007**, *111*, 1220–1227. [[CrossRef](#)]
51. Gwinn, K.D.; Gavin, A.M. Relationship between endophyte infestation level of tall fescue seed lots and *Rhizoctonia zae* seedling disease. *Plant Dis.* **1992**, *76*, 911–914. [[CrossRef](#)]
52. Fernando, K.; Reddy, P.; Hettiarachige, I.K.; Spangenberg, G.C.; Rochfort, S.J.; Guthridge, K.M. Novel antifungal activity of *Lolium*-associated *Epichloë* endophytes. *Microorganisms* **2020**, *8*, 955. [[CrossRef](#)]
53. Niones, J.T.; Takemoto, D. An isolate of *Epichloë festucae*, an endophytic fungus of temperate grasses, has growth inhibitory activity against selected grass pathogens. *J. Gen. Plant Pathol.* **2014**, *80*, 337–347. [[CrossRef](#)]
54. Purev, E.; Kondo, T.; Takemoto, D.; Niones, J.T.; Ojika, M. Identification of  $\epsilon$ -Poly-L-lysine as an antimicrobial product from an *Epichloë* endophyte and isolation of fungal  $\epsilon$ -PL synthetase gene. *Molecules* **2020**, *25*, 1032. [[CrossRef](#)]
55. Niones, J.T.; Takemoto, D. VibA, a homologue of a transcription factor for fungal heterokaryon incompatibility, is involved in antifungal compound production in the plant-symbiotic fungus *Epichloe festucae*. *Eukaryot. Cell* **2015**, *14*, 13–24. [[CrossRef](#)] [[PubMed](#)]
56. Clarke, B.B.; White, J.F., Jr.; Hurley, R.H.; Torres, M.S.; Sun, S.; Huff, D.R. Endophyte-mediated suppression of dollar spot disease in fine fescues. *Plant Dis.* **2006**, *90*, 994–998. [[CrossRef](#)]
57. Paňka, D.; Jeske, M.; Troczyński, M. Occurrence of *Neotyphodium* and *Epichloë* fungi in meadow fescue and red fescue in Poland and screening of endophyte isolates as potential biological control agents. *Acta Sci. Pol. Hortorum Cultus* **2013**, *12*, 67–83.
58. Christensen, M.; Latch, G.; Tapper, B. Variation within isolates of *Acremonium* endophytes from perennial rye-grasses. *Mycol. Res.* **1991**, *95*, 918–923. [[CrossRef](#)]
59. Holzmann-Wirth, A.; Dapprich, P.; Eierdanz, S.; Heerz, D.; Paul, V. Anti-fungal substances extracted from *Neotyphodium* endophytes. In Proceedings of the 3rd International Conference on Harmful and Beneficial Microorganisms in Grassland, Pasture and Turf, Soest, Germany, 26 September 2000.
60. Pérez, L.I.; Gundel, P.E.; Omacini, M. Can the defensive mutualism between grasses and fungal endophytes protect non-symbiotic neighbours from soil pathogens? *Plant Soil* **2016**, *405*, 289–298. [[CrossRef](#)]
61. Zhou, L.; Zhang, X.; Li, C.; Christensen, M.J.; Nan, Z. Antifungal activity and phytochemical investigation of the asexual endophyte of *Epichloë* sp. from *Festuca sinensis*. *Sci. China Life Sci.* **2015**, *58*, 821. [[CrossRef](#)]
62. Lian-Yu, Z.; Song, Z.; Hong-Mei, D.; Feng, Q. Antimicrobial activity and composition of volatile substance of *Epichloë* sp. endophyte isolated from *Festuca sinensis*. *Nat. Prod. Res. Dev.* **2019**, *31*, 1543.
63. Wäli, P.R.; Helander, M.; Nissinen, O.; Saikkonen, K. Susceptibility of endophyte-infected grasses to winter pathogens (snow molds). *Botany* **2006**, *84*, 1043–1051. [[CrossRef](#)]
64. Wang, X.; Qin, J.; Chen, W.; Zhou, Y.; Ren, A.; Gao, Y. Pathogen resistant advantage of endophyte-infected over endophyte-free *Leymus chinensis* is strengthened by pre-drought treatment. *Eur. J. Plant Pathol.* **2016**, *144*, 477–486. [[CrossRef](#)]
65. Hume, D.E.; Drummond, J.B.; Rolston, M.P.; Simpson, W.R.; Johnson, R.D. *Epichloë* endophyte improves agronomic performance and grain yield of rye (*Secale cereale*). In Proceedings of the 10th International Symposium on Fungal Endophytes of Grasses, Salamanca, Spain, 18–21 June 2018.
66. Chen, W.; Liu, H.; Gao, Y.; Card, S.D.; Ren, A. The advantages of endophyte-infected over uninfected tall fescue in the growth and pathogen resistance are counteracted by elevated CO<sub>2</sub>. *Sci. Rep.* **2017**, *7*, 1–12. [[CrossRef](#)]
67. Bonos, S.A.; Wilson, M.M.; Meyer, W.A.; Funk, C.R. Suppression of red thread in fine fescues through endophyte-mediated resistance. *Appl. Turfgrass Sci.* **2005**, *2*, 1–7. [[CrossRef](#)]
68. Guo, Y.; Gao, P.; Li, F.; Duan, T. Effects of AM fungi and grass endophytes on perennial ryegrass *Bipolaris sorokiniana* leaf spot disease under limited soil nutrients. *Eur. J. Plant Pathol.* **2019**, *154*, 659–671. [[CrossRef](#)]
69. Li, F.; Duan, T.; Li, Y. Effects of the fungal Endophyte *Epichloë festucae* var. *lolii* on growth and physiological responses of perennial ryegrass cv. Fairway to combined drought and pathogen stresses. *Microorganisms* **2020**, *8*, 1917. [[CrossRef](#)]



70. Pańka, D.; Piesik, D.; Jeske, M.; Baturo-Cieśniewska, A. Production of phenolics and the emission of volatile organic compounds by perennial ryegrass (*Lolium perenne* L.)/*Neotyphodium lolii* association as a response to infection by *Fusarium Poae*. *J. Plant Physiol.* **2013**, *170*, 1010–1019. [[CrossRef](#)]
71. Lowe, K.F.; Bowdler, T.M.; Hume, D.E.; Casey, N.D.; Tapper, B.A. The effect of endophyte on the performance of irrigated perennial ryegrasses in subtropical Australia. *Aust. J. Agric. Res.* **2008**, *59*, 567–577. [[CrossRef](#)]
72. Ma, M.; Christensen, M.J.; Nan, Z. Effects of the endophyte *Epichloë festucae* var. *lolii* of perennial ryegrass (*Lolium perenne*) on indicators of oxidative stress from pathogenic fungi during seed germination and seedling growth. *Eur. J. Plant Pathol.* **2015**, *141*, 571–583. [[CrossRef](#)]
73. Wheatley, W.M.; Nicol, H.I.; Hunt, E.R.; Nikandrow, A.; Cother, N. An association between perennial ryegrass endophyte, a leafspot caused by (*Pyrenophora seminiperda*) and preferential grazing by sheep. In Proceedings of the 3rd International Conference on Harmful and Beneficial Microorganisms in Grassland, Pastures and Turf, Soest, Germany, 26 September 2000.
74. Liu, L.; Guo, C.; Lv, H.; Gu, L.; Li, C. Effects of the *Epichloë gansuensis* endophyte on the disease resistance of drunken horse grass to powdery mildew. *Acta Prataculturae Sin.* **2015**, *24*, 65–71.
75. Xia, C.; Zhang, X.; Christensen, M.J.; Nan, Z.; Li, C. *Epichloë* endophyte affects the ability of powdery mildew (*Blumeria graminis*) to colonise drunken horse grass (*Achnatherum inebrians*). *Fungal Ecol.* **2015**, *16*, 26–33. [[CrossRef](#)]
76. Xia, C.; Li, N.; Zhang, X.; Feng, Y.; Christensen, M.J.; Nan, Z. An *Epichloë* endophyte improves photosynthetic ability and dry matter production of its host *Achnatherum inebrians* infected by *Blumeria graminis* under various soil water conditions. *Fungal Ecol.* **2016**, *22*, 26–34. [[CrossRef](#)]
77. Kou, M.-Z.; Bastías, D.A.; Christensen, M.J.; Zhong, R.; Nan, Z.-B.; Zhang, X.-X. The plant salicylic acid signalling pathway regulates the infection of a biotrophic pathogen in grasses associated with an *Epichloë* endophyte. *J. Fungi* **2021**, *7*, 633. [[CrossRef](#)]
78. Zhang, H.; Li, X.; White, J.F.; Wei, X.; He, Y.; Li, C. *Epichloë* endophyte improves ergot disease resistance of host (*Achnatherum inebrians*) by regulating leaf senescence and photosynthetic capacity. *J. Plant Growth Regul.* **2021**, 1–10. [[CrossRef](#)]
79. Shi, X.; Qin, T.; Liu, H.; Wu, M.; Li, J.; Shi, Y.; Gao, Y.; Ren, A. Endophytic fungi activated similar defense strategies of *Achnatherum sibiricum* host to different trophic types of pathogens. *Front. Microbiol.* **2020**, *11*, 1607. [[CrossRef](#)] [[PubMed](#)]
80. Perez, L.I.; Gundel, P.E.; Marrero, H.J.; Arzac, A.G.; Omacini, M. Symbiosis with systemic fungal endophytes promotes host escape from vector-borne disease. *Oecologia* **2017**, *184*, 237–245. [[CrossRef](#)]
81. Wang, Y.; Luo, Y.; Tian, P.; Peng, H.; Feng, J. Preliminary evaluation of the disease resistance of *Festuca sinensis* infected by *Epichloë sinensis*. *J. Phytopathol.* **2021**, *169*, 623–629. [[CrossRef](#)]
82. Iannone, L.J.; Vignale, M.V.; Pinget, A.D.; Re, A.; Cargo, P.D.M.; Novas, M.V. Seed-transmitted *Epichloë* sp. endophyte alleviates the negative effects of head smut of grasses (*Ustilago bullata*) on *Bromus Auleticus*. *Fungal Ecol.* **2017**, *29*, 45–51. [[CrossRef](#)]
83. Kauppinen, M.; Helander, M.; Anttila, N.; Saloniemi, I.; Saikkonen, K. *Epichloë* endophyte effects on leaf blotch pathogen (*Rhynchosporium* sp.) of tall fescue (*Schedonorus phoenix*) vary among grass origin and environmental conditions. *Plant Ecol. Divers.* **2018**, *11*, 625–635. [[CrossRef](#)]
84. Wiewióra, B.; Żurek, G.; Żurek, M. Endophyte-mediated disease resistance in wild populations of perennial ryegrass (*Lolium perenne*). *Fungal Ecol.* **2015**, *15*, 1–8. [[CrossRef](#)]
85. Greulich, F.; Horio, E.; Shimanuki, T.; Yoshihara, T. Field results confirm natural plant protection by the endophytic fungus *Epichloë typhina* against the pathogenic fungus *Cladosporium phlei* on timothy leaves. *Jpn. J. Phytopathol.* **1999**, *65*, 454–459. [[CrossRef](#)]
86. Shimanuki, T. Studies on the mechanisms of the infection of timothy with purple spot disease caused by *Cladosporium phlei* (Gregory) de Vries. *Res. Bull. Hokkaido Natl. Agric. Exp. Stn.* **1987**, *148*, 1–56.
87. Panka, D.; Podkowka, L.; Lamparski, R. Preliminary observations on the resistance of meadow fescue (*Festuca pratensis* Huds.) infected by *Neotyphodium uncinatum* to diseases and pest and nutritive value. In Proceedings of the 5th International Symposium on *Neotyphodium*/ Grass Interactions, University of Arkansas, Fayetteville, AK, USA, 23–26 May 2004.
88. Andrews, J.H. Biological control in the phyllosphere. *Annu. Rev. Phytopathol.* **1992**, *30*, 603–635. [[CrossRef](#)]
89. Whitaker, B.K.; Bakker, M.G. Bacterial endophyte antagonism toward a fungal pathogen in vitro does not predict protection in live plant tissue. *FEMS Microbiol. Ecol.* **2018**, *95*, fiy237.
90. Yakti, W.; Kovács, G.M.; Franken, P. Differential interaction of the dark septate endophyte *Cadophora* sp. and fungal pathogens in vitro and in planta. *FEMS Microbiol. Ecol.* **2019**, *95*, fiz164. [[CrossRef](#)]
91. Blackenship, J.D.; Spiering, M.J.; Wilkinson, H.H.; Fannin, F.F.; Bush, L.P.; Schardl, C.L. Production of loline alkaloids by the grass endophyte, *Neotyphodium uncinatum*, in defined media. *Phytochemistry* **2001**, *58*, 395–401. [[CrossRef](#)]
92. Spanu, P.D. The genomics of obligate (and nonobligate) biotrophs. *Annu. Rev. Phytopathol.* **2011**, *50*, 91–109. [[CrossRef](#)] [[PubMed](#)]
93. Zabalgoageazcoa, I. Fungal endophytes and their interaction with plant pathogens. *Span. J. Agric. Res.* **2008**, *6*, 138–146. [[CrossRef](#)]
94. De Kesel, J.; Conrath, U.; Flors, V.; Luna, E.; Mageroy, M.H.; Mauch-Mani, B.; Pastor, V.; Pozo, M.J.; Pieterse, C.M.; Ton, J. The induced resistance lexicon: Do's and don'ts. *Trends Plant Sci.* **2021**, *26*, 685–691. [[CrossRef](#)]
95. Viterbo, A.; Horwitz, B.A. Mycoparasitism. In *Cellular and Molecular Biology of Filamentous Fungi*; American Society for Microbiology Press: Washington, DC, USA, 2010; pp. 676–693.
96. Christensen, M.J.; Zhang, X.; Scott, B. Regulation switching of *Epichloë typhina* within elongating perennial ryegrass leaves. *Mycol. Res.* **2008**, *112*, 1056–1062. [[CrossRef](#)] [[PubMed](#)]

97. Christensen, M.J.; Bennett, R.J.; Ansari, H.A.; Koga, H.; Johnson, R.D.; Bryan, G.T.; Simpson, W.R.; Koolaard, J.P.; Nickless, E.M.; Voisey, C.R. *Epichloë* endophytes grow by intercalary hyphal extension in elongating grass leaves. *Fungal Genet. Biol.* **2008**, *45*, 84–93. [[CrossRef](#)]
98. Yoshihara, T.; Togiya, S.; Koshino, H.; Sakamura, S.; Shimanuki, T.; Sato, T.; Tajimi, A. Three fungitoxic cyclopentanoid sesquiterpenes from stromata of *Epichloë Typhina*. *Tetrahedron Lett.* **1985**, *26*, 5551–5554. [[CrossRef](#)]
99. Koshino, H.; Terada, S.-I.; Yoshihara, T.; Sakamura, S.; Shimanuki, T.; Sato, T.; Tajimi, A. Three phenolic acid derivatives from stromata of *Epichloë typhina* on *Phleum Pratense*. *Phytochemistry* **1988**, *27*, 1333–1338. [[CrossRef](#)]
100. Koshino, H.; Togiya, S.; Yoshihara, T.; Sakamura, S.; Shimanuki, T.; Sato, T.; Tajimi, A. Four fungitoxic C-18 hydroxy unsaturated fatty acids from stromata of *Epichloë Typhina*. *Tetrahedron Lett.* **1987**, *28*, 73–76. [[CrossRef](#)]
101. Koshino, H.; Yoshihara, T.; Sakamura, S.; Shimanuki, T.; Sato, T.; Tajimi, A. A ring B aromatic sterol from stromata of *Epichloë Typhina*. *Phytochemistry* **1989**, *28*, 771–772. [[CrossRef](#)]
102. Bultman, T.L.; Leuchtman, A. Biology of the *Epichloë-Botanophila* interaction: An intriguing association between fungi and insects. *Fungal Biol. Rev.* **2008**, *22*, 131–138. [[CrossRef](#)]
103. Schiestl, F.P.; Steinbrunner, F.; Schulz, C.; von Reub, S.; Francke, W.; Weymuth, C.; Leuchtman, A. Evolution of ‘pollinator’-attracting signals in fungi. *Biol. Lett.* **2006**, *2*, 401–404. [[CrossRef](#)]
104. Koulman, A.; Lane, G.; Christensen, M.; Fraser, K.; Tapper, B.A. Peramine and other fungal alkaloids are exuded in the guttation fluid of endophyte-infected grasses. *Phytochemistry* **2007**, *68*, 355–360. [[CrossRef](#)]
105. Pieterse, C.M.; van der Does, D.; Zamioudis, C.; Leon-Reyes, A.; van Wees, S.C. Hormonal modulation of plant immunity. *Annu. Rev. Cell Dev. Biol.* **2012**, *28*, 489–521. [[CrossRef](#)]
106. Glazebrook, J. Contrasting mechanisms of defense against biotrophic and necrotrophic pathogens. *Annu. Rev. Phytopathol.* **2005**, *43*, 205–227. [[CrossRef](#)]
107. Schmid, J.; Day, R.; Zhang, N.; Dupont, P.-Y.; Cox, M.P.; Schardl, C.L.; Minards, N.; Truglio, M.; Moore, N.; Harris, D.R. Host tissue environment directs activities of an *Epichloë* endophyte, while it induces systemic hormone and defense responses in its native perennial ryegrass host. *Mol. Plant-Microbe Interact.* **2017**, *30*, 138–149. [[CrossRef](#)]
108. Moy, M.; Belanger, F.; Duncan, R.; Freehoff, A.; Leary, C.; Meyer, W.; Sullivan, R.; White, J.F., Jr. Identification of epiphyllous mycelial nets on leaves of grasses infected by clavicipitaceous endophytes. *Symbiosis* **2000**, *28*, 291–302.
109. Tadych, M.; White, J. Ecology of epiphyllous stages of endophytes and implications for horizontal dissemination. *NZGA Res. Pract. Ser.* **2006**, *13*, 157–161. [[CrossRef](#)]
110. Wang, H.; Sun, S.; Ge, W.; Zhao, L.; Hou, B.; Wang, K.; Lyu, Z.; Chen, L.; Xu, S.; Guo, J.; et al. Horizontal gene transfer of *Fhb7* from fungus underlies *Fusarium* head blight resistance in wheat. *Science* **2020**, *368*, eaba5435. [[CrossRef](#)] [[PubMed](#)]
111. Wulff, B.B.H.; Jones, J.D.G. Breeding a fungal gene into wheat. *Science* **2020**, *368*, 822. [[CrossRef](#)] [[PubMed](#)]
112. Ambrose, K.V.; Belanger, F.C. SOLiD-SAGE of endophyte-infected red fescue reveals numerous effects on host transcriptome and an abundance of highly expressed fungal secreted proteins. *PLoS ONE* **2012**, *7*, e53214. [[CrossRef](#)]
113. Wang, R.; Luo, S.; Clarke, B.B.; Belanger, F.C. The *Epichloë festucae* antifungal protein Efe-AfpA is also a possible effector protein required for the interaction of the fungus with its host grass *Festuca rubra* subsp. *rubra*. *Microorganisms* **2021**, *9*, 140. [[CrossRef](#)]
114. Torres, M.; Singh, A.; Vorsa, N.; Gianfagna, T. Were endophytes pre-adapted for defensive mutualism? *NZGA Res. Pract. Ser.* **2006**, *13*, 63–67. [[CrossRef](#)]
115. Xu, X.; Jeger, M. More ecological research needed for effective biocontrol of plant pathogens. In *How Research Can Stimulate the Development of Commercial Biological Control Against Plant Diseases*; Springer: Berlin/Heidelberg, Germany, 2020; pp. 15–30.
116. Kuldau, G.; Bacon, C. Clavicipitaceous endophytes: Their ability to enhance resistance of grasses to multiple stresses. *Biol. Control* **2008**, *46*, 57–71. [[CrossRef](#)]
117. Glare, T.; Caradus, J.; Gelernter, W.; Jackson, T.; Keyhani, N.; Köhl, J.; Marrone, P.; Morin, L.; Stewart, A. Have biopesticides come of age? *Trends Biotechnol.* **2012**, *30*, 250–258. [[CrossRef](#)] [[PubMed](#)]
118. Schardl, C.L.; Craven, K.D.; Speakman, S.; Stromberg, A.; Lindstrom, A.; Yoshida, R. A novel test for host-symbiont codivergence indicates ancient origin of fungal endophytes in grasses. *Syst. Biol.* **2008**, *57*, 483–498. [[CrossRef](#)] [[PubMed](#)]
119. Popay, A.J.; Bonos, S.A. Biotic responses in endophytic grasses. In *Neotyphodium in Cool-Season Grasses*; Roberts, C.A., Charles, C.P., Spiers, D.E., Eds.; Blackwell Publishing: Ames, IA, USA, 2005; pp. 163–185.
120. Bultman, T.L.; Aguilera, A.; Sullivan, T.J. Influence of fungal isolates infecting tall fescue on multitrophic interactions. *Fungal Ecol.* **2012**, *5*, 372–378. [[CrossRef](#)]
121. Omacini, M.; Chaneton, E.J.; Ghersa, C.M.; Müller, C.B. Symbiotic fungal endophytes control insect host–parasite interaction webs. *Nature* **2001**, *409*, 78–81. [[CrossRef](#)]
122. Fuchs, B.; Krischke, M.; Mueller, M.J.; Krauss, J. Peramine and lolitrem B from endophyte-grass associations cascade up the food chain. *J. Chem. Ecol.* **2013**, *39*, 1385–1389. [[CrossRef](#)]
123. Casas, C.; Torretta, J.P.; Exeler, N.; Omacini, M. What happens next? Legacy effects induced by grazing and grass-endophyte symbiosis on thistle plants and their floral visitors. *Plant Soil* **2016**, *405*, 211–229. [[CrossRef](#)]
124. Roberts, E.L.; Ferraro, A. Rhizosphere microbiome selection by *Epichloë* endophytes of *Festuca Arundinacea*. *Plant Soil* **2015**, *396*, 229–239. [[CrossRef](#)]
125. Zhong, R.; Xia, C.; Ju, Y.; Li, N.; Zhang, X.; Nan, Z.; Christensen, M.J. Effects of *Epichloë gansuensis* on root-associated fungal communities of *Achnatherum inebrians* under different growth conditions. *Fungal Ecol.* **2018**, *31*, 29–36. [[CrossRef](#)]

126. Mormile, B.W. Influence of Seed Microbiome on Fitness of *Epichloë* Infected Tall Fescue Seedlings. Master's Thesis, Southern Connecticut State University, New Haven, CT, USA, 2016.
127. Ju, Y.; Zhong, R.; Christensen, M.J.; Zhang, X. Effects of *Epichloë gansuensis* endophyte on the root and rhizosphere soil bacteria of *Achnatherum inebrians* under different moisture conditions. *Front. Microbiol.* **2020**, *11*, 747. [[CrossRef](#)]
128. Liu, Q.; Parsons, A.J.; Xue, H.; Fraser, K.; Ryan, G.D.; Newman, J.A.; Rasmussen, S. Competition between foliar *Neotyphodium lolii* endophytes and mycorrhizal *Glomus* spp. fungi in *Lolium perenne* depends on resource supply and host carbohydrate content. *Funct. Ecol.* **2011**, *25*, 910–920. [[CrossRef](#)]
129. Pozo, M.J.; López-Ráez, J.A.; Azcón-Aguilar, C.; García-Garrido, J.M. Phytohormones as integrators of environmental signals in the regulation of mycorrhizal symbioses. *New Phytol.* **2015**, *205*, 1431–1436. [[CrossRef](#)]
130. Vignale, M.V.; Iannone, L.J.; Novas, M.V. *Epichloë* endophytes of a wild grass promote mycorrhizal colonization of neighbor grasses. *Fungal Ecol.* **2020**, *45*, 100916. [[CrossRef](#)]
131. Arrieta, A.M.; Iannone, L.J.; Scervino, J.M.; Vignale, M.V.; Novas, M.V. A foliar endophyte increases the diversity of phosphorus-solubilizing rhizospheric fungi and mycorrhizal colonization in the wild grass *Bromus Auleticus*. *Fungal Ecol.* **2015**, *17*, 146–154. [[CrossRef](#)]
132. Chu-Chou, M.; Guo, B.; An, Z.-Q.; Hendrix, J.; Ferriss, R.; Siegel, M.; Dougherty, C.; Burrus, P. Suppression of mycorrhizal fungi in fescue by the *Acremonium coenophialum* endophyte. *Soil Biol. Biochem.* **1992**, *24*, 633–637. [[CrossRef](#)]
133. Kalosa-Kenyon, E.; Slaughter, L.C.; Rudgers, J.A.; McCulley, R.L. Asexual *Epichloë* endophytes do not consistently alter arbuscular mycorrhizal fungi colonization in three grasses. *Am. Midl. Nat.* **2018**, *179*, 157–165. [[CrossRef](#)]
134. Mack, K.M.; Rudgers, J.A. Balancing multiple mutualists: Asymmetric interactions among plants, arbuscular mycorrhizal fungi, and fungal endophytes. *Oikos* **2008**, *17*, 310–320. [[CrossRef](#)]
135. Müller, J. Artificial infection by endophytes affects growth and mycorrhizal colonisation of *Lolium Perenne*. *Funct. Plant Biol.* **2003**, *30*, 419–424. [[CrossRef](#)]
136. Novas, M.V.; Cabral, D.; Godeas, A.M. Interaction between grass endophytes and mycorrhizas in *Bromus setifolius* from Patagonia, Argentina. *Symbiosis* **2005**, *40*, 23–30.
137. Novas, M.V.; Iannone, L.J.; Godeas, A.M.; Cabral, D. Positive association between mycorrhiza and foliar endophytes in *Poa bonariensis*, a native grass. *Mycol. Prog.* **2009**, *8*, 75. [[CrossRef](#)]
138. Omacini, M.; Eggers, T.; Bonkowski, M.; Gange, A.; Jones, T. Leaf endophytes affect mycorrhizal status and growth of co-infected and neighbouring plants. *Funct. Ecol.* **2006**, *20*, 226–232. [[CrossRef](#)]
139. Vignale, M.V.; Iannone, L.J.; Scervino, J.M.; Novas, M.V. *Epichloë* exudates promote in vitro and in vivo arbuscular mycorrhizal fungi development and plant growth. *Plant Soil* **2018**, *422*, 267–281. [[CrossRef](#)]
140. Vignale, M.V.; Iannone, L.J.; Pinget, A.D.; de Battista, J.P.; Novas, M.V. Effect of epichloid endophytes and soil fertilization on arbuscular mycorrhizal colonization of a wild grass. *Plant Soil* **2016**, *405*, 279–287. [[CrossRef](#)]
141. Larimer, A.L.; Bever, J.D.; Clay, K. Consequences of simultaneous interactions of fungal endophytes and arbuscular mycorrhizal fungi with a shared host grass. *Oikos* **2012**, *121*, 2090–2096. [[CrossRef](#)]
142. Liu, H.; Wu, M.; Liu, J.; Qu, Y.; Gao, Y.; Ren, A. Tripartite interactions between endophytic fungi, arbuscular mycorrhizal fungi, and *Leymus Chinensis*. *Microb. Ecol.* **2020**, *79*, 98–109. [[CrossRef](#)]
143. Bastías, D.A.; Jauregui, R.; Applegate, E.R.; Altermann, E.; Card, S.D.; Johnson, L.J. Complete genome sequence of *Paenibacillus* sp. strain E222, a bacterial symbiont of an *Epichloë* fungal endophyte of ryegrass. *Microbiol. Resour. Announc.* **2020**, *9*, e00786-20. [[CrossRef](#)] [[PubMed](#)]
144. Bastías, D.A.; Johnson, L.J.; Card, S.D. Symbiotic bacteria of plant-associated fungi: Friends or foes? *Curr. Opin. Plant Biol.* **2020**, *56*, 1–8. [[CrossRef](#)]
145. Partida-Martinez, L.P.; de Looß, C.F.; Ishida, K.; Ishida, M.; Roth, M.; Buder, K.; Hertweck, C. Rhizonin, the first mycotoxin isolated from the zygomycota, is not a fungal metabolite but is produced by bacterial endosymbionts. *Appl. Environ. Microbiol.* **2007**, *73*, 793–797. [[CrossRef](#)] [[PubMed](#)]
146. Hoffman, M.T.; Gunatilaka, M.K.; Wijeratne, K.; Gunatilaka, L.; Arnold, A.E. Endohyphal bacterium enhances production of indole-3-acetic acid by a foliar fungal endophyte. *PLoS ONE* **2013**, *8*, e73132.
147. Tudzynski, B.; Sharon, A. Biosynthesis, biological role and application of fungal phytohormones. In *Industrial Applications*; Springer: Berlin/Heidelberg, Germany, 2002; pp. 183–211.
148. Sharaf, E.F.; Farrag, A.A. Induced resistance in tomato plants by IAA against *Fusarium Oxysporum Lycopersici*. *Pol. J. Microbiol.* **2004**, *53*, 111. [[PubMed](#)]
149. Romo, M.; Leuchtman, A.; García, B.; Zabalgoeazcoa, I. A totivirus infecting the mutualistic fungal endophyte *Epichloë Festucae*. *Virus Res.* **2007**, *124*, 38–43. [[CrossRef](#)] [[PubMed](#)]
150. Zabalgoeazcoa, I.; Benito, E.P.; Ciudad, A.G.; Criado, B.G.; Eslava, A.P. Double-stranded RNA and virus-like particles in the grass endophyte *Epichloë Festucae*. *Mycol. Res.* **1998**, *102*, 914–918. [[CrossRef](#)]
151. Petisco, C.; Garcia-Criado, B.; Zabalgoeazcoa, I.; Vázquez-de-Aldana, B.R. A spectroscopy approach to the study of virus infection in the endophytic fungus *Epichloë festucae*. *Virol. J.* **2011**, *8*, 1–9. [[CrossRef](#)]
152. Burdon, J.J.; Zhan, J. Climate change and disease in plant communities. *PLoS Biol.* **2020**, *18*, e3000949. [[CrossRef](#)] [[PubMed](#)]
153. Martinelli, F.; Scalenghe, R.; Davino, S.; Panno, S.; Scuderi, G.; Ruisi, P.; Villa, P.; Stroppiana, D.; Boschetti, M.; Goulart, L.R. Advanced methods of plant disease detection. A review. *Agron. Sustain. Dev.* **2015**, *35*, 1–25. [[CrossRef](#)]

154. Kocmánková, E.; Trnka, M.; Juroch, J.; Dubrovský, M.; Semerádová, D.; Možný, M.; Žalud, Z. Impact of climate change on the occurrence and activity of harmful organisms. *Plant Prot. Sci.* **2009**, *45*, S48. [[CrossRef](#)]
155. Misra, A.; Yadav, S.; Mishra, S.; Tripathi, M. Impact of meteorological variables and climate change on plant diseases. In *Plant Pathogens*; Apple Academic Press: Palm Bay, FL, USA, 2020; pp. 313–327.
156. Yáñez-López, R.; Torres-Pacheco, I.; Guevara-González, R.G.; Hernández-Zul, M.I.; Quijano-Carranza, J.A.; Rico-García, E. The effect of climate change on plant diseases. *Afr. J. Biotechnol.* **2012**, *11*, 2417–2428. [[CrossRef](#)]
157. Hu, S.; Firestone, M.K.; Chapin, F.S., III. Soil microbial feedbacks to atmospheric CO<sub>2</sub> enrichment. *Trends Ecol. Evol.* **1999**, *14*, 433–437. [[CrossRef](#)]
158. Hunt, M.G.; Rasmussen, S.; Newton, P.C.; Parsons, A.J.; Newman, J.A. Near-term impacts of elevated CO<sub>2</sub>, nitrogen and fungal endophyte-infection on *Lolium perenne* L. growth, chemical composition and alkaloid production. *Plant Cell Environ.* **2005**, *28*, 1345–1354. [[CrossRef](#)]
159. Ueno, A.C.; Gundel, P.E.; Ghersa, C.M.; Demkura, P.V.; Card, S.D.; Mace, W.J.; Martínez-Ghersa, M.A. Ontogenetic and trans-generational dynamics of a vertically transmitted fungal symbiont in an annual host plant in ozone-polluted settings. *Plant Cell Environ.* **2020**, *43*, 2540–2550. [[CrossRef](#)]
160. Pareek, A.; Dhankher, O.P.; Foyer, C.H. Mitigating the impact of climate change on plant productivity and ecosystem sustainability. *J. Exp. Bot.* **2020**, *71*, 451–456. [[CrossRef](#)]
161. Qiu, J. *Nitrogen Fertilizer Warning for China*; Nature Publishing Group: Berlin, Germany, 2009.
162. Dordas, C. Role of nutrients in controlling plant diseases in sustainable agriculture. A review. *Agron. Sustain. Dev.* **2008**, *28*, 33–46. [[CrossRef](#)]
163. FAO. Special Event on Impact of Climate Change, Pests and Diseases on Food Security and Poverty Reduction. Background Document. In Proceedings of the 31st Session of the Committee on World Food Security, Rome, Italy, 13–16 April 2005.
164. Philippot, L.; Raaijmakers, J.M.; Lemanceau, P.; van der Putten, W.H. Going back to the roots: The microbial ecology of the rhizosphere. *Nat. Rev. Microbiol.* **2013**, *11*, 789–799. [[CrossRef](#)] [[PubMed](#)]
165. Card, S.D.; Faville, M.J.; Simpson, W.R.; Johnson, R.D.; Voisey, C.R.; de Bonth, A.C.; Hume, D.E. Mutualistic fungal endophytes in the Triticeae—survey and description. *FEMS Microbiol. Ecol.* **2014**, *88*, 94–106. [[CrossRef](#)] [[PubMed](#)]
166. Simpson, W.R.; Faville, M.J.; Moraga, R.A.; Williams, W.M.; Mcmanus, M.T.; Johnson, R.D. *Epichloë* fungal endophytes and the formation of synthetic symbioses in Hordeae (= Triticeae) grasses. *J. Syst. Evol.* **2014**, *52*, 794–806. [[CrossRef](#)]
167. Simpson, W.R. Hordeae *Epichloë* endophytes and the formation of synthetic symbioses with cereal grasses. Ph.D. Thesis, Massey University, Palmerston North, New Zealand, 2016.
168. Li, C.; Wang, Z.; Chen, T.; Nan, Z. Creation of novel barley germplasm using an *Epichloë* endophyte. *Chin. Sci. Bull.* **2021**, *66*, 2608. [[CrossRef](#)]
169. O’Hanlon, K.A.; Knorr, K.; Jørgensen, L.N.; Nicolaisen, M.; Boelt, B. Exploring the potential of symbiotic fungal endophytes in cereal disease suppression. *Biol. Control* **2012**, *63*, 69–78. [[CrossRef](#)]
170. Lewis, J.A.; Papavizas, G.C. Biocontrol of plant diseases: The approach for tomorrow. *Crop Prot.* **1991**, *10*, 95–105. [[CrossRef](#)]
171. Card, S.; Johnson, L.; Teasdale, S.; Caradus, J. Deciphering endophyte behaviour: The link between endophyte biology and efficacious biological control agents. *FEMS Microbiol. Ecol.* **2016**, *92*. [[CrossRef](#)] [[PubMed](#)]
172. Bryant, R.H.; Cameron, N.E.; Edwards, G.R. Response of black beetle and redheaded pasture cockchafer larvae to loline alkaloids in meadow fescue roots. *N. Z. Plant Prot.* **2010**, *63*, 219–223. [[CrossRef](#)]
173. Rostás, M.; Cripps, M.G.; Silcock, P. Aboveground endophyte affects root volatile emission and host plant selection of a belowground insect. *Oecologia* **2015**, *177*, 487–497. [[CrossRef](#)] [[PubMed](#)]
174. Qawasmeh, A.; Raman, A.; Wheatley, W. Volatiles in perennial ryegrass infected with strains of endophytic fungus: Impact on African black beetle host selection. *J. Appl. Entomol.* **2015**, *139*, 94–104. [[CrossRef](#)]
175. Swadling, I.R.; Jeffries, P. Isolation of microbial antagonists for biocontrol of grey mould disease of strawberries. *Biocontrol Sci. Technol.* **1996**, *6*, 125–136. [[CrossRef](#)]