# *Streptomyces* spp. as biocontrol agents against *Fusarium* species

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## Abstract

Streptomycetes are the largest taxon of antibiotic producers in the microbial world. Nevertheless, they are less studied than other biocontrol agents against Fusarium diseases and, perhaps, plant diseases in general. Plant diseases incited by *Fusarium* species are notably challenging. Four species complexes in the genus are pathogenic: *Fusarium fujikuroi*, *F. graminearum*, *F. solani* and *F. oxysporum*. Being a vascular pathogen, *F. oxysporum* is particularly difficult to control by using microbial antagonists. Most research has remained at early experimental stages, and only few *Streptomyces* spp. strains have been assayed under diverse conditions. Few commercial products consisting of *Streptomyces* spp. have often provided fluctuating results across trials. Five biocontrol trials conducted in the field using streptomycetes report reductions of diverse Fusarium wilts by 0–55%, with one case (cucumber) of yield increase by 1.3-fold. Among 38 articles dealing with pot-experiments, 16 report a disease control level above 50%, seven of which with a level above 70%. The chitinolytic activity of *Streptomyces* spp. strains plays an important role in the biocontrol of Fusarium diseases, and the plant growth promotion trait is a cherished outcome. More attention is being paid to strains endophytic, producing volatile organic compounds, or to the identification of antibiotics and metabolites responsible for the biocontrol. Bioformulation is a critical point in the use of biocontrol agents, but it has been still poorly considered in the experiments. The biocontrol efficacy of well-designed streptomycete consortia or the so-called microbial synthetic communities, possibly in proper bioformulations, and the role of streptomycetes in the reduction of mycotoxins in the grains are aspects that would merit further investigation in the future.

**Keywords:** *Streptomyces* spp., *Fusarium oxysporum*, Fusarium wilt, Streptomycetes, Biological control, Plant vascular disease

**Review Methodology**: I searched the databases Web of Science, PubMed and CAB Abstracts using the following search terms: 'Streptomyces' or 'Streptomycetes' or Actinomycetes' in the abstract, along with '*Fusarium*' in the title. In addition, I used the references from the articles obtained by this method to check for additional relevant material.

## Diseases Incited by *Fusarium* Species

The ascomycete *Fusarium* genus contains many agronomically important plant pathogens, mycotoxin producers, and opportunistic human pathogens. It is estimated to comprise at least 300 genealogically distinct phylogenetic species, with fewer than half being formally described [1]. Four out of 20 species complexes in the *Fusarium* phylogenetic clade, diverged in the middle Cretaceous 91.3 million years ago [2], account for most of the known plant pathogens in the genus *Fusarium* [1]. The *F. fujikuroi* species complex includes causal agents of Bakanae of rice, ear rot of maize and pitch canker of pine. The *F. graminearum* species complex includes species causing Fusarium head blight of wheat and barley. The *F. solani* species complex causes foot and root rots. Finally, the *Fusarium oxysporum* species complex is an outstanding example of host-specialization, as it comprises more than 100 *formae speciales* causing vascular wilt diseases of economically important crops worldwide [1]. Both *F. fujikuroi* and *F. graminearum* species complexes

can also contaminate grains with mycotoxins such as fumonisin, zearalenone and trichothecene, which have important implications for human health as well as animal health, welfare and productivity [3, 4]. The economic impact of mycotoxins includes loss of human and animal life, increased health care and veterinary care costs, reduced livestock production, and disposal of contaminated foods and feeds [5, 6]. Exposure to mycotoxins is mainly by ingestion of contaminated food, but it may also occur by the dermal and inhalation routes [7].

Several resistance genes have been found against *F. oxysporum* [8], but in crops where they are lacking an integrated management is practiced [9]. Numerous biocontrol agents have been studied against Fusarium wilts, including *Pseudomonas* spp., *Bacillus* spp. [10], nonpathogenic *Fusarium* strains (e.g. Fo47) [11, 12] and a number of other bacterial and fungal strains [13].

## Why *Streptomyces* spp.?

Streptomycetes are Gram positive, filamentous bacteria in the *Streptomycetaceae* family (Phylum *Actinobacteria*, Order *Actinomycetales*), with the genus *Streptomyces* as the sole member and more than 500 species [14, 15]. They are widely distributed in soil (nearly 40% of soil bacteria) and rhizosphere [16, 17], where they form very dynamic assemblies [16], but they also colonize water and a variety of other natural environments. Streptomycetes have a major role in biodegradation of relatively complex and recalcitrant plant and animal residues, including polysaccharides (e.g. starch, pectin and chitin), proteins (e.g. keratin and elastine), lignocellulose and aromatic compounds. Compared with Gram-negative bacteria, streptomycetes play only a minor role as plant pathogens (e.g. *Streptomyces scabies*, causing potato scab) or animal and human pathogens (some strains of *S. somaliensis*, *S. griseus* and few other species, causing mycetomas) [15].

Nearly two-thirds of naturally occurring antibiotics are produced by streptomycetes. Around 7600 out of 43 000 biologically active secondary metabolites have been characterized so far, and about 100 000 antibiotic molecules of pharmaceutical and agricultural importance are estimated to be produced by the genus *Streptomyces* [18, 19]. More than 50% of clinical-useful antibiotics are derived from *Streptomyces* spp. They also produce a wide variety of bioactive secondary metabolites, such as antifungal, antiviral, antitumour, anti-hypertensive and immunosuppressant molecules [20, 21]. Finally, streptomycetes have an exceptionally large number of hydrolytic enzymes enabling them to interact with others in the environment [22]. Such plethora of enzymes, antibiotics and secondary metabolites make them formidable competitors in natural environments as well as very attractive organisms for biotechnological purposes [23].

Few *Streptomyces* species are known pathogens of plants (scab-causing streptomycetes) and humans (*S. somaliensis* and *S. sudanensis*), but in many cases they are beneficial for insects, plants and marine animals. Recently, more attention has been paid to streptomycetes as beneficial endophytes of plants, fungi and animals [24].

Taken together, all these biological features suggest *Streptomyces* spp. as excellent candidates for developing biological control agents. Nevertheless, only very few commercial products are registered as plant protection products: *S. griseoviridis* K61 (Mycostop®, Finland), *S. lydicus* WYEC 108 (Actinovate®, Micro108®, Action Iron®, USA) and *S. saraceticus* KH400 (YAN TEN *S. saraceticus*, Taiwan). However, this may also be due to the fact that many strains are commercialized as plant strengthener or under similar definitions in organic matrixes.

## Literature Overview

To the best of my knowledge, the earliest report dealing with a *Fusarium* disease control by streptomycetes dates back to 1953, when Skinner demonstrated the inhibition of *F. culmorum* by *S. albidoflavus* in soil amended with small amounts of readily available carbohydrates [25]. One year later, the same author found that clays and soil suspensions or extracts inactivated an antibiotic present in culture filtrates of *S. albidoflavus* [26].

Since then, much advance has been done about *Streptomyces* spp. [23, 27] and their biocontrol activity. In the last decade, there has been an increasing interest of research in the control of *Fusarium*-induced diseases by harnessing streptomycetes. In fact, of 244 articles indexed on this topic by the CAB Abstracts database since 1970, about one-half has been published in the last 10 years. Many articles, supposed to have an international relevance because written in English, come mainly from USA and India, while others with a national impact have been produced in China. Nevertheless, streptomycetes as biocontrol agents against Fusarium diseases, or plant diseases in general, have been studied less than other important taxa such as *Trichoderma* spp. (950 articles searched with the same strategy), *Bacillus* spp. (610 articles) and *Pseudomonas* spp. (510 articles), while *Glomus* spp., for example, ranks lower (114 articles). Apparently, this sounds strange if we think that streptomycetes are the largest antibiotic producers in the microbial world [21–23]. However, this evidence is also reported by Raza *et al.* [28], who reviewed the microbial genera evaluated for the biological control of Fusarium wilts of cucumber, banana, and tomato since 2000.

In 45 articles retrieved from the literature and dealing with the biocontrol of Fusarium diseases using streptomycetes, at least 34 formally identified *Streptomyces* species have been evaluated for the control of five pathogenic *Fusarium* species and 12 *F. oxysporum formae speciales* in 17 plant species, being tomato, cucumber, wheat and watermelon the most studied (Table 1).

**Table 1.** List of literature dealing with biocontrol trials using *Streptomyces* spp. against Fusarium diseases conducted under field, commercial greenhouse or pot conditions

| Biocontrol agents | Application | Target pathogen | Host plant | Experimental conditions | Best disease reduction | Best fold-change of plant growth promotion or yield increase | Reference |
|---|---|---|---|---|---|---|---|
| *S. tsusimaensis* CAI-24, *S. caviscabies* CAI-121, *S. setonii CAI-127*, *S. africanus* KAI-32 and *Streptomyces* sp. KAI-90 | Seed bacterization or culture filtrate | *F. oxysporum* f. sp. *ciceris* | Chickpea | Pot and field | 76% (pot), 19% (field) | | [29] |
| *S. albospinus* CT205 | Spore suspension or organic fertilizer enriched with *T. harzianum* SQR-T037 | *F. oxysporum* | Cucumber | Pot and field | 70% (pot), 55% (field) | 1.3 (yield in the field) | [30] |
| *S. griseorubens* E44G | Spore suspension or culture filtrate | *F. oxysporum* f. sp. *lycopersici* | Tomato | Field | 50% | 2 | [31] |
| *S. lydicus* WYEC 108 (Actinovate®) | Formulated spore suspension | *F. oxysporum* f. sp. *niveum* | Watermelon | Field | 0 | | [32] |
| *S. kurssanovii* RCM Ac-1504 D | Crystalline crab chitin | *F. culmorum* | Wheat | Field | | | [33] |
| *S. griseoviridis* K61 (Mycostop®) | Formulated spore suspension with or without soil solarization | *F. oxysporum* f. sp. *radicis-lycopersici* | Tomato | Greenhouse | | | [34] |
| *S. griseoviridis* K61 (Mycostop®) | Formulated spore suspension with filtration and UV treatment of irrigation water | *F. oxysporum* f. sp. *chrysanthemi* | Gerbera | Soilless greenhouse | | | [35] |
| *S. miharaensis* | filipin III (purified antibiotic) | *F. oxysporum* f. sp. *lycopersici* | Tomato | Pot | 100% | | [36] |
| *S. corchorusii and/or S. mutabilis* with pendimethalin or metribuzin | Spore and hyphae suspension | *F. oxysporum* f. sp. *lycopersici* | Tomato | Pot | 100% | | [37] |
| *S. griseoviridis* K61 (Mycostop®) | Formulated spore suspension | *F. oxysporum*f. sp. *radicis-cucumerinum* | Cucumber | Rock wool blocks | 96% | | [38] |
| *S. roseodiastaticus* # 8, *S. erumpens* # 11, *S. aurantiacus* # 42 and *S. rameus* # 59 | Oat bran with or without a commercial seaweed extract | *F. oxysporum* f. sp. *lycopersici* | Tomato | Pot | 88% | 7.5 | [39] |
| *Streptomyces* sp. CB-75 | Fermentation broth with spores | *F. oxysporum* f. sp. *cubense* race 4 | Banana | Pot | 83% | 4.5 | [40] |
| *S. psammoticus* KP1404 | Purified strevertenes A and B | *F. oxysporum* f. sp. *lycopersici* | Tomato | Pot | 78% | | [41] |
| *Streptomyces* spp. | Seed bacterization | *F. culmorum* | Barley | Pot | 76% | | [42] |
| *Streptomyces* sp. 385 with *Paenibacillus* Pb300 at different ratio | Spore suspension | *F. oxysporum* f. sp. *cucumerinum* | Cucumber | Pot | 71% | | [43] |
| *S. thermocarboxydus* GYRRK | Culture filtrate | *F. oxysporum* | *Aloe vera* | Pot | 68% | | [44] |

**Table 1.** (Continued)

| Biocontrol agents | Application | Target pathogen | Host plant | Experimental conditions | Best disease reduction | Best fold-change of plant growth promotion or yield increase | Reference |
|---|---|---|---|---|---|---|---|
| *S. bikiniensis* HD-087 | Seed bacterization or culture filtrate | *F. oxysporum* f. sp. *cucumerinum* | Cucumber | Pot | 68% | 0 | [45] |
| *S. goshikiensis* YCXU | Organic fertilizer | *F. oxysporum* f. sp. *niveum* | Watermelon | Pot | 67% | 8 | [46] |
| *Streptomyces* spp. DAUFPE 11470 and DAUFPE 14632 | Spore suspension | *F. moniliforme* | Maize | Pot | 62% | | [47] |
| *Streptomyces* spp. | Spore suspension | *F. oxysporum* f. sp. *cubense* race 4 | Banana | Pot | 60% | 1.9 | [48] |
| *S. spectabilis* QLP12 or other two *Streptomyces* spp. strains | Solid fermentation substrate combined with *F. oxysporum* Fo47 | *F. oxysporum* f. sp. *niveum* | Watermelon | Pot | 59% | 1.8 | [49] |
| *Streptomyces* sp. KS62 or other four strains | Seed bacterization | *F. oxysporum* f. sp. *ciceris* | Chickpea | Pot | 55% | 1.5 | [50] |
| *S. bikiniensis* HD-087 | Fermentation broth | *F. oxysporum* | Cucumber | Pot | 54% | | [51] |
| *S. spectabilis* QLP12 or other two *Streptomyces* spp. strains | Solid fermentation substrate combined with *F. oxysporum* Fo47 | *F. oxysporum* f. sp. *vasinfectum* | Cotton | Pot | 52% | 2 | [49] |
| *Streptomyces* sp. G10 | Spore suspension | *F. oxysporum* f. sp. *cubense* race 4 | Banana | Pot | 47% | 0 | [52] |
| *S. roseochromogenus* K5 | Spore suspension | *F. oxysporum* f. sp. *vasinfectum* | Cotton | Pot | 47% | | [53] |
| *Streptomyces* sp. S96 | Spore suspension | *F. oxysporum* f. sp. *cubense* race 4 | Banana | Pot | 46% | 1.6 | [54] |
| *Streptomyces* spp. NSP2 | Spore suspension | *F. oxysporum* f. sp. *capsici* | Chili pepper | Pot | 44% | | [55] |
| *Streptomyces* sp. BN1 | Spray | *F. graminearum* | Wheat | Pot | 40% | 0 | [56] |
| *S. fulvoviolaceus* | Corn grain | *F. oxysporum* | Tomato | Pot | 33% | 1.6 | [57] |
| *S. rimosus* M527 | Fermentation broth | *F. oxysporum* f. sp. *cucumerinum* | Cucumber | Pot | 30% | 1.1 | [58] |
| *S. rochei* ACTA1551 | Seed bacterization | *F. oxysporum* f. sp. *lycopersici* | Tomato | Pot | 30% | 1.5 | [59] |
| *S. griseoviridis* K61 (Mycostop®) | Formulated spore suspension or seed bacterization | *F. oxysporum* f. sp. *basilici* | Basil | Pot | 26% | | [60] |
| *S. griseoviridis* K61 (Mycostop®) | Formulated spore suspension | *Fusarium* spp. | Douglas-fir | Pot | 16% | | [61] |
| *S. asterosporus* SNL2 or other two *Streptomyces* sp. strains | Seed bacterization | *F. oxysporum* f. sp. *radicis lycopersici* | Tomato | Pot | 13% | 2 | [62] |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Streptomyces* sp. ME2-27-19° | Purified metabolite | *F. oxysporum* f. sp. *asparagi* and *F. moniliforme* | Asparagus | Pot | 0 (though inoculum reduction) | 0 | [63] |
| *S. chibaensis* | Spore suspension | *F. oxysporum* | *L. termis* | Pot | | 2 | [64] |
| *S. antibioticus* S3 and S12, and *S. peruviensis* S40 | Spore suspension | *F. solani* f. sp. *pisi* | Pea | Pot | | 1.4 | [65] |
| *S. kasugaensis* A43 | Spore suspension | *Fusarium* sp. | *Pinus taeda* | Pot | | 2 | [66] |
| *S. griseus* var. *autotrophicus* ATCC 53668 | Spore suspension or faeriefungin | *F. oxysporum* f. sp. *asparagi* | Asparagus | Pot | | | [67] |
| *S. olivaceus* | Dry crude extract | *F. oxysporum* f. sp. *melonis* | Cucumber | Pot | | | [68] |
| *S. flavofuscus* CPP-53 | Spore suspension | *F. oxysporum* f. sp. *lycopersici* | Tomato | Pot | | | [69] |
| Actinomycetes | Spore suspension | *F. oxysporum* f. sp. *lycopersici* | Tomato | Pot | | | [70] |
| *S. lydicus* WYEC 108 (Actinovate®) | Formulated spore suspension combined with cover crops | *F. oxysporum* f. sp. *niveum* | Watermelon | Pot | | | [71] |
| *S. luteogriseus* A-23 | Spore suspension | *F. culmorum* | Wheat | Pot | | | [72] |
| *S. spororaveus* | Seed coating | *F. udum* | Wheat | Pot | | | [73] |

The *Streptomyces* species assayed *in planta* include: *S. africanus*, *S. albospinus*, *S. antibioticus*, *S. asterosporus*, *S. aurantiacus*, *S. bikiniensis*, *S. caviscabies*, *S. chibaensis*, *S. corchorusii*, *S. erumpens*, *S. flavofuscus*, *S. fulvoviolaceus*, *S. goshikiensis*, *S. griseorubens*, *S. griseoviridis* K61 (the commercial product Mycostop), *S. griseus* var. *autotrophicus*, *S. kasugaensis*, *S. kurssanovii*, *S. luteogriseus*, *S. lydicus* WYEC 108 (the commercial product Actinovate), *S. miharaensis*, *S. mutabilis*, *S. olivaceus*, *S. peruviensis*, *S. rameus*, *S. rimosus*, *S. rochei*, *S. roseochromogenus*, *S. roseodiastaticus*, *S. setonii*, *S. spectabilis*, *S. spororaveus*, *S. thermocarboxydus* and *S. tsusimaensis*. However, a so high number of species, nearly corresponding to the number of strains tested (identified based on the 16S-rDNA sequence), might be over-estimated because the streptomycetes taxonomy remains somewhat confused, and a conclusive definition of species is still unresolved [14, 74].

The *Fusarium* species include: *F. culmorum*, *F. graminearum*, *F. fujikuroi* (formerly *F. moniliforme* var. *subglutinans* or *F. verticillioides*), *F. solani* f. sp. *pisi*, *F. udum* and *F. oxysporum* with its *formae speciales asparagi*, *basilici*, *capsici*, *ciceris*, *cubense*, *cucumerinum*, *lycopersici*, *melonis*, *niveum*, *radicis-cucumerinum*, *radicis-lycopersici* and *vasinfectum* (Table 1).

In addition, other five *Streptomyces* species (*S. alboflavus*, *S. hygroscopicus*, *S. plicatus*, *S. tendae* and *S. violaceusniger*) have been assayed solely *in vitro* against four additional *Fusarium* species [*F. avenaceum*, *F. equiseti*, *F. roseum* (formerly *F. sambucinum*) and *F. solani*] (Table 2). About two dozens of *Streptomyces* spp. strains have also been tested *in planta* and *in vitro*.

The overall magnitude of disease reduction has been 31 ± 26% in field trials (mean ± 95% confidence interval) and 57 ± 9% under controlled conditions, with a plant growth promotion of 2.1 ± 1.1-fold (Figure 1).

## Field Trials with Commercial Products Containing *Streptomyces* spp.

The commercial products containing *S. lydicus* WYEC 108 (Actinovate® SP, Actinovate® AG, Novozymes BioAg Inc., Wisconsin, USA) and especially that containing *S. griseoviridis* K61 (Mycostop®, Verdera, Finland) have been repeatedly evaluated for the control of several soil-borne diseases, including Fusarium wilts, but they were often characterized by fluctuating results (Table 1). Both these bio-fungicides are registered for the use as seed treatment, soil drench and foliar spray, and their manufacturer's labels report very wide target pathogen ranges.

At two locations in 2010, the application protocol of Actinovate® recommended by the manufacturer significantly increased marketable watermelon yield in field plots inoculated with *F. oxysporum* f. sp. *niveum* compared with untreated plots, inoculated or not with the pathogen [32]. Two years later, however, this result was not confirmed, and no significant biocontrol was observed [71].

**Table 2.** List of literature dealing with the antagonistic activities of *Streptomyces* spp. against *Fusarium* species *in vitro*

| Biocontrol agents | Application | Target pathogen | Host plant | Reference |
|---|---|---|---|---|
| *S. hygroscopicus* | Seed coating | *F. avenaceum* | Winter rye and red clover | [75] |
| Actinomycetes | | *F. equiseti* | | [76] |
| *S. alboflavus* TD-1 | | *F. moniliforme* | | [77] |
| *S. tendae* HS5 | | *F. oxysporum* | | [78] |
| *Streptomyces* sp. EN27 | Spore suspension | *F. oxysporum* | *Arabidopsis thaliana* | [79] |
| *S. griseorubiginosus*-like | | *F. oxysporum* f. sp. *cubense* | | [80] |
| *S. violaceusniger* G10 | | *F. oxysporum* f. sp. *cubense* race 4 | | [81] |
| *S. griseus* | Spore suspension or kaolin/alginate formulations | *F. oxysporum* f. sp. *cubense* tropical race 4 | | [82] |
| *S. griseus* | | *F. oxysporum* f. sp. *cubense* tropical race 4 | | [83] |
| *S. griseorubens* E44G | | *F. oxysporum* f. sp. *lycopersici* | | [84] |
| *Streptomyces* spp. | | *F. oxysporum* f. sp. *lycopersici* | | [85] |
| *Streptomyces* spp. | | *F. oxysporum* f. sp. *lycopersici* | | [86] |
| *S. griseus* MTCC-*4734 | | *F. oxysporum* f. sp. *lycopersici* | | [87] |
| Actinomycetes | | *F. oxysporum* f. sp. *lycopersici*, F. *solani*, *F. moniliforme* | | [88] |
| *Streptomyces* sp. C-1 | | *F. sambucinum* | | [89] |
| *S. griseus* NCRRT | | *F. solani* | | [90] |
| *S. plicatus* and other *Streptomyces* spp. | | *F. solani* | | [91] |
| *Streptomyces* sp. | | *F. subglutinans* | | [92] |
| *Streptomyces* spp. | | *F. verticillioides* | | [93] |
| *Marmoricola* sp. MIM116 | Spray | *Fusarium* spp. | Wheat and barley grains | [94] |

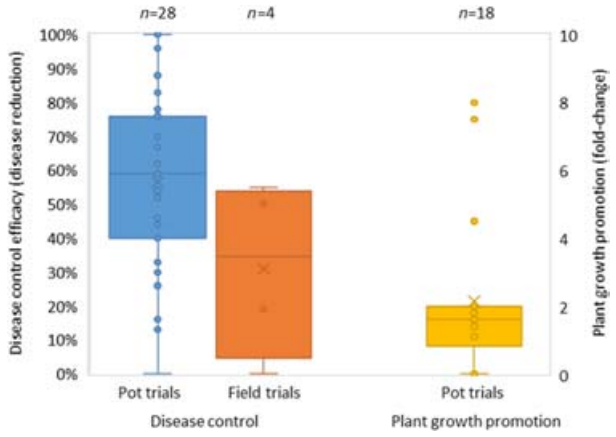


**Figure 1.** Data of the maximum Fusarium wilt control efficacy obtained in 28 pot experiments and four field trials using *Streptomyces* spp. strains. The maximum plant growth promotion effect is referred to 18 pot experiments. Data are reported in Table 1.

Mycostop® was effective against *F. oxysporum* f. sp. *lycopersici* in two of four independent trials, and soil spraying with $10^7$ CFU/m$^2$ was surprisingly more effective (60% disease reduction) than soil drench (50%) with $5 \times 10^6$ CFU/m$^2$ to control tomato wilt.

The bacterial antagonist was not effective against *F. oxysporum* f. sp. *radicis-lycopersici*. Possible additive effects in the biocontrol and tomato yield increase were detected when Mycostop® was combined with soil solarization, though most effects did not result statistically significant [34].

Rose *et al.* [38] experienced a significant biocontrol of *F. oxysporum* f. sp. *radicis-cucumerinum* using Mycostop® in two out of three trials.

In Douglas fir (*Pseudotsuga menziesii* var. *glauca*), Mycostop® was not effective in the control of *F. oxysporum*, *F. proliferatum* and *F. sporotrichioides*. Also, it had a synergistic negative effect with *Fusarium* against plant emergence. Mycostop®, however, reduced by 16% the number of seedlings infected by *Fusarium* spp., but within infected plants the proportion of seedlings infected by and *F. oxysporum* and especially by *F. proliferatum* was significantly increased by 40% [61].

The integration of Mycostop® with slow sand filtration and a nutrient solution pH higher than 6.0 induced a significant reduction of *F. oxysporum* f. sp. *chrysanthemi* infections in gerbera plants grown in closed soilless systems [35].

This product increased the percentage of healthy plants by 2–26% under *F. oxysporum* f. sp. *basilici* pressure, though a statistically significant protection occurred only in one of four trials [60]. Mycostop® was also effective against *F. oxysporum* f. sp. *lycopersici* in one of two independent trials, but ineffective substantially ineffective against *F. oxysporum* f. sp. *radicis-lycopersici* [34]. Its applications combined with slow sand filtration were effective in reducing *F. oxysporum* f. sp. *chrysanthemi* propagules in a closed soilless system where gerbera plants were grown [35]. Based on several trials in diverse pathosystems,

however, the authors concluded that biocontrol agents such as *Streptomyces* spp., *Trichoderma* spp. and *Fusarium* sp., integrated with other control means may represent an efficient alternative to the methyl bromide use in closed soilless cultivation systems [95].

## Examples of Biocontrol in the Field Using Experimental Strains

Out of 45 articles recovered from the literature, only eight deal with field or commercial greenhouse trials, whereas the remaining report pot-experiments (Table 1).

In a field trial, applications of *S. albospinus* CT205 spore suspensions reduced the incidence of Fusarium wilt of cucumber (*F. oxysporum* f. sp. *cucumerinum*) by 22% and plant death by 33%, with a concomitant 1.3-fold increase of cucumbers yield. If vectored into the soil within an organic fertilizer enriched with *T. harzianum* SQR-T037, *S. albospinus* CT205 determined higher disease control (55% incidence reduction and 63% plant death reduction) and yield (1.4). The treatment also significantly reduced the numbers of *Fusarium* colony forming units and improved the microbial community structure in the cucumber rhizosphere. *S. albospinus* CT205 was previously selected for the high levels of chitinase, β-glucanase and heat-resistant antagonistic substances, and provided a disease reduction up to 70% under greenhouse conditions [30].

Control levels ranging from 4 to 19% were obtained against *F. oxysporum* f. sp. *ciceris* using five *Streptomyces* spp. strains (CAI-24, CAI-121, CAI-127, KAI-32 and KAI-90) isolated from herbal vermicomposts. The best results were obtained with bacterial culture filtrates applied as soil drench. On the other hand, in a previous greenhouse experiment of the same research, seed bacterization was superior to soil drench and determined up to 76% Fusarium wilt control [29].

Drenches with cell-free culture filtrate or spore suspension of *S. griseorubens* E44G increased yield of tomato by 2- or 1.7-fold, respectively, compared with the control inoculated with *F. oxysporum* f. sp. *lycopersici*. The same treatments reduced the disease index to 1 or 2, respectively, while the score was 4 on the inoculated control [31]. The chitinolytic activity of *S. griseorubens* E44G was demonstrated and a thermostable chitinase enzyme of 45 kDa was purified using gel filtration chromatography [31, 84].

Preparations produced by cultivation of *S. kurssanovii* RCM Ac-1504 D on a medium containing crystalline crab chitin were proved to be an efficient treatment against *F. culmorum* in wheat [33].

It should be noted that most streptomycetes used in those field trials, after an obvious preliminary selection for their antagonistic activity (*in vitro* antibiosis), were characterized by a chitinolytic activity and a plant growth promoting effect. Successful applications were not only the simple drench with spore suspension, but they also included the drench with cell-free culture filtrate (containing the bacterial metabolites) and the use of an organic amendments or a chitin-based medium as carrier.

## The Most Successful Biocontrol Experiments Under Controlled Conditions

Among 38 articles dealing with pot-experiments, 16 report a disease control level (disease reduction) above 50%, seven of which with a level above 70% (Table 1). A total of 15 articles document a plant growth promotion activity by *Streptomyces* spp. strains.

In three research work, it was demonstrated a complete suppression of *F. oxysporum* f. sp. *lycopersici* in tomato. Seed bacterization with *S. miharaensis* KPE62302H determined a Fusarium wilt reduction of 60 or 80% in two independent experiments. A purified antibiotic namely FP-1 and identified as filipin III was effective in inhibiting Fusarium wilt of tomato at 10 μg/ml, with no phytotoxicity effects even at 500 μg/ml [36]. The same research team isolated strevertenes A and B from *S. psammoticus* KP1404 and demonstrated a nearly complete suppression of tomato Fusarium wilt following their application [41]. Applications of *S. corchorusii* culture suspension combined with the herbicides pendimethalin or metribuzin, each $2 \times 10^{-3}$ M, suppressed completely tomato Fusarium wilt and reduced drastically or hindered plant tissue colonization by the pathogen. The same results were obtained if the treatment was combined with a culture suspension of *S. mutabilis* and assayed concurrently against Fusarium wilt and bacterial wilt (*Pseudomonas solanacearum*) of tomato [37].

At least two other good results were obtained against Fusarium wilt of tomato. Soil incorporation of oat bran colonized with *S. roseodiastaticus* # 8, *S. erumpens* # 11, *S. aurantiacus* # 42 and *S. rameus* # 59 two weeks after the pathogen-inoculation resulted in a 70% disease reduction, a level higher than that obtained with the strains inoculated separately. The treatment doubled the microbial activity in the soil and increased plant biometric parameters in the range of 2.4–6-fold changes, compared with untreated, pathogen-inoculated control. When the treatment was combined with the application of a commercial seaweed extract, the disease control level reached 88%, and plant growth was increased by 2.4–6-fold, with an extraordinary peak of 7.5-fold increase in shoot dry weight (31.3 g in treated plants, compared with 4.16 g in untreated, pathogen-inoculated control) [39]. Drench with spore suspension of *S. flavofuscus* CPP-53 1 week after pathogen inoculation provided an evident visible protection from Fusarium wilt and growth promotion, although no data were presented [69].

Application of Mycostop® to cavity of rock wool blocks inoculated 24 h later with *F. oxysporum* f. sp. *radicis-cucumerinum* and planted with cucumber reduced the

percentage of diseased plants by 30%, though without a statistical significance support. Under semi-commercial propagation conditions, the application of Mycostop® 48 h prior to pathogen-inoculation resulted in a significant reduction of disease severity index by 75 or 96% in two independent trials. Other biocontrol agents and amendments were also tested. Among them, the addition of chitin (4%, vol./vol.) to a peat-based medium significantly enhanced cucumber seedling growth and reduced the pathogen population in the soil, but the disease severity increased. A greenhouse compost was significantly more suppressive than the other two composts, and the suppression was partially eliminated by sterilization [38].

A streptomycete strain isolated from banana rhizosphere and identified as *Streptomyces* sp. CB-75 (though with a 99.93% sequence similarity with *S. spectabilis*) was very effective against Panama disease, as provided an 83% control efficacy and increments by 72–82% or 113–195% in the fresh or dry weights, respectively, of shoots and roots. Such results were obtained once CB-75 was inoculated as fermentation broth including living spores, and interestingly were superior to those obtained with the fermentation broth deprived from the spores (e.g. 10% disease control efficacy). The crude extract of *Streptomyces* sp. CB-75 caused deformation, shrinkage, collapse, and tortuosity in pathogenic fungi when observed by scanning electron microscopy. Among 18 chemical constituents identified in the CB-75's crude extract by gas chromatography-mass spectrometry (GC-MS), (*Z*)-13-docosenamide was the major constituent [40].

On barley, seed treatment significantly reduced the occurrence of *F. culmorum* symptoms on seedlings. Amongst six streptomycetes, the strains TW3, RI3 and TW2, related to *S. gancidicus* and *S. pseudogriseolus*, showed the best performances with 76, 65 and 62% disease reduction, respectively. The disease severity on treated plants was 0.4, 0.8 and 0.9, respectively, compared with a value of 17 on the control. A negative effect on barley plant emergence was detected, and it consisted of a 30% reduction with the RI3 strain. When uninoculated seeds were treated with RI3, only 63% seeds emerged (95.7% in the control) and a 30% reduction in seedling weight and length was observed. Such negative effects were ascribed by the authors to the ability of some streptomycetes to produce phytotoxic metabolites with a herbicidal property [42].

In the abovementioned experiments, it can be noted the use of fermentation broth, purified metabolites, the use of seed bacterization as application method, the treatment prior to pathogen inoculation rather than the concurrent inoculation of antagonist and pathogen, and the combination with an organic fertilizer like a seaweed extract. Unlike the articles dealing with field experiments, in these research works the chitinolytic and plant growth promoting activities of *Streptomyces* spp. strains were not investigated.

## Reduction of Mycotoxins in the Grains

Only two examples of mycotoxin reduction in the grains have been reported in the literature.

The inoculation of *Marmoricola* sp. MIM116 cell suspension into 1000 kernels of wheat and barley resulted in a deoxynivalenol decrease from approximately 3 mg/kg to <1 mg/kg [94]. Some organic amendments reduced fumonisin FB1 and FB2 levels by 69 and 93%, respectively. A number of *Streptomyces* spp. strains isolated from those amendments were antagonistic against *F. verticillioides* (currently denoted *F. fujikuroi*). *In vitro*, the best *Streptomyces* spp. strains decreased the FB1 and FB2 amounts by 88 and 98%, respectively [93].

Both these studies are extremely interesting if we consider that a meta-analysis revealed a mean expected control of deoxynivalenol by tebuconazole equal to 21.6% [96].

## Role of Streptomycetes in the *Fusarium*-Suppressive Soils

A soil is referred to as disease-suppressive if a plant pathogen does not establish or persist, if a pathogen establishes but causes little or no disease, or if a pathogen causes disease only in a limited time period after its establishment. Suppressive soils are often surrounded by conducive soils, with which they share the same climatic conditions and agronomic management [97–100]. Disease suppressiveness may develop because of certain crop rotations, as documented for Rhizoctonia-induced diseases [100–105], or after years of severe disease under continuous monoculture, as for Fusarium wilt of strawberry [106] or Fusarium wilt (*F. oxysporum*) and take-all of wheat (*Gaeumannomyces graminis* var. *tritici*) [100].

In a given soil, biotic factors such as a higher microbial diversity or particular compositions of the microbiota are amongst the key factors contributing to the soil suppressiveness, and in turn the microbiota populations (including streptomycetes) and their pathogen-antagonistic members are structured by the cropping history and soil management [98, 99, 107–111]. In early studies, disease suppressiveness was partly attributed to populations of fluorescent *Pseudomonas* spp. or non-pathogenic *Fusarium* spp. [100, 112], but recently the role of streptomycetes has emerged, as demonstrated by the case of *Streptomyces* spp. secreting lantipeptides in strawberry rhizosphere [106]. *Streptomyces* spp. populations associated with naturally occurring suppressive soils have been found generally more abundant, compared with conducive soils, and characterized by a higher antagonistic:saprophytic strains ratio [107, 113]. The population of *Streptomyces* spp., as well as *Pseudomonas* spp., carrying the non-ribosomal peptide synthetase gene, was related to the soil suppressiveness to Panama disease with an impact on disease

incidence more significant than the total bacterial community and chemical properties of soil [114].

Besides its natural occurrence, the disease suppressiveness in soil has been induced using certain agronomic practices such as green manuring. The incorporation of green manures has been shown to increase the density and diversity of soil microbiota, including streptomycetes [115, 116]. *Streptomyces* spp. population increased after manuring with sorghum-sudangrass hybrid or common buckwheat, and reduced the *F. graminearum* survival on wheat residues, which is a key factor for Fusarium head blight epidemics [117]. Also following the incorporation of *Brassica juncea* seed meal, streptomycetes increased in the soil though the total bacterial population density decreased. Such treatment completely suppressed Fusarium wilt of pepper [118]. A higher density of actinomycetes along with those of *Trichoderma*, *Aspergillus* and *Pseudomonas* were observed after the applications of three on-farm green composts, which determined on average a 25% reduction of Fusarium wilts of melon, tomato and basil [119].

## Mechanisms Underlying the Biocontrol

### *Chitinolytic activity*

Streptomycetes play an important role in the decomposition of various biopolymers, such as lignin, cellulose, starch, xylan (hemicellulose), pectin (polygalacturonic acid) and chitin. Ecologically, streptomycetes have key roles in the natural recycling of the globally abundant cell walls of fungi and plants. The widespread ability of streptomycetes to degrade chitin has attracted the attention of plant pathologists because it is a component of the fungal cell wall (as well as of the exoskeleton of crustaceans and arthropods). Colloidal chitin is even used for semi-selective isolation of streptomycetes [15, 22].

For this reason, chitinolytic *Streptomyces* spp. strains have been widely studied for the Fusarium biocontrol. Some of those studies are already described here as examples of good Fusarium biocontrol [30, 31, 33, 42, 84], but others are also worthy of description.

Chitinase and β-1,3-glucanase activity was investigated in *Paenibacillus* sp. 300 and *Streptomyces* sp. 385, which provided a 71 or 64% reduction of Fusarium wilt incidence in cucumber once added to the potting medium in 1:1 or 4:1 mixture, respectively [43]. *S. goshikiensis* YCXU, a strain producing catalase, β-1,3-glucanase, chitinase, urease, antifungal diffusible and volatile organic compounds, decreased by 67% Fusarium wilt of watermelon when vectored by an organic fertilizer. The treatment also reduced by 89% the pathogen population in soil and decreased the stress indicator enzymes and malondialdehyde content by 55–70 and 62%, respectively. Significant variations in the soil fungal and bacterial community structures following the treatments were also observed [46].

A crude and a partially purified chitinase enzyme of *S. griseus* were as effective as the dipping into spore suspension against Fusarium wilt of tomato (50–60%) [120].

Other works involved *Streptomyces* sp. KS62 or other four strains against Fusarium wilt of chickpea (55% disease reduction and 1.5-fold plant growth promotion) [50], and *S. asterosporus* SNL2 or other two *Streptomyces* sp. strains against Fusarium wilt of tomato (13% disease reduction and 2-fold plant growth promotion) [62]. Finally, some studies were conducted solely *in vitro* for the characterization of strains of *S. griseus* [83, 87] and *S. tendae* [78] (Table 2).

### *Endophytic trait*

The concept of *Streptomyces* spp. as symbionts of plant has been recently considered with much more attention [17, 24, 121, 122]. Cao *et al.* [80] isolated actinomycetes from banana plants, and found that most of them were close to *S. griseorubiginosus*. The community diversity was higher in wilting than in healthy leaves, whereas similar actinomycete communities were found in wilting and healthy roots. On the other hand, the proportion of streptomycetes antagonists of *F. oxysporum* f. sp. *cubense* in healthy roots was higher than that in wilting roots, but no difference was found between antagonistic strains isolated from healthy and wilting leaves [80]. One year later, the same research team demonstrated the efficacy of *Streptomyces* sp. S96, an endophytic and siderophore-producing strain, in the control of Panama disease (*F. oxysporum* f. sp. *cubense*) and in the growth increase of banana plants [54]. Actinomycetes were found as a predominant taxon in the endophytic microbiome of banana plants. Although the metagenomics revealed *Mycobacterium* and *Nocardia* as dominant genera in banana shoots, only streptomycetes were isolated, probably due to likely because of an isolation procedure-related bias. However, those streptomycetes reduced Panama disease by 60% and increased the banana plant growth by 1.9-fold [48].

Endophytic, 1-aminocyclopropane-1-carboxylate (ACC) deaminase-producing actinomycetes were found to be significantly more effective in reducing the incidence and severity of tomato wilt disease under greenhouse conditions compared with ACC deaminase-non-producing isolates. The application of ACC deaminase-producing isolates resulted in the reduction of the endogenous levels of ACC, the immediate precursor of ethylene, in both roots and shoots and increased plant growth compared with isolates that did not produce the ACC deaminase [70].

### *Volatile organic compounds*

Volatile organic compounds are known to be involved in the biocontrol as well as in the interactions between

plants, pathogen/pests and beneficial microbes [123]. Streptomycetes produce volatile organic compounds [17, 124], but they are still scarcely characterized in the interaction with *Fusarium* spp.

Amini *et al.* [50] found that volatile compounds were less effective on mycelial growth inhibition (20.2–33.4% of *F. oxysporum* f. sp. *ciceris* growth inhibition) than non-volatile extracts of five *Streptomyces* strains (50% inhibition).

The mycelial growth, sporulation, spore germination and membrane permeability of *F. moniliforme* (currently re-classified as *F. fujikuroi*) were significantly compromised by the *S. alboflavus* TD-1 volatiles. A GC-MS analysis revealed 31 volatile compounds produced by *S. alboflavus* TD-1, and one of them, 2-methylisoborneol, exhibited a fumigant activity against *F. moniliforme* [77].

### *Plant resistance induction*

The literature dealing with the induction of resistance in plants mediated by biocontrol agents is huge [17, 125]. However, this important aspect has been poorly investigated in *Streptomyces* spp. controlling Fusarium wilts.

Using a fine molecular approach, it was demonstrated that the resistance to *F. oxysporum* mediated by the endophytic strain *Streptomyces* sp. EN27 involved primarily the systemic acquired resistance pathway, since it occurred via an NPR1-dependent manner and required salicylic acid, while it was jasmonate/ethylene independent [126]. Later, with a proteomics approach (two-dimensional difference gel electrophoresis or DIGE), proteins induced by *F. oxysporum* and *Streptomyces* sp. EN27 were isolated, and grouped into functions of defense-related, cell redox and metabolism after LC-MS/MS analysis. Quantitative polymerase chain reaction analysis showed that *Streptomyces* sp. EN27-mediated defense resulted in increased expression of LLP and Hel. The streptomycete suppressed jasmonate signalling, known to induce the pathogen-mediated early leaf chlorosis and senescence [79].

In *Lupinus termis* seeds, *S. chibaensis* was proved to increase peroxidase and catalase and to induce three novel proteins, with molecular masses of 27, 32.9 and 24 kDa [64].

The fermentation broth of *S. bikiniensis* HD-087 suppressed *F. oxysporum* and triggered plant defense mechanisms in cucumber. It significantly increased the activities of peroxidase, phenylalanine ammonia-lyase, β-1,3-glucanase and the levels of chlorophyll and soluble sugars in cucumber leaves [51].

## Formulation of *Streptomyces* spp. Strains

Formulations of biocontrol agents affect significantly the biocontrol efficacy [127], but they have been insufficiently evaluated in the biocontrol of Fusarium diseases using for *Streptomyces* spp. strains.

When different mixtures of *Paenibacillus* sp. 300 and *Streptomyces* sp. 385 were tested with several formulations, a zeolite-based, chitosan-amended formulation provided a cucumber Fusarium wilt protection superior to a peat-based formulation with or without chitosan and to the non-formulated inoculants [43].

In the reduction of *F. oxysporum* f. sp. *cubense* race four soil inoculum, formulations in sodium alginate, kaolin clay and in alginate-kaolin were all advantageous for *S. griseus*, and kaolin was the best material [82].

On the other hand, Anitha and Rabeeth [120] did not find improvement of *S. griseus* efficacy with a chitin amendment in seed treatment. Moreover, two commercial formulate products such as Mycostop® and Actinovate® have provided inconstant results across trials [32, 34, 35, 38, 60, 61, 71, 95].

## Conclusion

Although the streptomycetes are the largest taxon of antibiotic producers in the microbial world, they are less studied than other biocontrol agents against Fusarium diseases and, perhaps, plant diseases in general. Very likely, they are more attractive for biotechnological and pharmaceutical purposes.

Plant diseases induced by *Fusarium* species are notably challenging. One of them, *F. oxysporum*, is particularly difficult to control by using microbial antagonists because, being a vascular pathogen, it evades the contact with them as soon as it enters in the plant xylem, unless the antagonist is endophytic. However, successful biocontrol has been achieved in several experiments, of which the tomato/*F. oxysporum* f. sp. *lycopersici* pathosystem was the most studied. This is not in agreement with the review by Raza *et al.* [28], who concluded that the overall biocontrol efficiency of different microbial genera is higher against the Fusarium wilt of cucumber compared with the Fusarium wilts of banana and tomato. Biocontrol of Fusarium wilts has also been reviewed by other authors [11, 13].

From 45 *in planta* biocontrol studies retrieved from the literature we learn that, besides the obvious *in vitro* initial selection for antibiosis, the chitinolytic activity of *Streptomyces* spp. strains play an important role in the biocontrol of Fusarium diseases, and the plant growth promotion trait is a cherished outcome. Other biocontrol mechanisms appear less relevant, or they have been just less studied so far in the *Streptomyces–Fusarium* interaction. Some of them, however, merit further studies, since overall they are being considered, or re-considered, attractive; it is the case, for example, of strains endophytic or producing volatile organic compounds [24, 123]. The identification of specific antibiotics or metabolites responsible for the biocontrol is challenging and, for this reason, not frequent,

but some good examples teach us that it deserves more efforts.

Bioformulation is a crucial point in the use of biocontrol agents [127], but overall poorly considered in the biocontrol of Fusarium diseases using streptomycetes. Recently, secondary metabolite-based formulations have been receiving much interest because of a much longer shelf-life and a higher efficiency against soil-borne plant pathogens [127]. Also, microbial polysaccharides [128], consortia of antimicrobial metabolites and narrower target pathogen ranges of biopesticides [127] are new trends for the bioformulations. Different new microbial formulations such as nanosuspension, nanoemulsion and nanocapsule suspensions are expected to be released soon in the market [127]. Other weak points in the Fusarium wilts biocontrol have been already reviewed by several authors [12, 28, 129, 130].

The soil incorporation of organic amendments (concurrently or colonized) with *Streptomyces* spp. has determined sometimes additive or synergistic effects on the biocontrol or plant growth promotion. Also, the mixture of several *Streptomyces* spp. strains has been often positively correlated with the biocontrol efficacy. In this view, consortia-based formulations are being considered in agriculture [127], and should be taken into account for *Streptomyces* spp. as well. Associations of *Rhizobia* and mycorrhiza used on legume crops, combinations of phosphate-solubilizing bacteria with phosphate and potassium rocks, or mixtures of cyanobacteria, microalgae and *Azotobacter* used as biostimulators and biofertilizers, consortia of *Bacillus* spp., *Streptomyces* spp., *Azotobacter* spp. and *Frauteria* spp. are intelligently tactical bioformulations. Nevertheless, the combination of biocontrol strains should be designed accurately, with the aim to sum different modes of actions avoiding cross-inhibition. Actually, such combinations of strains should be the so-called synthetic communities, viz. extremely simplified artificial community resembling the natural ones, thus with a stable and durable equilibrium along with a good fitness in the environment [131–134]. Microbial interactions in the soil are very intricate, and those involving streptomycetes make no exceptions [16, 135–137]. Herrera Paredes *et al.* [138] have elegantly demonstrated that it is possible to infer causal relationships between microbiota membership and host phenotypes, and these inferences can be used to rationally design novel communities.

## References


1. Aoki T, O'Donnell K, Geiser DM. Systematics of key phytopathogenic *Fusarium* species: current status and future challenges. Journal of General Plant Pathology 2014;80(3):189–201.
2. O'Donnell K, Rooney AP, Proctor RH, Brown DW, McCormick SP, Ward TJ, *et al.* Phylogenetic analyses of RPB1 and RPB2 support a middle cretaceous origin for a clade comprising all agriculturally and medically important *Fusaria*. Fungal Genetics and Biology 2013;52:20–31.
3. Placinta CM, D'Mello JPF, Macdonald AMC. A review of worldwide contamination of cereal grains and animal feed with *Fusarium* mycotoxins. Animal Feed Science and Technology 1999;78(1):21–37.
4. D'Mello JPF, Placinta CM, Macdonald AMC. Fusarium mycotoxins: a review of global implications for animal health, welfare and productivity. Animal Feed Science and Technology 1999;80(3):183–205.
5. Hussein HS, Brasel JM. Toxicity, metabolism, and impact of mycotoxins on humans and animals. Toxicology 2001;167(2):101–34.
6. Zain ME. Impact of mycotoxins on humans and animals. Journal of Saudi Chemical Society 2011;15(2):129–44.
7. Peraica M, Radić B, Lucić A, Pavlović M. Toxic effects of mycotoxins in humans. Bulletin of the World Health Organization 1999;77(9):754–66.
8. Michielse CB, Rep M. Pathogen profile update: *Fusarium oxysporum*. Molecular Plant Pathology 2009;10(3):311–24.
9. Gordon TR. *Fusarium oxysporum* and the Fusarium wilt syndrome. Annual Review of Phytopathology 2017;55(1):23–39.
10. Khan N, Maymon M, Hirsch A. Combating *Fusarium* infection using *Bacillus*-based antimicrobials. Microorganisms 2017;5(4):75.
11. Alabouvette C, Lemanceau P, Steinberg C. Recent advances in the biological control of Fusarium wilts. Pesticide Science 1993;37(4):365–73.
12. Alabouvette C, Olivain C, Migheli Q, Steinberg C. Microbiological control of soil-borne phytopathogenic fungi with special emphasis on wilt-inducing *Fusarium oxysporum*. New Phytologist 2009;184(3):529–44.
13. Monda E. Biological control of Fusarium wilt of tomato – a review. Journal of Tropical Microbiology 2002;1:74–8.
14. Anderson AS, Wellington EM. The taxonomy of *Streptomyces* and related genera. International Journal of Systematic and Evolutionary Microbiology 2001;51:797–814.
15. Korn-Wendisch F, Kutzner HJ. The family Streptomycetaceae. In: Dworkin M, editor. The Prokaryotes: an Evolving Electronic Resource for the Microbiological Community. Release 3.0 of 5/21/1999, 2nd ed. Springer-Verlag, New York; 1999.
16. Vetsigian K, Jajoo R, Kishony R. Structure and evolution of *Streptomyces* interaction networks in soil and *in silico*. PLoS Biology 2011;9(10):e1001184.
17. Viaene T, Langendries S, Beirinckx S, Maes M, Goormachtig S. Streptomyces as a plant's best friend? FEMS Microbiology Ecology 2016;92(8).
18. Watve MG, Tickoo R, Jog MM, Bhole BD. How many antibiotics are produced by the genus *Streptomyces*? Archives of Microbiology 2001;176(5):386–90.
19. Subramaniam G, Arumugam S, Rajendran V. Plant Growth Promoting Actinobacteria: A New Avenue for Enhancing the Productivity and Soil Fertility of Grain Legumes. Springer, Singapore; 2016.
20. Liu G, Chater KF, Chandra G, Niu G, Tan H. Molecular regulation of antibiotic biosynthesis in *Streptomyces*. Microbiology and Molecular Biology Reviews 2013;77(1):112–43.

21. de Lima Procópio RE, da Silva IR, Martins MK, de Azevedo JL, de Araújo JM. Antibiotics produced by *Streptomyces*. The Brazilian Journal of Infectious Diseases 2012;16(5):466–71.
22. Chater KF, Biro S, Lee KJ, Palmer T, Schrempf H. The complex extracellular biology of *Streptomyces*. FEMS Microbiology Reviews 2010;34(2):171–98.
23. Chater KF. Recent advances in understanding *Streptomyces*. F1000Research 2016;5:2795.
24. Seipke RF, Kaltenpoth M, Hutchings MI. *Streptomyces* as symbionts: an emerging and widespread theme? FEMS Microbiology Reviews 2012;36(4):862–76.
25. Skinner FA. Inhibition of Fusarium culmorum by Streptomyces albidoflavus. Nature 1953;172(4391):1191.
26. Skinner FA. The effect of adding clays to mixed cultures of *Streptomyces albidoflavus* and *Fusarium culmorum*. Journal of General Microbiology 1956;14(2):393–405.
27. Schrempf H. The family Streptomycetaceae, Part II: molecular biology. In: Dworkin M, Falkow S, Rosenberg E, Schleifer K-H, Stackebrandt E, editors. The Prokaryotes: Volume 3: Archaea Bacteria: Firmicutes, Actinomycetes. Springer, New York; 2006. p. 605–22.
28. Raza W, Ling N, Zhang R, Huang Q, Xu Y, Shen Q. Success evaluation of the biological control of Fusarium wilts of cucumber, banana, and tomato since 2000 and future research strategies. Critical Reviews in Biotechnology 2017;37(2):202–12.
29. Gopalakrishnan S, Pande S, Sharma M, Humayun P, Kiran BK, Sandeep D, *et al*. Evaluation of actinomycete isolates obtained from herbal vermicompost for the biological control of Fusarium wilt of chickpea. Crop Protection 2011;30(8):1070–8.
30. Wang SM, Liang Y, Shen T, Yang H, Shen BA. Biological characteristics of *Streptomyces albospinus* CT205 and its biocontrol potential against cucumber Fusarium wilt. Biocontrol Science and Technology 2016;26(7):951–63.
31. Rashad YM, Al-Askar AA, Ghoneem KM, Saber WIA, Hafez EE. Chitinolytic *Streptomyces griseorubens* E44G enhances the biocontrol efficacy against Fusarium wilt disease of tomato. Phytoparasitica 2017;45(2):227–37.
32. Himmelstein J, Everts K, Maul J. Efficacy of *Streptomyces lydicus* and cover crops for management of Fusarium wilt of watermelon. Phytopathology 2010;100(6):S51.
33. Tatarinova NY, Grinchenko OS, Varlamov VP, Pospekhov GV, Vasikova IS, Dzhavakhiya VG. A complex of chitinolytic enzymes from *Streptomyces kurssanovii* and its use as treatment for *Fusarium culmorum*, a wheat pathogen. Applied Biochemistry and Microbiology 1996;32(2):223–6.
34. Minuto A, Spadaro D, Garibaldi A, Gullino ML. Control of soilborne pathogens of tomato using a commercial formulation of *Streptomyces griseoviridis* and solarization. Crop Protection 2006;25(5):468–75.
35. Minuto A, Gaggero L, Gullino ML, Garibaldi A. Influence of pH, nutrient solution disinfestation and antagonists application in a closed soil less system on severity of Fusarium wilt of gerbera. Phytoparasitica 2008;36(3):294–303.
36. Kim JD, Han JW, Hwang IC, Lee D, Kim BS. Identification and biocontrol efficacy of *Streptomyces miharaensis* producing filipin III against Fusarium wilt. Journal of Basic Microbiology 2012;52(2):150–9.
37. El-Shanshoury AR, Abu-El-Sououd SM, Awadalla OA, El-Bandy NB. Effects of *Streptomyces corchorusii*, *Streptomyces mutabilis*, pendimethalin, and metribuzin on the control of bacterial and Fusarium wilt of tomato. Canadian Journal of Botany 1996;74(7):1016–22.
38. Rose S, Parker M, Punja ZK. Efficacy of biological and chemical treatments for control of Fusarium root and stem rot on greenhouse cucumber. Plant Disease 2003;87(12):1462–70.
39. Al-Shugairan NMI. Biological control of *Fusarium oxysporum* wilt disease of tomato by antagonistic and plant growth promoting actinomycetes [PhD Thesis]. United Arab Emirates University; 2008. http://scholarworks.uaeu.ac.ae/all_theses/552 (last accessed 1 August 2018).
40. Chen Y, Zhou D, Qi D, Gao Z, Xie J, Luo Y. Growth promotion and disease suppression ability of a Streptomyces sp. CB-75 from banana rhizosphere soil. Frontiers in Microbiology 2018;8:2704.
41. Kim JD, Han JW, Lee SC, Lee D, Hwang IC, Kim BS. Disease control effect of strevertenes produced by *Streptomyces psammoticus* against tomato Fusarium wilt. Journal of Agricultural and Food Chemistry 2011;59(5):1893–9.
42. Yekkour A, Sabaou N, Zitouni A, Errakhi R, Mathieu F, Lebrihi A. Characterization and antagonistic properties of *Streptomyces* strains isolated from Saharan soils, and evaluation of their ability to control seedling blight of barley caused by *Fusarium culmorum*. Letters in Applied Microbiology 2012;55(6):427–35.
43. Singh PP, Shin YC, Park CS, Chung YR. Biological control of Fusarium wilt of cucumber by chitinolytic bacteria. Phytopathology 1999;89(1):92–9.
44. Kawuri R, Suprapta DN, Nitta Y. Antagonistic activity of *Streptomyces thermocarboxydus* to *Fusarium oxysporum*: the cause of leaf rot disease on *Aloe vera* (*Aloe barbadensis* Mill.) in Bali, Indonesia. Malaysian Journal of Microbiology 2018;14(1):10–5.
45. Zhao S, Tian CY, Du CM. Production of hybrids of *Streptomyces bikiniensis* strain HD-087 by genome shuffling and enhancement of its bio-control activity against *Fusarium oxysporum* f. sp *cucumerinum*. Journal of Horticultural Science and Biotechnology 2014;89(2):147–52.
46. Faheem M, Raza W, Zhong W, Nan Z, Shen QR, Xu YC. Evaluation of the biocontrol potential of *Streptomyces goshikiensis* YCXU against *Fusarium oxysporum* f. sp *niveum*. Biological Control 2015;81:101–10.
47. Bressan W, Figueiredo JEF. Efficacy and dose-response relationship in biocontrol of Fusarium disease in maize by *Streptomyces* spp. European Journal of Plant Pathology 2008;120(3):311–6.
48. Du X, Zhai Y, Deng Q, Tan H, Cao L. Illumina-based sequencing analysis directed selection for actinobacterial probiotic candidates for banana plants. Probiotics and Antimicrobial Proteins 2018;10(2):284–92.
49. Zhang J, Chen J, Jia RM, Ma Q, Zong ZF, Wang Y. Suppression of plant wilt diseases by nonpathogenic *Fusarium oxysporum* Fo47 combined with actinomycete strains. Biocontrol Science and Technology 2018;28(6):562–73.
50. Amini J, Agapoor Z, Ashengroph M. Evaluation of *Streptomyces* spp. against *Fusarium oxysporum* f. sp. *ciceris* for the management of chickpea wilt. Journal of Plant Protection Research 2016;56(3):257–64.
51. Zhao S, Du CM, Tian CY. Suppression of *Fusarium oxysporum* and induced resistance of plants involved in the biocontrol of

cucumber Fusarium wilt by *Streptomyces bikiniensis* HD-087. World Journal of Microbiology and Biotechnology 2012;28(9):2919–27.

52. Getha K, Vikineswary S, Wong WH, Seki T, Ward A, Goodfellow M. Evaluation of *Streptomyces* sp. strain g10 for suppression of Fusarium wilt and rhizosphere colonization in pot-grown banana plantlets. Journal of Industrial Microbiology and Biotechnology 2005;32(1):24–32.

53. Zhang Q, Chen J, Tong Y, Xu J. Isolation and identification of actinomyces K5 antagonistic against *Fusarium oxysporum* f. sp. *vasinfectum*. Chinese Journal of Biological Control 2008;24(4):325–8.

54. Cao LX, Qiu ZQ, You JL, Tan HM, Zhou SN. Isolation and characterization of endophytic streptomycete antagonists of Fusarium wilt pathogen from surface-sterilized banana roots. FEMS Microbiology Letters 2005;247(2):147–52.

55. Seangnak V, Chaisiri C, Nalumpang S. Use of antagonistic *Streptomyces* spp. against chili wilt disease caused by *Fusarium oxysporum* f. sp. *capsici*. International Journal of Agricultural Technology 2013;9(7):1895–908.

56. Jung B, Park SY, Lee YW, Lee J. Biological efficacy of *Streptomyces* sp. strain BN1 against the cereal head blight pathogen *Fusarium graminearum*. Plant Pathology Journal 2013;29(1):52–8.

57. Tewfike TA. Biocontrol activity of *Streptomyces fulvoviolaceus* against *Fusarium oxysporum* and *Rhizoctonia solani* pathogens of tomato plants. Annals of Agricultural Science, Moshtohor 2000;38(3):1503–20.

58. Lu D, Ma Z, Xu X, Yu X. Isolation and identification of biocontrol agent *Streptomyces rimosus* M527 against *Fusarium oxysporum* f. sp. *cucumerinum*. Journal of Basic Microbiology 2016;56(8):929–33.

59. Kanini GS, Katsifas EA, Savvides AL, Karagouni AD. *Streptomyces rochei* ACTA1551, an indigenous Greek isolate studied as a potential biocontrol agent against *Fusarium oxysporum* f. sp. *lycopersici*. BioMed Research International 2013:387230.

60. Minuto A, Minuto G, Migheli Q, Mocioni M, Gullino ML. Effect of antagonistic *Fusarium* spp. and of different commercial biofungicide formulations on Fusarium wilt of basil (*Ocimum basilicum* L.). Crop Protection 1997;16(8):765–9.

61. Dumroese RK, James RL, Wenny DL. Interactions among *Streptomyces griseoviridis*, Fusarium root disease, and Douglas-fir seedlings. New Forests 1998;15(2):181–91.

62. Goudjal Y, Zamoum M, Sabaou N, Mathieu F, Zitouni A. Potential of endophytic *Streptomyces* spp. for biocontrol of Fusarium root rot disease and growth promotion of tomato seedlings. Biocontrol Science and Technology 2016;26(12):1691–705.

63. Elson MK, Kelly JF, Nair MG. Influence of antifungal compounds from a soil-borne actinomycete on *Fusarium* spp. in asparagus. Journal of Chemical Ecology 1994;20(11):2835–46.

64. Nafie EM. The possible induction of resistance in *Lupinus termis* L. against *Fusarium oxysporum* by *Streptomyces chibaensis* and its mode of action: I. Changes in certain morphological criteria and biochemical composition related to induced resistance. International Journal of Agriculture and Biology 2003;5(4):463–72.

65. Soltanzadeh M, Nejad MS, Bonjar GHS. Application of soil-borne actinomycetes for biological control against Fusarium wilt of chickpea (*Cicer arietinum*) caused by *Fusarium solani* f. sp. *pisi*. Journal of Phytopathology 2016;164(11–12):967–78.

66. Vasconcellos RLFd, Cardoso EJBN. Rhizospheric streptomycetes as potential biocontrol agents of Fusarium and Armillaria pine rot and as PGPR for *Pinus taeda*. Biocontrol 2009;54(6):807–16.

67. Smith J, Putnam A, Nair M. In vitro control of Fusarium diseases of *Asparagus Officinalis* L. with a *Streptomyces* or its polyene antibiotic, faeriefungin. Journal of Agricultural and Food Chemistry 1990;38(8):1729–33.

68. Bonjar GHS, Farrokhi PR, Shafii B, Aghighi S, Mahdavi MJ, Aghelizadeh A. Laboratory preparation of a new antifungal agent from *Streptomyces olivaceus* in control of *Fusarium oxysporum* f. sp. *melonis* of cucurbits in greenhouse. Journal of Applied Sciences 2006;6(3):607–10.

69. Ranveer K, Sharma AK. Control of Fusarium wilt using biological agent *Streptomyces* sp. CPP-53 isolated from compost with plant growth promoting effect on tomato under greenhouse condition. Journal of Microbiology and Antimicrobials 2014;6(6):97–103.

70. El-Tarabily K, McKenna F. Biological control of wilt disease of tomato caused by *Fusarium oxysporum* f. sp *lycopersici* by endophytic ACC-deaminase producing actinomycetes in the United Arab Emirates. Phytopathology 2008;98(6):S51–S.

71. Himmelstein JC, Everts K, Balci Y. Efficacy of a *Vicia villosa* green manure and *Streptomyces lydicus* for management of Fusarium wilt of watermelon in the greenhouse and in vitro. Phytopathology 2012;102(7):53-.

72. Domracheva LI, Shirokikh IG, Fokina AI. Anti-*Fusarium* activity of cyanobacteria and actinomycetes in soil and rhizosphere. Microbiology (Moscow) 2010;79(6):871–6.

73. Al-Sahli AA, Abdulkhair WM. Biocontrol of *Fusarium udum* diseases for some wheat cultivars by *Streptomyces sporoaveus*. African Journal of Microbiology Research 2012;6(1):190–6.

74. Kämpfer P. The family Streptomycetaceae, Part I: taxonomy. In: Dworkin M, Falkow S, Rosenberg E, Schleifer K-H, Stackebrandt E, editors. The Prokaryotes: Volume 3: Archaea Bacteria: Firmicutes, Actinomycetes. Springer, New York; 2006. p. 538–604.

75. Sysuev VA, Shirokikh IG, Merzaeva OV. Biological efficiency of *Streptomyces hygroscopicus* A-4 against phytopathogenic fungus *Fusarium avenaceum* 7/2 in the rhizosphere. Journal of Fungal Research 2008;6(2):83–7.

76. Pérez-Corral DA, García-González NY, Gallegos-Morales G, Ruiz-Cisneros MF, Berlanga-Reyes DI, Ríos-Velasco C. Isolation of actinomycetes associated to apple trees rhizosphere antagonistic to *Fusarium equiseti*. Revista Mexicana de Ciencias Agrícolas 2015;6(7):1629–38.

77. Wang ZF, Wang CL, Li FJ, Li ZJ, Chen MH, Wang YR, *et al.* Fumigant activity of volatiles from *Streptomyces alboflavus* TD-1 against *Fusarium moniliforme* Sheldon. Journal of Microbiology 2013;51(4):477–83.

78. Abdulkhair WM. Chitinolytic activity of highly halotolerant *Streptomyces tendae* against *Fusarium oxysporum* PTK2. African Journal of Biotechnology 2012;11(89):15529–38.

79. Bernardo KT, Franco CMM, Chataway T. Proteomic Analysis in *Arabidopsis thaliana* Inoculated with a Beneficial Endophytic *Streptomyces* sp. in Response to a Challenge by the Pathogen

*Fusarium Oxysporum*. Deutsche Phytomedizinische Gesellschaft e.V. Verlag, Braunschweig; 2013. p. 78–87.

80. Cao LX, Qiu ZQ, Dai X, Tan HM, Lin YC, Zhou SN. Isolation of endophytic actinomycetes from roots and leaves of banana (*Musa acuminata*) plants and their activities against *Fusarium oxysporum* f. sp. *cubense*. World Journal of Microbiology and Biotechnology 2004;20(5):501–4.

81. Getha K, Vikineswary S. Antagonistic effects of *Streptomyces violaceusniger* strain G10 on *Fusarium oxysporum* f. sp. *cubense* race 4: indirect evidence for the role of antibiosis in the antagonistic process. Journal of Industrial Microbiology and Biotechnology 2002;28(6):303–10.

82. Zacky FA, Ting S. Biocontrol of *Fusarium oxysporum* f. sp. *cubense* tropical race 4 by formulated cells and cell-free extracts of *Streptomyces griseus* in sterile soil environment. Biocontrol Science and Technology 2015;25(6):685–96.

83. Zacky FA, Ting S. Investigating the bioactivity of cells and cell-free extracts of *Streptomyces griseus* towards *Fusarium oxysporum* f. sp. *cubense* race 4. Biological Control 2013;66(3):204–8.

84. Al-Askar AA, Baka ZA, Rashad YM, Ghoneem KM, Abdulkhair WM, Hafez EE, *et al.* Evaluation of *Streptomyces griseorubens* E44G for the biocontrol of *Fusarium oxysporum* f. sp. *lycopersici*: ultrastructural and cytochemical investigations. Annals of Microbiology 2015;65(4):1815–24.

85. Mujoko T, Sastrahidayat IR, Hadiastono T, Djauhari S. Antagonistic effect of *Streptomyces* spp. on spore germination and mycelial growth of *Fusarium oxysporum* f. sp. *lycopersici*. International Journal of Biosciences 2014;5(9):414–22.

86. Soares ACF, Sousa CdS, Garrido MdS. Streptomycetes antagonism against *Cladosporium fulvum* Cooke and *Fusarium oxysporum* f. sp. *lycopersici*. Ciencia Rural 2009;39(6):1897–900.

87. Anitha A, Rebeeth M. Self-fusion of *Streptomyces griseus* enhances chitinase production and biocontrol activity against *Fusarium oxysporum* f. sp. *lycopersici*. Biosciences, Biotechnology Research Asia 2009;6(1):175–80.

88. Hatamy N, Bonjar GHS, Sadeghy B. Screening and isolation of Actinomycetes isolates in biological control of *Fusarium solani, f. moniliforme* and *F. subglutinans* the causal agent of rot root of greenhouse cucumber *in vitro* conditions. Archives of Phytopathology and Plant Protection 2014;47(4):437–41.

89. Sadeghy B, Hatamy N. Several physiological features of *Streptomyces* sp. isolate C-1 showing bioactivity against *Fusarium sambucinum* and *Verticillium dahliae*. Archives of Phytopathology and Plant Protection 2013;46(20):2519–27.

90. El-Khonezy MI, El-Gammal EW, Atwa NA, El-Abd MA. Partial purification and characterization of an alkaline serine protease produced by *Streptomyces griseus* NCRRT and its antifungal effect on *Fusarium solani*. World Applied Sciences Journal 2015;33(5):831–42.

91. Aghighi S, Bonjar GHS, Rawashdeh R, Batayneh S, Saadoun I. First report of antifungal spectra of activity of Iranian actinomycetes strains against *Alternaria solani*, *Alternaria alternata*, *Fusarium solani*, *Phytophthora megasperma*, *Verticillium dahliae* and *Saccharomyces cerevisiae*. Asian Journal of Plant Sciences 2004;3(4):463–71.

92. Sadeghy B, Hatamy N. Isolation and investigation of extracellular metabolites of *Streptomyces* sp. for biological control of *Fusarium subglutinans*, the causal agent of wilting cucumber greenhouse. Archives of Phytopathology and Plant Protection 2014;47(2):171–7.

93. Nguyen PA, Strub C, Durand N, Alter P, Fontana A, Schorr-Galindo S. Biocontrol of *Fusarium verticillioides* using organic amendments and their actinomycete isolates. Biological Control 2018;118:55–66.

94. Ito M, Sato I, Koitabashi M, Yoshida S, Imai M, Tsushima S. A novel actinomycete derived from wheat heads degrades deoxynivalenol in the grain of wheat and barley affected by Fusarium head blight. Applied Microbiology and Biotechnology 2012;96(4):1059–70.

95. Minuto A, Garibaldi A. Prevention of root diseases in soilless cultures used as methyl bromide alternatives. Proceedings of the VI$^{th}$ International Symposium on Chemical and Non-Chemical Soil and Substrate Disinfestation 2005(698):241–9.

96. Paul PA, Lipps PE, Hershman DE, McMullen MP, Draper MA, Madden LV. A quantitative review of tebuconazole effect on Fusarium head blight and deoxynivalenol content in wheat. Phytopathology 2007;97(2):211–20.

97. Dignam BEA, O'Callaghan M, Condron LM, Raaijmakers JM, Kowalchuk GA, Wakelin S. Challenges and opportunities in harnessing soil disease suppressiveness for sustainable pasture production. Soil Biology and Biochemistry 2016;95:100–11.

98. Mazzola M. Assessment and management of soil microbial community structure for disease suppression. Annual Review of Phytopathology 2004;42:35–59.

99. Garbeva P, van Veen JA, van Elsas JD. Microbial diversity in soil: selection of microbial populations by plant and soil type and implications for disease suppressiveness. Annual Review of Phytopathology 2004;42(1):243–70.

100. Mazzola M. Mechanisms of natural soil suppressiveness to soilborne diseases. Antonie van Leeuwenhoek 2002;81(1):557–64.

101. Henis Y, Ghaffar A, Baker R. Factors affecting suppressiveness to *Rhizoctonia solani* in soil. Phytopathology 1979;69(11):1164–9.

102. Wijetunga C, Stack RW, Baker R. Induction of suppressiveness to *Rhizoctonia solani* in an unmodified loamy soil. Phytopathology 1984;74(7):862-.

103. Nelson EB, Kuter GA, Hoitink HAJ. Induction of suppressiveness to Rhizoctonia damping-off by species of *Trichoderma* and *Gliocladium virens* from composted hardwood bark. Phytopathology 1982;72(7):1011.

104. Chet I, Baker R. Induction of suppressiveness to *Rhizoctonia solani* in soil. Phytopathology 1980;70(10):994–8.

105. Mazzola M, Gu Y-H. Wheat genotype-specific induction of soil microbial communities suppressive to disease incited by *Rhizoctonia solani* anastomosis group (AG)-5 and AG-8. Phytopathology 2002;92(12):1300–7.

106. Kim D-R, Jeon C-W, Shin J-H, Weller DM, Thomashow L, Kwak Y-S. Function and distribution of a lantipeptide in strawberry Fusarium wilt disease-suppressive soils. Molecular Plant-Microbe Interactions 2018. doi: 10.1094/MPMI-05-18-0129-R.

107. Jauri PV, Altier N, Pérez CA, Kinkel L. Cropping history effects on pathogen suppressive and signaling dynamics in *Streptomyces* communities. Phytobiomes 2017;2(1):14–23.

108. Bakker MG, Glover JD, Mai JG, Kinkel LL. Plant community effects on the diversity and pathogen suppressive activity of soil streptomycetes. Applied Soil Ecology 2010;46(1):35–42.

109. Peralta AL, Sun Y, McDaniel MD, Lennon JT. Crop rotational diversity increases disease suppressive capacity of soil microbiomes. Ecosphere (Washington, D.C) 2018;9(5): e02235.

110. Xiong W, Li R, Ren Y, Liu C, Zhao Q, Wu H, *et al.* Distinct roles for soil fungal and bacterial communities associated with the suppression of vanilla Fusarium wilt disease. Soil Biology and Biochemistry 2017;107:198–207.

111. Xiong W, Zhao QY, Zhao J, Xun WB, Li R, Zhang RF, *et al.* Different continuous cropping spans significantly affect microbial community membership and structure in a vanilla-grown soil as revealed by deep pyrosequencing. Microbial Ecology 2015;70(1):209–18.

112. Scher FM, Baker R. Mechanism of biological control in a *Fusarium*-suppressive soil. Phytopathology 1980;70(5):412–7.

113. Kinkel LL, Schlatter DC, Bakker MG, Arenz BE. Streptomyces competition and co-evolution in relation to plant disease suppression. Research in Microbiology 2012;163(8):490–9.

114. Zhao M, Yuan J, Zhang R, Dong M, Deng X, Zhu C, *et al.* Microflora that harbor the NRPS gene are responsible for Fusarium wilt disease-suppressive soil. Applied Soil Ecology 2018;132:83–90.

115. Wiggins E, Kinkel LL. Green manures and crop sequences influence alfalfa root rot and pathogen inhibitory activity among soil-borne streptomycetes. Plant and Soil 2005;268(1–2):271–83.

116. Wiggins BE, Kinkel LL. Green manures and crop sequences influence potato diseases and pathogen inhibitory activity of indigenous streptomycetes. Phytopathology 2005;95(2):178–85.

117. Perez C, Dill-Macky R, Kinkel LL. Management of soil microbial communities to enhance populations of *Fusarium graminearum*-antagonists in soil. Plant and Soil 2008;302(1–2):53–69.

118. Ren G, Ma Y, Guo D, Gentry TJ, Hu P, Pierson EA, *et al.* Soil bacterial community was changed after brassicaceous seed meal application for suppression of Fusarium wilt on pepper. Frontiers in Microbiology 2018;9:185.

119. De Corato U, Salimbeni R, De Pretis A. Suppression of soil-borne pathogens in container media amended with on-farm composted agro-bioenergy wastes and residues under glasshouse condition. Journal of Plant Diseases and Protection 2018;125(2):213–26.

120. Anitha A, Rabeeth M. Control of *Fusarium* wilt of tomato by bioformulation of *Streptomyces griseus* in green house condition. African Journal of Basic and Applied Sciences 2009;1(1–2):1–14.

121. Vurukonda SSKP, Giovanardi D, Stefani E. Plant growth promoting and biocontrol activity of *Streptomyces* spp. as endophytes. International Journal of Molecular Sciences 2018;19(4):952.

122. Shimizu M. Endophytic actinomycetes: biocontrol agents and growth promoters. In: Maheshwari DK, editor. Bacteria in Agrobiology: Plant Growth Responses. Springer, Berlin, Heidelberg; 2011. p. 201–20.

123. Weisskopf L, Ryu CM, Raaijmakers JM, Garbeva P. Editorial: smelly fumes: volatile-mediated communication between bacteria and other organisms. Frontiers in Microbiology 2016;7:2031.

124. Citron CA, Barra L, Wink J, Dickschat JS. Volatiles from nineteen recently genome sequenced actinomycetes. Organic and Biomolecular Chemistry 2015;13(9):2673–83.

125. Pieterse CM, Zamioudis C, Berendsen RL, Weller DM, Van Wees SC, Bakker PA. Induced systemic resistance by beneficial microbes. Annual Review of Phytopathology 2014;52:347–75.

126. Conn VM, Walker AR, Franco CM. Endophytic Actinobacteria induce defense pathways in *Arabidopsis thaliana*. Molecular Plant-Microbe Interactions 2008;21(2):208–18.

127. Keswani C, Bisen K, Singh V, Sarma BK, Singh HB. Bioformulations: for Sustainable Agriculture. Springer, New Delhi, India; 2016.

128. Figueiredo MdVB, Bonifacio A, Rodrigues AC, de Araujo FF, Stamford NP. Beneficial microorganisms: current challenge to increase crop performance. In: Arora NK, Mehnaz S, Balestrini R, editors. Bioformulations: for Sustainable Agriculture. Springer India, New Delhi; 2016. p. 53–70.

129. Ploetz RC. Management of Fusarium wilt of banana: a review with special reference to tropical race 4. Crop Protection 2015;73:7–15.

130. Law JW-F, Ser H-L, Khan TM, Chuah L-H, Pusparajah P, Chan K-G, *et al.* The potential of *Streptomyces* as biocontrol agents against the rice blast fungus, *Magnaporthe oryzae* (*Pyricularia oryzae*). Frontiers in Microbiology 2017;8:3.

131. Kim HJ, Boedicker JQ, Choi JW, Ismagilov RF. Defined spatial structure stabilizes a synthetic multispecies bacterial community. Proceedings of the National Academy of Sciences 2008;105(47):18188.

132. Großkopf T, Soyer OS. Synthetic microbial communities. Current Opinion in Microbiology 2014;18:72–7.

133. Johns NI, Blazejewski T, Gomes ALC, Wang HH. Principles for designing synthetic microbial communities. Current Opinion in Microbiology 2016;31:146–53.

134. De Roy K, Marzorati M, Van den Abbeele P, Van de Wiele T, Boon N. Synthetic microbial ecosystems: an exciting tool to understand and apply microbial communities. Environmental Microbiology 2014;16(6):1472–81.

135. Moody MJ, Jones SE, Crisante DA, Elliot MA. *Streptomyces* bacteria: specialized metabolism, inter-species interations and non-coding RNAs. In: Leitão AL, Enguita FJ, editors. Non-coding RNAs and Inter-Kingdom Communication. Springer International Publishing, Cham, Switzerland; 2016. p. 83–101.

136. Essarioui A, LeBlanc N, Kistler HC, Kinkel LL. Plant community richness mediates inhibitory interactions and resource competition between *Streptomyces* and *Fusarium* populations in the rhizosphere. Microbial Ecology 2017;74(1):157–67.

137. Strap JL. Actinobacteria–plant interactions: a boon to agriculture. In: Maheshwari DK, editor. Bacteria in Agrobiology: Plant Growth Responses. Springer, Berlin, Heidelberg; 2011. p. 285–307.

138. Herrera Paredes S, Gao T, Law TF, Finkel OM, Mucyn T, Teixeira PJPL, *et al.* Design of synthetic bacterial communities for predictable plant phenotypes. PLoS Biology 2018;16(2): e2003962.