Department of Agricultural Science

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Ph.D. Thesis in Sustainable Agricultural And Forestry Systems And Food Security

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Characterization and selection of *Beauveria bassiana* isolates for their potential as dual biocontrol agents

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Chapter 1: General introduction

1. Biological control

Biological control or biocontrol may include different phenomena and can be associated to naturally occurring or anthropogenic application-based agricultural settings. Initially, the former system considers the major ecological forces of nature and involves the regulation of plant and animal populations by their natural enemies (Debach and Rosen, 1991). Later, in the twentieth century, the application of biological control in agriculture was established as a strategy for pest management. However, the rapid spread and development of different biological control approaches and practices together with scientific advancements in the field led to biocontrol fragmentation into subspecialties (Barratt *et al*. 2018). For example, in their books on biological control of plant pathogens, Baker and Cook (1974, 1983) noted that their definitions and terminology differed from those of entomologists. This difference has continued for several decades, prompting Eilenberg *et al.* (2001) and later Heimpel and Mills (2017) to suggest a unifying terminology that could be accepted in all areas of biological control. More recently, Eilenberg *et al.* (2001), applied a definition revolving around 'the use of living organisms to suppress the population density or impact of a specific pest organism, making it less abundant or less damaging than it otherwise would be', with further emphasis that the term biological control should exclusively be used for living organisms, excluding other natural or semi-natural agents. This definition and classification have had some success, having been adopted and followed by many entomologists, but they are still largely non used by pathologists and weed scientists, as well as other stakeholders. Thus, as the application of biological control as an important element of IPM is escalating, there is an increasing need for cross-disciplinary terminological and conceptual harmonization. Despite the separate and divisive development between pathologists and entomologists, the general term biological control has acquired positive connotations in society, prompting both industrial and scientific interest groups to extend the concept to include the use of related biologically-derived agents and products (Gray *et al.* 2018; Santos *et al.,* 2011).

In entomology, biological control is described as the use of living predators, parasitoids, or entomopathogenic microorganisms to suppress pest populations (Pal and Gardener, 2006). For many years, the direct consumption of pests, phytopathogens, and weeds by antagonists, which leads to trophic cascades, has been considered to be the most important process for reducing plant damage in natural ecosystems (Hairston *et al.,* 1960). For example, predators kill and consume their prey (e.g., pests or weed seeds), whereas insect parasitoids oviposit their eggs on or in their hosts, which are subsequently consumed by the developing or maturing offspring. Similarly, some entomopathogenic living agents (especially fungi) may penetrate the external cuticle of insects, causing systemic infection, whereas others (especially bacteria and viruses) cause infection and death of the host

following ingestion. In entomology, biological control is defined using the following three approaches: classical, augmentative and conservative.

1) Classical biological control is defined as the introduction of non-native natural enemies into a new ecosystem to control non-native pests.

2) Augmentative biological control involves the release of biocontrol agents to control pests. These strategies include two methods: inoculative and inundative. Inundative control provides for the introduction of a large number of biocontrol agents with the goal of reducing the damage caused by pests. Inoculative control methods include the release of biocontrol agents, which are expected to provide pest control after propagation. The success of the latter type of application is highly dependent on the population of the biocontrol agent adapting to and reproducing where it has been released (Eilenberg *et al.*, 2001).

3) Conservative biological control is the adjustment of the environment or existing practices to protect and enhance the environmental conditions to promote the establishment of the native populations. The main difference in this approach from other biological control approaches is that natural enemies are not directly released in the environment (Eilenberg *et al.,* 2001).

In plant pathology, biological control is considered as a result of different types of interactions that can eventually occur among microorganisms. In most cases, pathogens are either directly or indirectly antagonized by the presence and activity of other microorganisms. The different modes of action used by biocontrol-active microorganisms may include parasitism, antibiosis, competition for space and nutrients, and induction of plant resistance (Cook, 1993).

Parasitism:

Parasitism is a nutritional relationship in which one organism feeds at the expense of the other (the host). This intermicrobial relationship is based on a very complex series of events that include recognition, attack, and subsequent penetration and killing of the host. The various mechanisms used by fungi to antagonize or parasitize their competitors include antibiotic production, secretion of lytic enzymes, hyphal interference and direct penetration of the host. Any particular prey-fungus/host-fungus interaction (mycoparasitism) may encompass more than one of those mechanisms either individually or simultaneously (Jeffries, 1994). Mycoparasitism involves morphological changes, such as coiling and formation of appressorium-like structures, which contain high concentrations of osmotic solutes such as glycerol to penetrate host cells. Lysis of the host cell wall is considered the key step of mycoparasitic attack (Kubicek *et al*., 2001; Howell, 2003).

Antibiosis:

Antibiosis is defined as an antagonistic interaction between two organisms in which one of them inhibits the proliferation of the other through the production of antibiotic compounds. Generally, antibiotics are microbe-derived molecules that can intoxicate/poison or kill other microorganisms at low concentrations. Some antibiotics produced by microorganisms have been shown to be particularly effective against plant pathogens and the diseases they cause (Howell and Stipanovic, 1980; Islam *et al*., 2005; Shanahan *et al*., 1992). In all cases, antibiotics have been shown to be particularly effective in suppressing the growth of the target pathogen *in vitro* and/or *in situ*.

Competition:

Competition occurs when two (or more) organisms require the same resource, and the rivalry between them excludes the availability of this resource to the other. Nutrient sources in the soil and in the rhizosphere are frequently insufficient for most microorganisms, and starvation is the most common cause of microorganism death. For successful colonization of the phyllosphere and rhizosphere, microbes must effectively compete for available nutrients. It is generally believed that competition between pathogens and non-pathogens for nutrient resources is an important issue in biocontrol. Competition is believed to be more critical for soil-borne pathogens, including *Fusarium* and *Pythium* species, that infect through mycelial contact than foliar pathogens that germinate directly on plant surfaces and infect through appressoria and infection pegs (Elad and Baker, 1985; Keel *et al*., 1989; Loper and Buyer, 1991). Competition for rare but essential micronutrients, such as iron, zinc and copper has also been shown to be important in biological disease control. Competition is also possible for oxygen, space and, in the case of autotrophs, light.

Induction of plant resistance:

Plants actively respond to a variety of environmental stimulating factors, including gravity, light, temperature, physical stress, water and nutrient availability, and chemicals produced by soil and plant-associated microorganisms. Such stimuli can either induce or condition plant host defenses through biochemical changes that enhance resistance against subsequent infections by a variety of pathogens. The induction of host defences can be local and/or systemic in nature, depending on the type, source, and amount of stimulating agents (Audenaert *et al*., 2002; De Meyer and Höfte, 1997; Kloepper *et al*., 1980; Leeman *et al.*, 1995).

1.1. *Beauveria bassiana*

Beauveria (Balsamo-Crivelli) Vuillemin is a global anamorphic genus of soil-borne facultative necrotrophic arthropod-pathogenic fungi (Roberts and Hajek, 1992), which also appear as saprotrophs in the soil and as plant endophytes (Vega *et al.,* 2008). The first studies of this fungus date back to the early 19th century, when silkworm farms in Italy and France were plagued with diseases which periodically decimated the European silk industry. In 1835, Agostino Bassi demonstrated that the agent threatening the Italian silkworm industry, named White Muscardine or Calcino disease was caused by a parasitic fungus (Steinhaus, 1956) infecting silkworm larvae. Previous reports of a fungal entomopathogen, possibly the organism that would come to be known as *Beauveria bassiana* (Balsamo) Vuillemin, came from China as far back as 2700 BC (Steinhaus, 1956). Balsamo Crivelli officially named the organism *Botrytis paradoxica*, eventually changing its name to *Botrytis bassiana* to honor the man who firstly described it. In 1912, Vuillemin determined that there were enough features characteristic to *Botrytis bassiana* to assign it to a new genus *Beauveria* (de Hoog, 1972). Currently, multiple species in the genus *Beauveria* Vuill., some including *B. bassiana*, *Beauveria brongniartii*, *and Beauveria alba*, which are important entomopathogens with a wide host range, including arthropods other than insects, are being used as biological control agents to control a variety of crop-damaging insects. *B. bassiana* is considered non-pathogenic to vertebrates, although there are only a handful of recorded cases of human infection by this fungus (Kisla *et al*., 2000; Tucker *et al*., 2004). However, these cases involved immune-compromised patients, having increased susceptibility to a wide range of opportunistic infections (Henke *et al*., 2002). Based on toxicity/safety tests, and considerations as a "natural product," *B. bassiana* was approved by the U.S. Environmental Protection Agency for Commercial Use as a biopesticide as: it is non-toxic to mammals, birds, and plants, and its use is not expected to have deleterious effects on human health or on the environment (EPA 2000). Strains and formulations of *B. bassiana* are commercially available in various parts of the world.

1.1.1 Biology

B. bassiana is a widely diffused genus of cosmopolitan soil fungi that has a remarkable ecological distribution and consists of many entomopathogenic species of economic importance (Rehner *et al*., 2011; Robène-Soustrade *et al*., 2015).

Although this ubiquitous fungus is a saprophyte, it can colonize plants as an avirulent endophyte and can also be a facultative pathogen of numerous arthropods, including insect pests harmful to

agriculture (Boomsma *et al*., 2014), where it is frequently employed as a biocontrol agent for arthropod species that pose a threat to the health of humans, animals, and plants.

B. bassiana is one of the most studied fungal species among entomopathogens and it is distinguished by a very broad host range that includes more than 700 species of insects and mites (Zimmermann, 2007). These strains are exploited as effective biological control agents (BCA) because of their high variability which enables the selection of virulent strains as specific antagonists of given target pests (Sasan and Bidochka, 2012; Lacey *et al*., 2015; Quesada-Moraga *et al*., 2006; Erler and Ates, 2015). In-depth research on host-pathogen interactions and antagonistic modes of action has also uncovered a variety of biologically active secondary metabolites associated with insect host disease and virulence, which have potential uses in industrial, medicinal, and agricultural fields (Wang *et al*., 2021). As a plant endophyte, *B. bassiana* is able to elicit defense responses in the host, which activates barriers against plant pathogenic fungi and pest insect attacks (Ownley *et al*., 2008; Jaber and Ownley, 2018). Due to *B. bassiana'*s multiple beneficial traits, biotechnologies and commercial biological products incorporating it as a microbial BCA have been developed, marketed globally as novel "low risk" biopesticides or alternatives to chemical insecticides. The extensive research on *B. bassiana* that has been done recently is amazing and has led to a better knowledge from both the standpoint of basic research and the development of its biotechnological applications.

This thesis aims to provide an overview of the most important data on *B. bassiana* that is currently known from the literature, addressing aspects of its biology, such as the generation of bioactive metabolites, mode of action, and traits that support its potential as an alternative in agricultural applications.

1.1.1.1. Taxonomy

The complete systematic position of *B. bassiana* according to Sung *et al*. (2006) and Halouane (2008) is as follows:

- Kingdom: Fungi,
- Phylum: Ascomycota,
- Class: Sordariomycetes,
- Order: Hypocreales,
- Family: Clavicipitaceae / Cordicipitaceae or Ophiocordicipitaceae,
- Genus: *Beauveria*,
- Species: *B. bassiana* (Bals.-Criv.) (Vuil., 1912).

Note: in some documents, the pathogen was considered to belong to Cordycipitaceae or Ophiocordicipitaceae (Sensagent 2000–2016).

1.1.1.2. Morphology

B. bassiana represents the anamorphic form of *Cordyceps bassiana*, which is distinguished by its exclusively asexual reproduction. This occurs through the production of "conidia" (from the Greek κόνις, which means dust), haploid single-celled reproductive structures, globose in shape and hyaline, with a size of 2-3 µm, produced by agamic way by specialized hyphae called "conidiophores," in turn produced at the extremity of the hyphae that make up the body of the fungus (Fig. 1.1). Different types of conidia can be produced by *B. bassiana* depending on the environment. In the presence of air (aerobic environment), the fungus produces spherical (1–4 µm in diameter) or oval (1.55–5.5 µm × 1–3 µm in size) conidia but in an anaerobic condition (in liquid media), it produces oval shape blastospores (2–3 µm in diameter and 7 µm in length) unicellular, budding yeast-like cells which are similar to *in vivo* produced hyphal bodies (Bidochka *et al.,* 1987; Jackson *et al.,* 1997; Wanchoo *et al.,* 2009). Blastospores and conidia are all infectious organs (Weiser, 1972; Lipa, 1975).

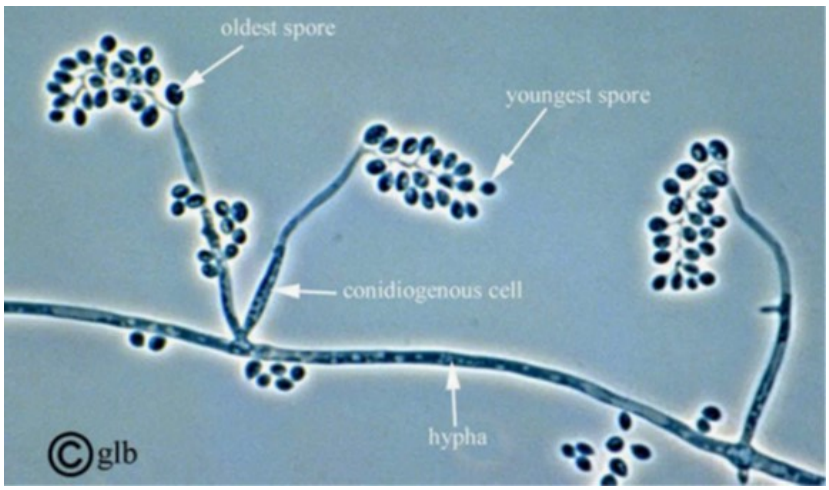

Figure 1.1. **Optical microscope image of a *Beauveria bassiana* hypha bearing conidiophores and conidial branches** [from SilkPathDB - Silkworm Pathogen Database, https://silkpathdb.swu.edu.cn].

1.2. Life cycle

Infection caused by *B. bassiana* begins when spores or aerial conidia attach to the host cuticle (Boucias & Pendland, 1991). Hyphae, aerial conidia, single-cell blastospores (the yeast-like form), and submerged conidia (specialized cells grown in minimum liquid medium) all appear to represent infectious life stages of the fungus (Holder *et al*., 2007). The degree to which these later fungal forms

infect insects in the wild is uncertain, although asexually generated (aerial) conidia are thought to be the principal infectious and dispersion structures because they can withstand diverse abiotic conditions to a greater extent than hyphae and blastospores. Conidia of *B. bassiana* are hydrophobic and adhere to the equally hydrophobic insect epicuticle or waxy layer, which is abundant in hydrocarbons, fatty acids, and wax esters (Holder and Keyhani, 2005). As a non-motile organism, the fungus targets insects through a passive process in which the first contact with prospective hosts is mediated by air, water-dispersion, and/or presence in the substrata over which insects would feed, such as the leaf surface and soil. As a result, infection might be seen as an opportunistic program initiated by conidia that just happen to locate themselves on a host cuticle. In this respect, although preferential sites of infection, typically those where sclerotization of the cuticle is lower (i.e., mouthparts and anus), have been noted for many insects, the fungus can initiate infection essentially anywhere on the host cuticle. In contrast, other microbial pathogens must consume host surfaces and/or use a more specific route of entry into the host. It appears that attachment itself consists of both general and particular components (Boucias *et al.,* 1988; Zhang *et al.,* 2011). With the outermost or rodlet layer of *B. bassiana* conidia made up of hydrophobin-containing proteins, hydrophobic interactions prevail. *B. bassiana* has at least two hydrophobin proteins that have been characterized: HYD1 and HYD2 (Cho *et al*., 2007; Kirkland & Keyhani, 2011). HYD1 is localized on the surface of aerial and submerged conidia, as well as on the base of germinating conidia, according to experiments utilizing antibodies against the tagged forms of HYD1 and HYD2. However, HYD1 was not found in blastospores. Similarly, HYD2 is located at the base of germinated conidia and on the surface of aerial conidia. However, the blastospores and submerged conidia did not contain HYD2. Furthermore, hyphae or hyphal bodies did not include neither HYD1 nor HYD2 proteins (Zhang *et al.,* 2011b). Despite loss of HYD1 (Δ*Bbhyd1* mutant) resulted in decreased virulence, whereas Δ*BbHyd2* mutants did not, the double mutants (Δ*Bbhyd1*Δ*Bbhyd2*) showed the most pronounced phenotype in terms of reduced adhesion and virulence. Both hydrophobins contribute to the rodlet layer structure as well as to cell surface hydrophobicity (Zhang *et al.*, 2011b). *Metarhizium robertsii*, a similar entomopathogenic fungus, contains a unique adhesion gene (*mad1*) that mediates attachment to insect cuticles (Wang and Leger, 2007). Although a homolog has been identified in the *B. bassiana* genome, its contribution to adhesion to insect surfaces and/or virulence is yet to be characterized. Besides, it has been described that surface signaling plays a major role in fungal infection (Kolattukudy *et al.,* 1995). Plant surface topographical features and chemicals on the surface can trigger germination of fungal spores and differentiation into appressoria by the plant pathogenic and stomatal penetrating fungus *Uromyces appendiculatus* (Hoch *et al.*, 1987). The formation of appressoria by *B. bassiana* strains remains controversial and may vary depending on the strain. For

instance, a SEM investigation of *B. bassiana* development on the red palm weevil found possible appressoria, but they were much less conspicuous than comparable experiments employing *M. anisopliae* (Güerri-Agulló *et al*., 2010). Additionally, it is uncertain to what extent appressoria created artificially (*i.e.* on a plastic surface) resemble those created during germination and growth on an insect's cuticle.

The life cycle of *B. bassiana* (Fan *et al*., 2007; Fang *et al*., 2005) proceeds through the following stages (Figures 1.2- 1.3).

1. Adhesion:

   The initial contact between conidia and the potential hosts is mediated by wind, rain splashing, arthropod vectors and/or presence in substrata over which insects would forage, *i.e.* the leaf surface and soil (Ortiz-Urquiza and Keyhani, 2013). For most entomopathogenic fungi, the host location is a random event, and conidial attachment is a passive process. The fungus can initiate infection essentially anywhere on the host cuticle, although preferential sites of infection, typically those where sclerotization of the cuticle is lower, such as mouthparts and anus, have been noted for many insects. The adhesion itself appears to include both nonspecific and specific components (Boucias *et al*., 1988; Zhang *et al*., 2011). It was found that the conidia of *B. bassiana* possessed an outer layer composed of interwoven fascicles of hydrophobic rodlets. This rodlet layer appears to be unique to the conidial stage and has not been detected in the vegetative cells. Adhesion is characterized by the recognition and compatibility mechanisms between the conidia of the host cuticle cells (Boucias *et al*., 1988). Conidia (or, in some cases, blastospores) attachment to the cuticle may involve specific receptor-ligand and/or nonspecific hydrophobic and electrostatic mechanisms (Mascarin and Jaronski, 2016). Hydrophobic interactions predominate with *B. bassiana* conidia containing an outermost or rodlet layer composed of proteins known as hydrophobins. Other factors involved in *B. bassiana* attachment are virulence-related lectins, which are carbohydrate-binding glycoproteins detected on the conidial surface.

2. Germination and differentiation:

   After adhesion, *B. bassiana* induces epicuticular modification through the production of mucilage (Wraight and Roberts, 1987) leading to conidia germination. The environmental conditions (availability of nutrients, oxygen, water, pH and temperature) can stimulate or inhibit the germination process, as well host physiology (biochemical composition of the host cuticle, including the presence of toxic host-surface compound) (Butt *et al*., 1995; Smith and

Grula,1982; Leger *et al*., 1989 a,b). Conidia or blastospores attached on the host cuticle by electrostatic forces, germinate and form a germ tube following rehydration and perception of chemical stimuli from the host (Mascarin and Jaronski, 2016). During this process the fungus produces specialized infection structures that can include penetration pegs and/or appressoria (*i.e.* an enlarged cell expression bearing key hydrolytic cuticle-degrading enzymes), which serves as inking point, enabling the growing hyphae to penetrate into the host integument (Mascarin and Jaronski, 2016). Scanning electron microscopy (SEM) revealed that conidia of *B. bassiana* attached to the cuticle of *Rhynchophorus ferrugineus* can germinate and differentiate appressoria. Moreover, the high frequency of *B. bassiana* appressoria differentiated on *R. ferrugineus* cuticle suggests that this structure provides the signals required for the triggering of this key event in fungus penetration of the host (Guerri-Agullò *et al*., 2010). Appressoria are produced on the arthropod cuticle, artificial substrates, and plants, suggesting that Entomopathogenic Fungi (EPF) respond to a wide range of cues. *Metarhizium flavoviride* and *M. anisopliae* will produce appressoria on synthetic, hard, hydrophobic substrates supplemented with traces of nutrients (Leger *et al*., 1989; Xavier-Santos *et al*., 1999). The MAP kinase gene *Bbmpk1* in *B. bassiana* is involved in appressorium production and cicada wing penetration, whereas *Bbhog1* controls the frequency of appressorium formation and reduces virulence (Zhang *et al.*, 2009, 2010). More targeted studies are required to elucidate how appressoria (if formed) contribute to virulence.

3. Penetration and colonization:

   At the beginning of the germination stage, the pathogen finds the first host immune barrier, the cuticle, which is a highly heterogeneous structure that can vary greatly in composition, even during the various life stages of a particular insect. The cuticle consists of different layers. The external layer, named the epicuticle, provides a hydrophobic barrier rich in lipids, followed by the procuticle (typically divided into the exo-, meso-, and endo-cuticular layers) that contains chitin and sclerotized protein. The procuticle, in turn, is followed by cells that constitute the epidermis, which sorrow the internal structures of the insect.

   The insect epicuticle does not consist only of lipids, but includes additional compounds, some of which having strong antimicrobial activity (e.g., n-alkanes, fatty acids, and aldehydes). The success of *B. bassiana* as an insect pathogen relies on its ability to overcome the antimicrobial barrier. From the appressorium or penetration peg and with the hydrolytic action of enzymes, mechanical pressure, and other factors (such as oxalic acid), the fungus is able to penetrate all cuticle layers until reaching the insect hemolymph to obtain nutrients for

its growth and reproduction. Once penetration has occurred, hyphae actively producing lytic enzymes (*i.e.* proteases, lipases, chitinases) (Leger *et al*., 1986; Krieger de Moraes *et al*., 2003; Fang *et al*., 2005) allow for colonization of internal host tissues, cause mechanical damage, toxicity, malnutrition, mummification, and finally victim's death. The presence of eight *Bt* cry-like genes in the *B. bassiana* genome, potentially responsible for the production of delta endotoxins similar to those produced by entomopathogenic bacteria such as *Bacillus thuringiensis* (Xiao *et al*., 2012), also suggests that *B. bassiana* might produce a battery of toxic compounds to successfully kill an insect host in 4-14 days, depending on the host species, size of the victim, inoculum potential and *B. bassiana* strain.

4. Evasion:

   After breaching the insect cuticle and reaching the haemocoel, the fungus undergoes a dimorphic transition, forming single-cell hyphal bodies called blastospores. This is a cryptic growth form, and this unique structure is thought to help blastospores to avoid detection by the host immune system. Blastospores proliferate via budding and use the circulating hemolymph as a source of nutrition as well a 'vehicle' for host colonization (Lewis *et al*., 2009). During this stage of infection, the fungus can also secrete toxic metabolites that help overcome the insect's immune defense mechanisms for successful colonization. Indeed, *Beauveria* can also produce wide-spectrum inhibitory metabolites including bassianolides, beauvericin (BEA), oxalic acid, oosporein, bassianin and tenellin. Upon insect death, the fungus produces oosporein, an antimicrobial compound that limits bacterial overgrowth and allows for full exploitation of host nutrient (Fan *et al*., 2017). Finally, *B. bassiana* hyphae cross the insect integument, preferentially at the inter-segmental level, allowing for fungal escape from the mummified victim, where new conidiophores and conidial branches are formed (Jaronski, 2014) for efficient dispersal in the environment.

5. Diffusion:

   Conidial spreading can occur passively (through wind, rain, etc.), actively (through living hosts moving among plants), or through vertical transmission (from the mother plant to the progeny through the seeds), as reported in *Papaver somniferum* L. (Quesada-Moraga *et al*., 2014).

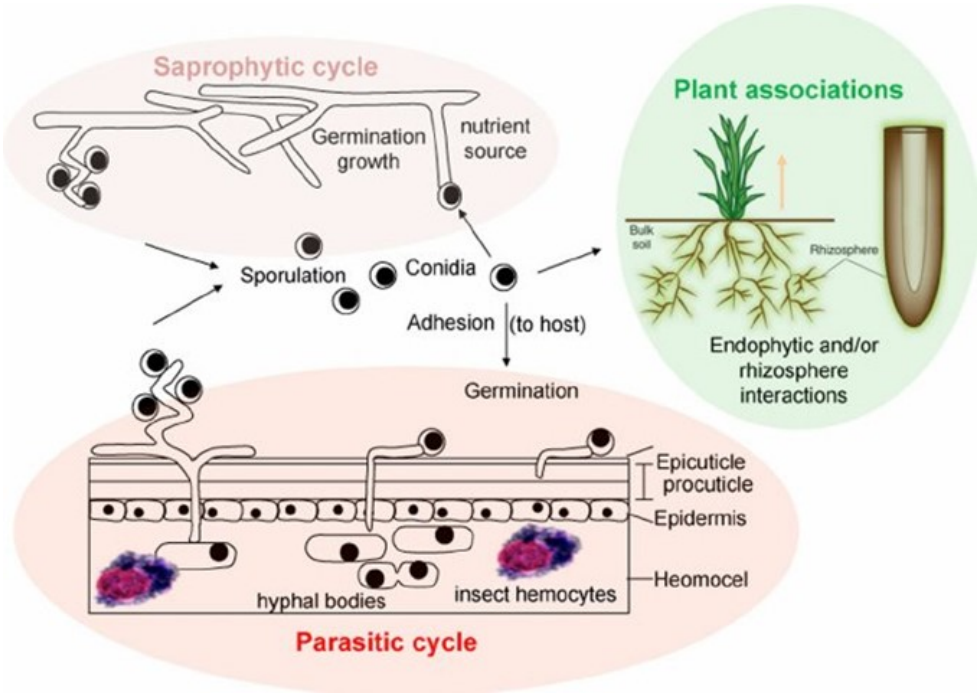

Figure 1.2. **Main phases of the *Beauveria bassiana* life cycle**. *B. bassiana* is a cosmopolitan and ubiquitous fungus capable of completing its life cycle both in the soil or in the air (Ortiz-Urquiza *et al.,* 2015).

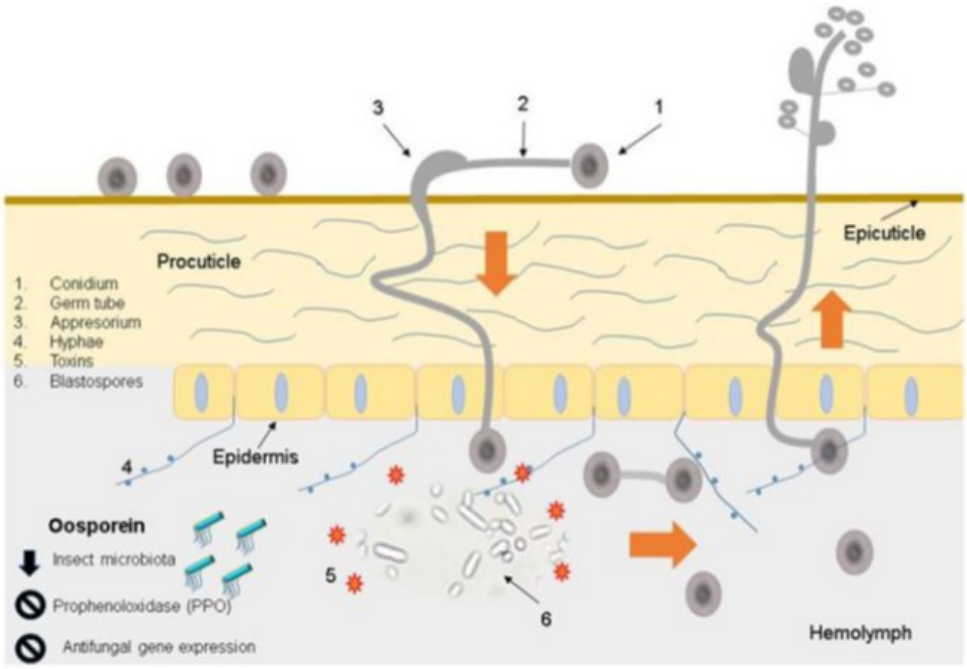

Figure 1.3. **Schematic representation of host insect entry, colonization and evasion by *Beauveria bassiana*** (Ávila-Hernández *et al*., 2020). Inside the host's body *B. bassiana* survives by producing toxins and blastospores useful for life cycle completion.

1.3. Ecology

Natural ecosystems (*e.g.* hedgerows) are important refuges for flora and fauna that do not thrive within the cultivated arable fields (Marshall and Moonen, 2002; Maudsley *et al*., 2002; Pywell *et al*., 2005). Regarding *B. bassiana*, hedgerows constitute a huge reservoir of genetic diversity compared to agricultural soil (Meyling, 2005).

The preservation of species variety and ecological functional groupings of organisms that are important for pest control in future sustainable agriculture, depends on heterogeneity in the agricultural environment. To avoid the loss of ecological heterogeneity at multiple spatial and temporal scales it is important to introduce management solutions that recreate that heterogeneity as the key to restoring and sustaining biodiversity in temperate agricultural systems (Benton *et al.,* 2003; Weibull and Ostman, 2003).

Landscape structure is also important when predicting the recruitment potential of organisms for biological control by changes in agricultural practices (Tscharntke *et al*., 2005). Both empirical evidence as well as simulation studies suggest that diversity in the guild of natural enemies is important for efficient biological pest control in agroecosystems (Wilby and Thomas, 2002; Cardinale *et al*., 2003).

1.3.1. Aerial dispersion

In Hypocreales, infectious propagules of EPF are passively spread, and this is mostly thought to occur due to the influence of weather phenomena such as wind and rain (Hajek, 1997; Inglis *et al*., 2001; Shah and Pell, 2003). The dispersal of the infective stages of a pathogen represents a key factor in disease development (Anderson and May, 1981). *B. bassiana* is considered an airborne fungus which is dispersed in the environment through meteorological events such as wind and rain, transmitted to plant parts via rain splashes or dispersed from them into the surrounding environment following rainfalls (Airaudi and Marchisio, 1996; Bruck and Lewis, 2002b; Inglis *et al*., 2000; Shimazu *et al*., 2002).

1.3.2. Soil propagation

The soil environment is usually the conventional isolation site for entomopathogenic fungi (Keller *et al*., 1989; Hajek, 1997) and several species can be found in both cultivated and natural habitats (Steenberg, 1995; Vänninen, 1996; Bidochka *et al*., 1998; Klingen *et al*., 2002; Keller *et al*., 2003; Meyling and Eilenberg, 2006b).

Entomopathogenic fungi can persist in the soil, but extensive proliferation and dispersal are limited. The increase in population depends on the conversion of host cadaver resources into infectious conidia that are gradually liberated from cadavers during sporulation. Both the fungus species and the host species, as well as the host size, affect the amount of conidia delivered per host (Gottwald and Tedders, 1982).

Cultivated agroecosystems are increasingly perturbed by human action as a result of tillage practices, which has an impact on the populations of natural enemies of crop pests. Indeed, entomopathogenic fungal communities in worked soil conditions differ from those in less disturbed habitats (Steenberg, 1995; Bidochka *et al*., 1998; Meyling and Eilenberg, 2006b). In corn fields, soil densities of *B. bassiana* (measured by colony forming units per gram of soil) were seemingly higher in no-tillage systems than in systems subjected to agricultural processing (Bing and Lewis, 1993). Likewise, conservation tillage regimes, using no-till, were more favorable to *B. bassiana* and *M. ansiopliae* populations in the soil than conventional tillage regimes (Hummel *et al*., 2002). Furthermore, no-till cultivation in soybean and wheat positively affected the population levels of *B. bassiana* and *M. anisopliae* compared to conventional tillage (Sosa-Gomez and Moscardi, 1994). These results of greater fungal densities in decreased tillage and no-till settings may represent observations of indirect effects caused by increasing levels of host populations of non-pest insects (Hummel *et al*., 2002). However, mechanical disturbance may not be the only process involved in the decrease in fungal population levels, as fungal inocula are inactivated by UV solar radiation (Fargues *et al*., 1996; Fargues *et al*., 1997) and temperature (Inglis *et al*., 2001). Indeed, temperature, moisture and UV radiation seem to be the most important factors for *B. bassiana* survival (Meikle *et al*., 2003). However, the persistence of applied fungal material in soils depends also on several other abiotic factors such as soil texture (Groden and Lockwood, 1991), pH values and moisture content (Lingg and Donaldson, 1981).

1.3.3. Dispersion by hosts

B. bassiana have been documented to occur naturally in >700 species of hosts (Inglis *et al.*, 2001). Indeed, *B. bassiana* could be found as a natural host in every insect taxon collected in temperate regions with host infection presumably being the only part of its life cycle in which the population size significantly increases through the production of a vast number of conidia. Generally, EPF are dispersed by living infected hosts which migrate and die away from the site where the infection occurred (Hajek, 1997). For example, aphids migrating long distances in the atmosphere harbour several entomopathogenic fungi (Entomophthorales and *B. bassiana*) (Feng *et al*., 2004). This

allows *B. bassiana* travelling over long distances leading to new infections and establishment far away from the original dispersal site.

The potential of arthropods to disperse and serve as vectors for entomopathogenic fungi has been demonstrated in different terrestrial ecosystems. In the soil, collembolans disperse *B. bassiana* and *M. anisopliae* conidia that are non-pathogenic on them (Dromph and Vestergaard, 2002), both by carrying conidia on their cuticle or by ingesting them. Moreover, collembolans are able to vector inoculum to other soil-dwelling insects and initiate infections in laboratory experiments (Dromph, 2003). Similarly, insects inhabiting nettle plants and predators are able to disperse *B. bassiana* propagules through their activity (Meyling *et al*., 2006) and could therefore be the distributors of naturally occurring *B. bassiana* isolates on nettle phylloplanes as an alternative to wind dispersal (Meyling and Eilenberg, 2006a; Meyling *et al.*, 2006). Interspecific vectoring of *B. bassiana* has also been shown in corn systems, where beetles likely feed on fungi growing in tunnels made by the larvae of the European corn borer *Ostrinia nubilalis* (Lepidoptera: Pyralidae) (Bruck and Lewis, 2002a). Insect activity may therefore influence the dispersal of *B. bassiana* conidia as depicted in Figure 1.4.

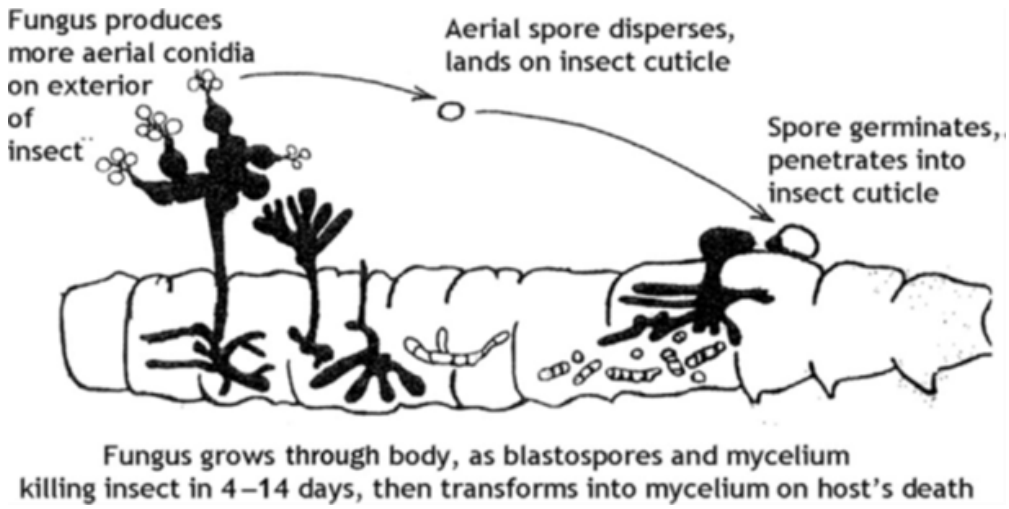

Figure 1.4. **Schematic representation of the life cycle of *Beauveria bassiana* on a host insect** (Jaronski, 2014). Conidia produced by the fungus adhere to the cuticle of the host insect, germinate and fungal propagules eventually penetrate into the insect body causing death. On the surface of the insect, the fungus will produce conidiophores and conidia from which, in the presence of a new host, a new cycle will start.

1.3.4. Association with plants

The term ‘‘endophyte” was coined by De Bary (1884) and is used to define fungi or bacteria occurring inside asymptomatic plant tissues. Fungal endophytes are ubiquitous and dominated by Ascomycota (Arnold and Lutzoni, 2007). Recent evidences suggest that both *B. bassiana* and *M. anisopliae* have

the potential to engage in fungus–plant interactions. *B. bassiana* has thus been included in this spectrum of fungi with endophytic activity (Bing and Lewis, 1991; Bing and Lewis, 1992; Bing and Lewis, 1993).

Endophytic fungi (EF) are often regarded as plant-defending mutualists (Saikkonen *et al.*, 2004) and the presence of *B. bassiana* in internal plant tissue has been discussed as an adaptive protection against herbivorous insects (Elliot *et al*., 2000; White *et al*., 2002). More than 20 plants, including *Zea mays*, *Solanum lycopersicum* L., and *Phaseolus vulgaris*, harbor the endophyte *B. bassiana* (McKinnon *et al*., 2017). The interior leaf apoplast, xylem, stomatal apertures, parenchyma, and vascular tissue are the sites of localization for *B. bassiana* (Vega, 2018). Besides natural occurrence in leaf tissue of corn, *B. bassiana* has been shown to exhibit endophytic activity in cacao (*Theobroma cacao*) (Posada and Vega, 2005), poppy (*P. somniferum*) (Quesada-Moraga *et al*., 2006), coffee (*Coffea* spp.) and tomato (*Lycopersicon esculentum*) plants (Vega, 2008). The utilization of EF as biological control agents (BCA) represents a potential alternative that meets the growing need for more eco-sustainable agricultural practices. According to this new perspective, in recent years many studies have been performed, through inoculation of EF on tomato plants to test their effects on plant performance (Sinno *et al*., 2021). Among these introduced EF, a consistent number of species belongs to a group of fungi classified as entomopathogens, fungi that are pathogens to insects, many isolated from asymptomatic plants, including *Akanthomyces* spp., *B. bassiana*, *Clonostachys rosea*, *Cordyceps farinosa* (formerly *Isaria farinosa*), *Lecanicillium* spp., and *Sarocladium* spp. (formerly *Acremonium* spp.) (Vega, 2008; Nicoletti and Becchimanzi, 2020; Bills and Polishook, 1991; Cherry *et al*., 1999; Pimentel *et al*., 2006; Orole *et al*., 2009). The natural occurrence of these fungi within the plant tissues suggests their ability to endophytically colonize a wide range of plants and to efficiently control insect pest populations of *Aphis gossypii* (Gurulingappa *et al.,* 2010) *Bemisia tabaci* (El-Deeb *et al*., 2012; Wei *et al*., 2020), *Helicoperva armigera* (Qayyum *et al*., 2015; Prabhukarthikeyan *et al*., 2017), *Nesidiocoris tenuis* (Garantonakis *et al*., 2018), *Spodoptera littoralis* (Resquín-Romero *et al.,* 2016), *Tuta absoluta* (Allegrucci *et al*., 2017; Klieber *et al*., 2016) and *Trialeurodes vaporariorum* (Menjivar *et al*., 2012). The overall effects observed on tomato pests included: increased mortality, feeding deterrence, reduced growth rate and reproduction, reduced infestation, egg masses colonization, and increased plant defense.

1.4. Virulence mechanisms on insects

Entomopathogenic fungi, such as *B. bassiana*, infect host insects by breaking through the insect cuticle, mainly through the hydrolytic activity of secreted enzymes. To adhere to the cuticle and

initiate germination, fungal conidia use non-specific hydrophobic processes (Boucias *et al*., 1988). The first line of defense against infection is the insect cuticle, which is mostly composed of a chitin matrix embedded with proteins (Clarkson *et al*., 1996). Extracellular proteases and chitinases produced by entomopathogenic fungi break down these proteinaceous and chitinous components, allowing hyphae to pass through the cuticle and enter the nutrient-rich insect hemolymph (Charnley *et al*.,1991). Important virulence factors for *B. bassiana* include proteases, such as subtilisin-like protease PR1 (Joshi *et al*., 1995) and chitinase BbCHIT1 (Fang *et al*., 2005).

Fungal produced compounds important in the penetration of the microorganism into the insect host include hydrophobins, adhesins, lectins, Mitogen-Activated Protein Kinases, lipases and proteases are described in more detail below.

Hydrophobins

The first step in the *B. bassiana* infection process on insects is the attachment of fungal single-celled dispersive forms, such as conidia or blastospores, to the insect cuticle (Holder and Keyhani, 2005; Holder *et al.*, 2007). A hydrophobic coating protects the aerial conidia of *B. bassiana*, which interacts with the hydrophobic surfaces of the insect cuticle. In *B. bassiana*, hydrophobins HYD1 and HYD2 have been shown to be essential for conidial adherence to the cuticle. Neither are they found on blastospores, submerged conidia, or fungal hyphae; rather, they are found on the surface of airborne conidia and at the base of germinating conidia. Although both genes have distinct roles, the *hyd1/hyd2* double-knockout mutants have less conidial adherence and pathogenicity. Conidia from the *hyd1* knock-out mutant have unchanged surface adherence in respect the wild-type strain but decreased virulence, in contrast to those of the *hyd2* knock-out mutant, which have reduced surface adhesion but unaltered pathogenicity (Zhang *et al*., 2011b).

Adhesins

Passive adhesion of *B. bassiana* can be triggered by hydrophobins such as HYD1 and HYD2 as well as by adhesins such as ADH1/MAD1, ADH2/MAD2, and ADH3 (Zang *et al*., 2011; Holder and Keyhani, 2005). ADH1/MAD1, ADH2/MAD2, and ADH3, filamentous hemagglutinin/adhesins and virulence factors in animal-pathogenic bacteria, have all been identified in *B. bassiana* (Zhou *et al.,* 2021). Only ADH2 was found to be significantly involved in fungal virulence, and several traits were linked to biological control. Conidial adhesion, blastospore formation, and conidiation capacity are all regulated by ADH2 (viability, hydrophobicity, and UV resistance).

Lectins

Lectins play essential physiological roles when fungi deal with various biotic and abiotic environmental conditions (Varrot *et al*., 2013). *B. bassiana* uses different lectins, which are carbohydrate-binding glycoproteins, to subvert host defenses and colonize host niches. The conidial surfaces of *B. bassiana* and its mycelia have been shown to contain lectins. It has been hypothesized that lectins are involved in the binding between conidia and insect cuticles (Kossowska *et al*., 1999). Two LyM proteins (BLY2 and BLYS5) display chitin-binding activities and protect fungal cell-wall from the host chitinase hydrolysis, which facilitate fungal colonization in the host haemocoel (Cen *et al*., 2017). More details about the lectin types and potential functions are still lacking in *B. bassiana* (Peng *et al*., 2021).

Mitogen-Activated Protein Kinases (MAPKs)

B. bassiana conidia can germinate after successfully adhering to the host cuticle in the presence of an external carbon source, optimum temperature and humidity levels. Conidia that germinate produce germ tubes that eventually turn into penetration pegs that pierce the cuticle of the host and invade the body. However, the genes responsible for host sensing and controlling the differentiation of penetration pegs are poorly understood. Conidial adhesion, appressorium development, and virulence are just a few of the activities in EPF that MAP kinases influence. Recent studies showed that homologs of HOG1 MAPKs are involved in fungal responses to osmotic stress (Dixon *et al*.,1999; Kojima *et al*., 2004; San José *et al*., 1996; Zhang *et al*., 2002), oxidative stress (Kawasaki *et al*., 2002; Sharma *et al*., 2005), heat shock (Kawasaki *et al*., 2002) and tolerance to a phenylpyrrole fungicide (Dixon *et al*.,1999; Kojima *et al*., 2004, Zhang *et al*., 2002) in several other fungi. For instance, deletion of *hog1*-encoding genes in *Candida albicans* (San José *et al*., 1996), *Neurospora crassa* (Zhang *et al.,* 2002), *Magnaporthe grisea* (Dixon *et al*.,1999), and *Colletotrichum lagenarium* (Kojima *et al*., 2004) results in a defect in adaptation to high-osmolarity conditions. A *hog1*-silenced strain of *Trichoderma harzianum* was highly sensitive to osmotic stress and showed intermediate levels of sensitivity to oxidative stress (Delgado-Jarana *et al*., 2006). In *B. bassiana* Δ*Bbhog1* mutants exhibited reduced pathogenicity, most likely due to a decrease in spore viability, a reduced ability to attach to insect cuticle, and a reduction in appressorium formation. The transcript levels of two hydrophobin-encoding genes, *hyd1* and *hyd2*, were dramatically decreased in a Δ*Bbhog1* mutant, suggesting that BBHOG1 may regulate the expression of genes associated with hydrophobicity or adherence (Zhang *et al.,* 2009).

Lipases

Once conidia germinate, penetration in the insect host requires cuticle degradation, a process mediated by the synergistic action of several different cuticle-degrading enzymes and mechanical pressure. A range of extracellular hydrolytic enzymes (including lipases, four different classes of proteases, chitinases and esterases) able to degrade the major components of insect cuticle (Leger *et al*., 1986) have been suggested to play an important role in pathogenesis. Further, to infect the insect, *B. bassiana* needs to enter the insect epicuticle, a hydrophobic layer consisting of lipids and other compounds, some of which have strong antimicrobial activities (e.g., n-alkanes, fatty acids, and aldehydes). The capacity of *B. bassiana* to overcome this antimicrobial barrier is crucial for its effectiveness as an insect pathogen. Indeed, enzymes capable of hydrolyzing these substances, such as lipases, are required for both host cuticular lipid hydrolysis, lipid droplet formation, mobilization and assimilation, and virulence (Fan *et al*., 2015; Ortiz-Urquiza *et al*., 2016). Neverthless, Feng (1998) reported a minimal association between the pathogenicity of different strains and their overall lipase activity. Although lipases are recognized as one of the primary methods by which these fungi penetrate the cuticle, fine molecular characterization of *B. bassiana* lipase genes is still missing (along with the mechanisms of chitin and protein hydrolysis). The use of comparative genomics and the creation of several knockout mutants can aid in the correlation between lipase function and pathogenesis, virulence, development, and fitness of *B. bassiana*.

Proteases

Aside lipases, fungal proteases are also believed to play an important role in cuticle penetration (Leger, 1995). Two proteases produced during the early stages of cuticle penetration have been detected in *B. bassiana*: PR1, a subtilisin-like serine protease, and PR2, a trypsin-like enzyme belonging to the serine protease group. PR1 plays an important role in cuticle penetration and a protease-defective mutant was found to have decreased virulence (Fang *et al*., 2009). High levels of PR1-like proteases produced by *B. bassiana* appear to be related to the early onset of mortality in the wax moth *Galleria mellonella* larvae (Gupta *et al*., 1994). PR2 plays a critical role in the degradation of extracellular proteins as a complement to PR1 and other enzymes (Dias *et al*., 2008). This means that PR2 is synthesized after PR1 activity to complete protein hydrolysis during the penetration process (Firouzbakht *et al*., 2015). PR1 and PR2 synthesis is controlled by multiple regulatory mechanisms, including carbon and nitrogen metabolite repression and derepression and by extracellular levels of N-acetyl-D-glucosamine (Bidochka *et al*., 1988a).

1.5. Secondary metabolites

The majority of entomopathogens are fungal members of the order Hypocreales, a distinct, specialized trophic subgroup of fungi. The genomes of these Hypocrealean EPF which generate a wide range of secondary metabolites (SMs), score highly for the number of expected, distinctive SM biosynthetic gene clusters. The producer fungus and its insect host interact in a variety of ways, and SMs from EPF can influence these interactions and play different roles in insect pathogenicity as virulence factors. Thus, in the context of integrated pest management systems, these SMs may serve as commercial biopesticides to support the role of EPF in crop protection (Zhang *et al*., 2020). Toxic secondary metabolites produced by EPF (Zhang *et al*., 2020) can either aid in fungal invasion (Altimira *et al*., 2022) or act as immunosuppressive agents to undermine host defenses (Lu and Leger, 2016). Filamentous fungi with a pathogenic lifestyle often produce a large variety of polyketide and non-ribosomal peptide natural products that act as immunosuppressors and general or host-specific toxins (von Döhren, 2004). Beauverolides (cyclic peptides), BEA, bassianolide (cyclooligomeric nonribosomal peptides), oosporein (dibenzoquinone), bassiatin (diketomorpholine), and tenellin (2-pyridone) are all produced by *Beauveria* species (Zhang *et al.,* 2020). Secondary metabolites are frequently associated with the pathogenicity of fungal strains, although their exact mode of action are not yet known (Pedrini, 2018; Butt *et al*., 2016; Zhang *et al*., 2020; Lu and Leger, 2016). The chemical structure and the biological activity of the main secondary metabolites produced by *B. bassiana* are shown in Figure 1.5 and Table 1.1.

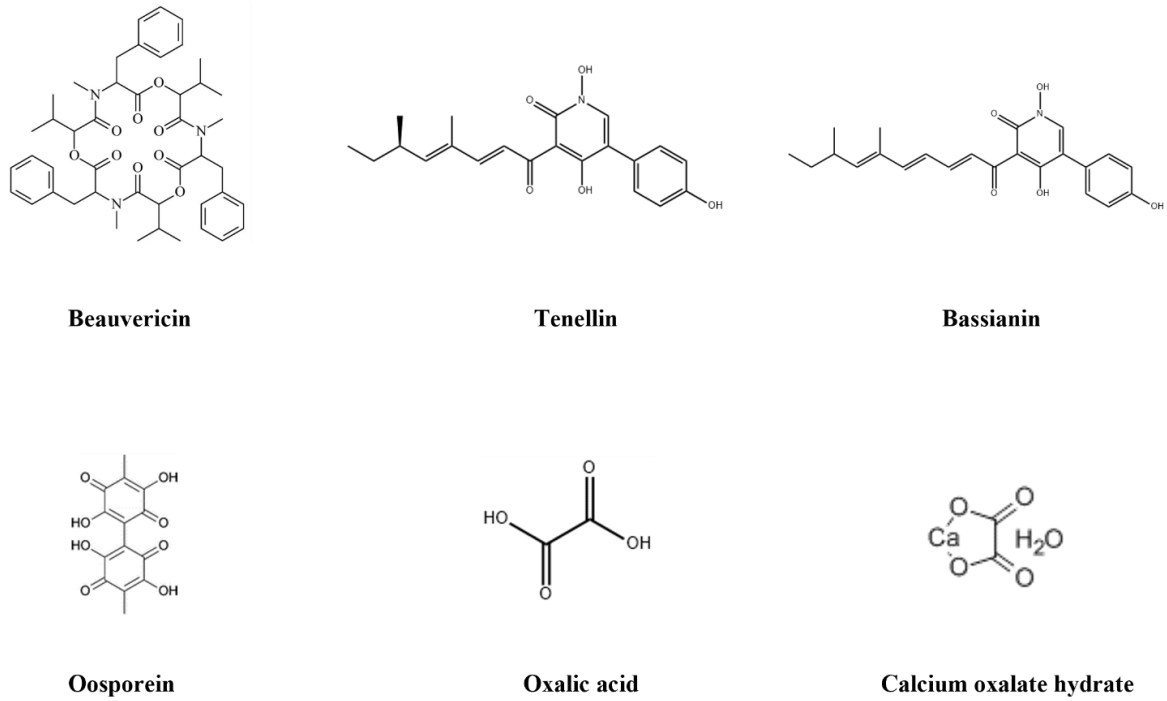

Figure 1.5. **Chemical structure of the main secondary metabolites produced by *Beauveria bassiana*.**

Table 1.1. **Biological activity of main secondary metabolites produced by *Beauveria bassiana*.**

Metabolite	Biological activity	References
Beauvericin	Antibacterial; insecticidal; anticancer; toxicity on animals and humans	Meca *et al*. (2010); Safavi (2013); Zhan *et al*. (2007); Křížová *et al*. (2021); Wu *et al.* (2018)
Tenellin	Protection against ROS	Jirakkakul *et al*. (2015)
Bassianin	Inhibition of erythrocyte membrane ATPase activity	Jeffs and Khachatourians (1997)
Oosporein	Inhibition of erythrocyte membrane ATPase activity; antibiotic; antiviral; antifungal; insecticidal	Jeffs and Khachatourians (1997); Brewer *et al*. (1984); Terry *et al*. (1992); Wainwright *et al*. (1986); Amin *et al*. (2010)
Oxalic acid	Promotion of plant cell wall disruption; bioremediation of organic pollutants; nitrogen fixation; acaricidal; insecticidal	Bateman and Beer (1965); Barr and Aust (1994); Trinchant *et al.* (1994); Kirkland *et al.* (2005); Bidochka and Khachatourians (1991)

BEA is a cyclic hexadepsipeptide produced by many fungi, such as *B. bassiana* and *Fusarium* spp. (Hamill *et al*., 1969; Logrieco *et al*., 1998). Additionally, BEA (Fig. 1.5) is a well-known mycotoxin belonging to the enniatin family of antibiotics. This natural bioactive compound is distributed worldwide. It has a dual nature as it occurs both as an antibacterial, antiviral, antifungal, antiparasitic, insecticidal, and anticarcinogenic compound, as well as a natural contaminant of food and feed commodities, and an emerging mycotoxin (Caloni *et al*., 2020). BEA is also known as an ionophore, compounds that can transport small ions across lipid membranes. The ionophoric activity produced by BEA in membranes has a direct effect on the intracellular ion concentration of mammalian cells. Disruption of normal physiological concentrations of important monovalent and divalent cations could be the reason for the non-specific toxicity of BEA. The ionophoric properties have effect on cell homeostasis and they are accompanied by ATP hydrolysis and acidification, which ultimately contributes to cell death (Kouri *et al*., 2005). BEA also acts as a mitochondrial uncoupler, disturbs physiological ionic balance and pH, challenges cellular metabolism, and causes ATP depletion and cytolysis. BEA has been described to have broad spectrum insecticidal activity against being active on *Aedes aegypti* (Grove and Pople, 1980), *Calliphora erythrocephala* (Grove and Pople, 1980), *Leptinotarsa decemlineata* (Gupta *et al*., 1991), *Lygus* spp. (Leland *et al*., 2005), *Schizaphis graminum* (Ganassi *et al*., 2002), *Spodoptera frugiperda* (Fornelli *et al*., 2004). BEA also displays

antibacterial properties against both Gram positive and Gram negative bacterias, including human, animal and plant pathogens (Sood *et al*., 2017). For instance, BEA exhibits antibacterial activity against *Bacillus* spp., *Peptostreptococcus* spp., *Clostridium perfringens* (Castlebury *et al*., 1999), *Enterococcus faecium, Listeria monocytogenes, Pseudomonas aeruginosa, Salmonella enterica, Shigella dysenteriae, Yersinia enterocolitica* (Meca *et al*., 2010), *Mycobacterium tuberculosis* (Nilanonta *et al*., 2000), *Staphylococcus haemolyticus* and *Escherichia coli* (Xu *et al*., 2010). Antifungal activities of BEA have also been reported: association of BEA with ketoconazole or miconazole exerted antifungal effects against *Candida parapsilosis*. Interestingly, BEA and ketoconazole alone are ineffective (Zhang *et al*., 2007). Moreover, BEA was able to block the activity of *C. albicans* ABC transporters and showed synergistic antifungal effects against multidrug-resistant *C. albicans* (Tong *et al*., 2016). Lastly, BEA showed phytotoxicity against tomato protoplasts (Paciolla *et al.,* 2004), anticarcinogenic activity in many cell lines (Zhan *et al*., 2007), and strong and specific inhibition of cholesterol acyltransferase (ACAT) (Tomoda *et al*., 1992).

Tenellin and bassianin (Fig. 1.5) are yellow 1,4-dihydroxy-2-pyridone pigments isolated from several *Beauveria* species. They are formed from a chain of reduced polyketide (pentaketide in the case of tenellin and hexaketide for bassianin), with the amide portion of the tyrosine (Molnár *et al*., 2010). These pigments are produced by *B. bassiana* and *B. tenella* (Patocka, 2016). From chemical and spectroscopic evidence, the nomenclature for tenellin and bassianin is 3- [(E,E)-4,6-dimethylocta-2,4-dienoyl] and 3-[(E,E,E)-6,8-dimethyldeca-2,4,6- trienoyl], respectively. These are derivatives of 1,4-dihydroxy-5-(p-hydroxyphenyl)- 2(1H)-pyridine (Patocka, 2016). However, structurally, they differ only in one side chain extension (Gibson *et al*., 2014). To date, there is no documented information on the physicochemical characteristics of both tenellin and bassianin. Hence, it is important to understand their interactions with the environment (Seger *et a*l., 2005). Scientific research on the tenellin pigment has been carried out to define its specific role in the infection process of *B. bassiana* on insects. Despite tenellin does not have the capacity to kill insect larvae (Eley *et al*., 2007) it is thought to play an important role in fungal protection against ROS (Jirakkakul *et al*., 2015). Besides, bassianin was reported (Jeffs and Khachatourians, 1997) to disrupt erythrocyte membranes, causing cell lysis and inhibiting membrane ATPase activity in a dose-dependent manner.

Oosporein (Fig. 1.5) is a 1,4-bibenzoquinone derivative red pigment produced by *B. bassiana* and *B. brongniarti* (Seger *et al*., 2005), which exhibits antibiotic, antiviral, antifungal, and insecticidal activities (Brewer *et al*., 1984; Terry *et al*., 1992; Wainwright *et al*., 1986; Amin *et al*., 2010). Oosporein was originally described in 1944 as a dye produced by the fungus *Oospora*

colorans (Kogl and Van Wessem, 1994). Oosporein inhibits Ca-dependent ATPases of erythrocyte membranes at relatively high concentrations (200 μg ml^{-1}), possibly by disturbing the membrane structure (Jeffs and Khachatourians, 1997). Previous studies have implicated a polyketide origin for oosporein, with the common fungal metabolite orsellinic acid as a likely intermediate that undergoes multiple oxidations and dimerizations by oxidative coupling to yield the final dibenzoquinone product. The first orsellinic acid synthase, nonribosomal (NR) polyketide synthase (PKS), was recently identified in *A. nidulans (*Schroeckh *et al*. 2009). Feng *et al*. (2015) demonstrated that oosporein might be biosynthesized through orsellinic acid by a PKS gene cluster in *Beauveria*. The physicochemical properties of oosporein indicate that at pH values above 3, the solubility (basal solubility Cs0 =24.8 ± 0.3 μM) and the degree of dissociation (ionization constant pKa =2.42 ± 0.02) increases exponentially. In addition, depending on the temperature, solubility increases in acidic aqueous solutions. Oosporein has three levels of deprotonation $[oosporein]^-$, followed by $[oosporein]^{2-}$ (pKa= 6.79 ± 0.08) and $[oosporein]^{3-}$(pKa= 9.19 ± 0.03). As for stability, the influence of pH and temperature decreased the half-life of the compound as it is a strong organic acid with very low lipophilicity (Seger *et al*., 2005). Recently, it has been demonstrated (Chen *et al*., 2022) that the pH signaling transcription factor *BbpacC* is involved in the regulation of oosporein production as oosporein production is disrupted when this gene is deleted.

Oxalic acid and oxalate crystals are phytopathogenic fungal virulence factors, with the abilitity to facilitate disruption of the plant cell wall while promoting the functions of fungal lytic enzymes that ultimately lead to wilting and disease progression (Bateman and Beer, 1965; Magro *et al*.,1984; Munir *et al*., 2001). Moreover, high concentrations of oxalate in plants are considered to inhibit insect foraging, although the exact physiological roles of plant oxalates on insects is unknown (Oke, 1969; Franceschi and Horner, 1980; McConn and Nakata, 2002). Oxalic acid has three chemical natures: it is as proton and electron source and a strong metal chelator, despite its simple chemical formula $(COOH)_2$. Due to its unique multiple chemical nature, it has received much attention for its various ecological qualities, such as:

(i) bioremediation of a wide variety of organic pollutants (Barr and Aust, 1994);
(ii) inactivation of copper-containing wood preservatives by wood-rotting fungi (Tsunoda *et al*., 1997; Murphy and Levy, 1983);
(iii) crop damage caused by oxalic acid-producing phytopathogens (Maxwell and Bateman, 1968; Magro *et al*., 1984);

(iv) being an electron source for nitrogen fixation in symbiotic rhizobia of legume plants (Trinchant *et al*., 1994).

Oxalic acid has been demonstrated to be toxic against the honeybee mite *Varroa destructor* and to reduce the biological fitness of the tarnished plant bug, *Lygus hesperus* (Palisot de Beauvois) (Alverson, 2003; Gregorc and Poklukar, 2003). Oxalate crystals have been identified on cadavers of insects infected by fungi, including *B. bassiana* (Moino *et al.,* 2002). Metabolic acids, including oxalate, have been implicated in *B. bassiana*-mediated virulence toward the migratory grasshopper, *Melanoplus sanguinipes* (F.) (Bidochka and Khachatourians, 1991). Additionally, oxalic acid has a pH-dependent toxicity against the adult stage of *Amblyomma americanum* and the production of oxalic acid by *B. bassiana* may contribute to the explanation for the acaracidal action of cell-free fungal culture. Oxalate is hypothesized by Kirkland *et al*. (2005) to be an important entomopathogenic fungal virulence factor, similar to observations concerning the importance of oxalate during phytopathogenic fungal infection on plant hosts. It is known to contribute to the ability of the fungus to penetrate the insect cuticle (Fan *et al*., 2012b; Kirkland *et al*., 2005). Indeed, oxalic acid is able to solubilize several components of insect cuticles, including elastin and collagen, and has been demonstrated to disrupt the integrity of *M. sanguinipes* cuticle directly (Bidochka and Khachatourians, 1991). Furthermore, Bidochka and Khachatourians (1993) demonstrated that the ability of *B. bassiana* to produce metabolic acids is stimulated by the presence of a utilizable carbon sources such as glucose, glycerol or trehalose that are found in insect haemocoel supporting the idea that insect mortality in *B. bassiana* infected hosts might depend on hemolymph acidosis.

Several pathways exist in fungi for oxalate biosynthesis. In *Aspergillus niger*, oxaloacetate hydrolase can catalyze the conversion of oxaloacetate to oxalate and acetate (Kubicek, 1987), whereas species of the phytopathogenic fungus *Sclerotium* can oxidize glyoxylate via the activity of a glyoxylate dehydrogenase (Balmforth and Thomson, 1984). These systems link oxalate production to the tricarboxylic acid (TCA) and glyoxylate cycles, respectively. However, *A. niger* also possesses both a cytoplasmic pyruvate decarboxylase and oxaloacetate acetylhydrolase that would be capable of forming oxalate without the reactions of the TCA cycle (Kubicek *et al*., 1988).

1.6. Biological role of environmental pH in soil-borne interactions

Microorganisms must be able to detect environmental changes and adapt to them in order to survive. In filamentous fungi, environmental pH has a significant impact on growth and organic acid excretion. When cultivated in an unbuffered media, some filamentous fungi rapidly acidify their surroundings to very low and sometimes even harmful pH levels (Magnuson and Lasure, 2004). The major mechanism behind this acidification is controversial but is most often attributed to either organic acid excretion (Magnuson and Lasure, 2004; Andersen *et al*., 2009) or proton release by the plasma membrane H+-ATPase (Sanders, 1988; Jernejc and Legisa, 2001). The capacity of fungi to produce natural organic acids (such as butyrate, oxalate, malate, citrate, gluconate, and succinate) is widely used in industry, especially with nonpathogenic *Aspergillus* sp. and *Rhizopus* sp. The amount of pH change is influenced by the availability of nutrients, the production of organic acids, and the fungus's ability to either excrete H^+ - ions as a consequence of $NH4^+$ absorption or remove ammonium ions from ammonium salt (Prusky *et al*., 2001; Bi *et al*., 2016). Along with acidifying host tissues, the generated acids also have the potential to reduce the activity of reactive oxygen species produced by the host (Chen and Dickman, 2005). The human pathogen *C. albicans* acidifies the environment in a carbohydrate-dependent fashion, allowing production of aspartyl proteases, which are virulence factors (Naglik *et al*., 2003). Many fungal pathogens modulate environmental pH as a means to escape host immune responses, facilitate destruction of the host tissues, and/or stimulate reproduction. For some fungi, such as the phytopathogens *Colletotrichum gloeosporioides* and *Magnaporthe oryzae*, acidic pH favors fungal colonization and invasion (Prusky *et al*., 2001; Landraud *et al*., 2013). The mildly acidic pH of the plant surface favors both germination of attached conidia and rapid differentiation of the germ tube into a specialized cell named appressorium. Once the appressorium penetrates the plant tissues, the fungus switches to necrotrophic development, associated with rapid ammonia release and increase in environmental pH, which triggers the expression of virulence factors (Bi *et al.,* 2016; Shnaiderman *et al*., 2013; Landraud *et al*., 2013; Alkan *et al*., 2009). Thus, the acidic environment serves as a signal in this fungus to switch from saprotrophic to pathogenic growth and damage the host. The acidic pH of host tissues further promotes the expression and activity of fungal proteases. Other fungi utilize nitrogen or carbon metabolism pathways to generate ammonia, which is released from the cell to raise the extracellular pH. Generation of alkaline pH favors morphogenetic and reproductive processes in fungi, such as germination, hyphal growth, and formation of fruiting bodies, all critical for disease progression. The alkaline pH increases fungal virulence by facilitating penetration into host surfaces and hindering or evasion of immune responses. From a biotechnological point of view, ambient pH is also an important process parameter, *e.g.*, in

Aspergillus niger maximal citric acid production occurs below pH 2 (Papagianni, 2007), gluconic acid production at pH 4.5–6.5 (McCullough *et al.,* 1986) and oxalic acid excretion above pH 5 (Ruijter *et al*., 1999). The excretion of a single organic acid may peak at a certain pH value, whereas the total amount of excreted organic acids seems to follow a different progress, although systematic investigations of this phenomenon for a broader range of organic acids are scarce. The only two available studies on this subject were performed with *N. crassa* (Slayman *et al.*, 1990) and *A. niger* (Andersen *et al*., 2009) and indicate that total organic acid excretion increases with rising pH despite huge differences in experimental conditions (*i.e.*, pH-stat incubation with non-growing hyphae versus bioreactor batch cultures). Entomopathogenic hyphomycetous fungi persistence and efficacy in soil is also dependent on pH (Inglis *et al.*, 2001). There are contradictory reports about the effect of pH on the survival, ecological distribution and virulence of entomopathogenic fungi. Soil pH and nitrogen fertilizers were found to have an impact on the germination of *B. bassiana* conidia, but not on its infection of the Colorado potato beetle (Groden & Dunn, 1996). Protease and hydrolase production by *B. bassiana* to facilitate breaching of the insect cuticle is also influenced by pH in the microenvironmental niche on the host cuticle (Caddick *et al*., 1986; Mekalanos, 1992; Leger *et al*., 1998). Similarly, the expression of the genes coding for the subtilisin protease and other putative virulence factors in the entomopathogenic fungus *Metarhizium anisopliae* is reported to be regulated by the pH on the insect cuticle (Leger *et al.,* 1998). Galani (1988) studied the influence of initial pH of the medium on biomass production in *B. bassiana*, *Verticillium lecanii*, and *Paecilomyces farinosus*, with the highest biomass produced when the initial pH was between 6 and 8.5. Studies on pH tolerance in *B. bassiana* have been carried out on only a few isolates and contradictory results were reported likely due to inter-isolate heretogeneity which might reflect adaptation to the different pH values fungal cells encounter in the different insect species (Schultz and Lechowicz, 1986). The pH-dependent regulation of expression in fungi is mediated by specific response elements in their genome. Among them the transcription factor *BbpacC* is one such element that enables *B. bassiana* to adapt its gene expression to ambient pH (Peñalva *et al*., 2008). Alkaline pH strongly induces *BbpacC*, leading to the upregulation of alkaline-expressed genes and the repression of acid-expressed genes (Zhou *et al*., 2014). Ambient pH can also be regulated by the secretion of compounds that acidify or alkalinize the surrounding microenvironment (Leger *et al*., 1999). Infection progression can be stimulated by acidification of the host tissue and the hemolymph. To this end the fungus secretes acidic metabolites such as oxalic acid (Bidochka and Khachatourians, 1991) which is known to contribute to the ability of the fungus to penetrate the insect cuticle (Fan *et al*., 2012b; Kirkland *et al*., 2005). Another factor known to be involved in mycelial acidification is the *Bbcsa1* gene (calcium

sensor and acidification regulator). Indeed, deletion of the *Bbcsa1* gene results in both reduced acidification and virulence (Fan *et al*., 2012b).

1.7. Biocontrol activity against plant pathogens

In recent years, evidence has shown that *B. bassiana* has potential as a dual-purpose microbial control organism for both insect pests and plant pathogens (Sinno *et al*., 2021). Isolates of *B. bassiana* inhibited mycelial growth in vitro against an array of soilborne and foliar plant pathogens, including *Gaeumannomyces graminis* var. *tritici* (Renwick *et al*., 1991), *Armillaria mellea*, *Fusarium oxysporum* (Reisenzein and Tiefenbrunner, 1997), *B. cinerea* (Bark *et al.,* 1996) and *Rhizoctonia solani* (Lee *et al*., 1999). In addition to the inhibition of mycelial growth, *B. bassiana* induced cell lysis of plant pathogenic species, such as *Pythium ultimum*, *P. debaryanum*, and *Septoria nodorum* (Veselý and Koubova, 1994). Barra-Bucarei *et al*. (2019) assessed the ability of native strains of *B. bassiana* (RGM393, 461,547, 557, 565, 570, 632, 644, 657, 731 and 2519) to inhibit the growth of *Botrytis cinerea*, a phytopathogenic fungus, in tomato plants *(S. lycopersicum*) and chili pepper plants (*Capsicum annuum*) L. In both conditions, all the strains displayed a biocontrol activity, with a significant reduction in symptoms compared to control. Moreover, Rivas-Franco *et al*. (2019) evaluated the effect of maize seeds coated with *Metarhizium* spp. and *B. bassiana* Bb21 in the presence of *Fusarium graminearum* and second-to third-instar larvae of *Costelytra giveni*. Their study showed that *B. bassiana* Bb21 exerted a negative effect on the germination of coated spore maize seeds at a concentration of 1×10^8 conidia mL^{-1}. This was due to a significant reduction in the dry weight of shoots and roots, suggesting that *B. bassiana* benefits from nutrients without synergistic benefits to the plant, possibly due to the lack of specificity of the entomopathogenic fungus to the maize plant. Meanwhile, it is not capable of infecting *C. giveni*, but decreases the symptoms of necrosis by *F. graminearum* in the roots by less than 30 %. In another study from Senthilraja *et al*. (2010), it was found that *B. bassiana* (strain B2) together with *Pseudomonas fluorescens* (TDK1 and Pf1 strains) have the ability to control the insect pest *Aproaerema modicella* as well as the plant pathogenic fungus *Sclerotium rolfsii*, which causes the collar rot disease. Additionally, Sinno *et al.* (2021) evaluated the ability of four *B. bassiana* wild and one commercial isolate to perform biocontrol against two foliar pathogens (*B. cinerea* and *Alternaria alternata*) and a sucking insect pest (*Macrosiphum euphorbiae*). Four out of five isolates efficiently controlled fungal pathogen infection, while all of them were capable of reducing aphid survival and fertility.

1.8. Aims of the work

B. bassiana has been described as a multifunctional organism (Ortiz-Urquiza, 2021), due to its ability to cover different lyfe-styles. Indeed, it has the ability to grow as an endophyte (establishing non-symptomatic interaction with plants), as a saprophyte (growing on decaying materials) and as a parasite (infecting insects). However, as previously reported not all *B. bassiana* isolates are capable of multiple biological activities (*i.e.* biocontrol of insects and phytopathogens, plant biostimulation or induction of resistance) that are desirable traits in beneficial microorganism to be used as alternatives to chemical products in agriculture.

This thesis aims to select and characterize ten different strains of *B. bassiana* (*Bb*) to determine their potential applications. Nine wild isolates (*Bb*716, *Bb*633, *Bb*672, *Bb*682, *Bb*688, *Bb*709, *Bb*632, *Bb*758, *Bb*762) received from the Agricultural University of Plovdiv (Bulgaria), while one commercial strain ATCC 74040 was isolated from the commercial product *Naturalis*® (CBC S.r.l., Grassobbio, Italy). The objective was to characterize the morphology, biology and ability to produce bioactive metabolites from each of these isolates in order to obtain an in-depth characterization of such potential beneficial microorganisms and to identify those able to both enhance plant growth and resistance. To achieve this goal, pathogenicity on the insect pest *S. littoralis*, promotion of tomato plant growth and resistance towards the fungal pathogen *F. oxysporum* f.sp. *lycopersici* and metabolic profiling were evaluated.

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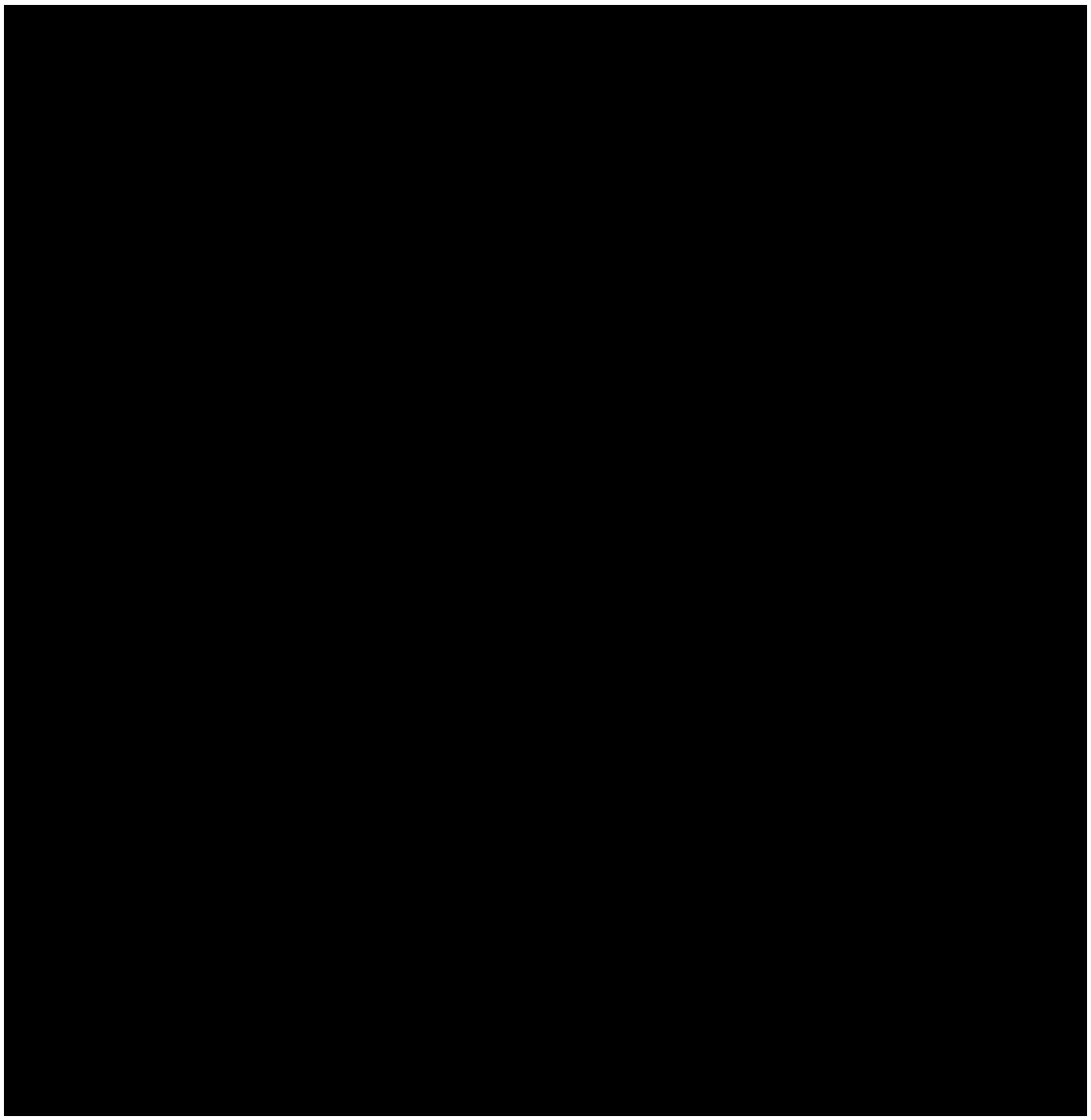

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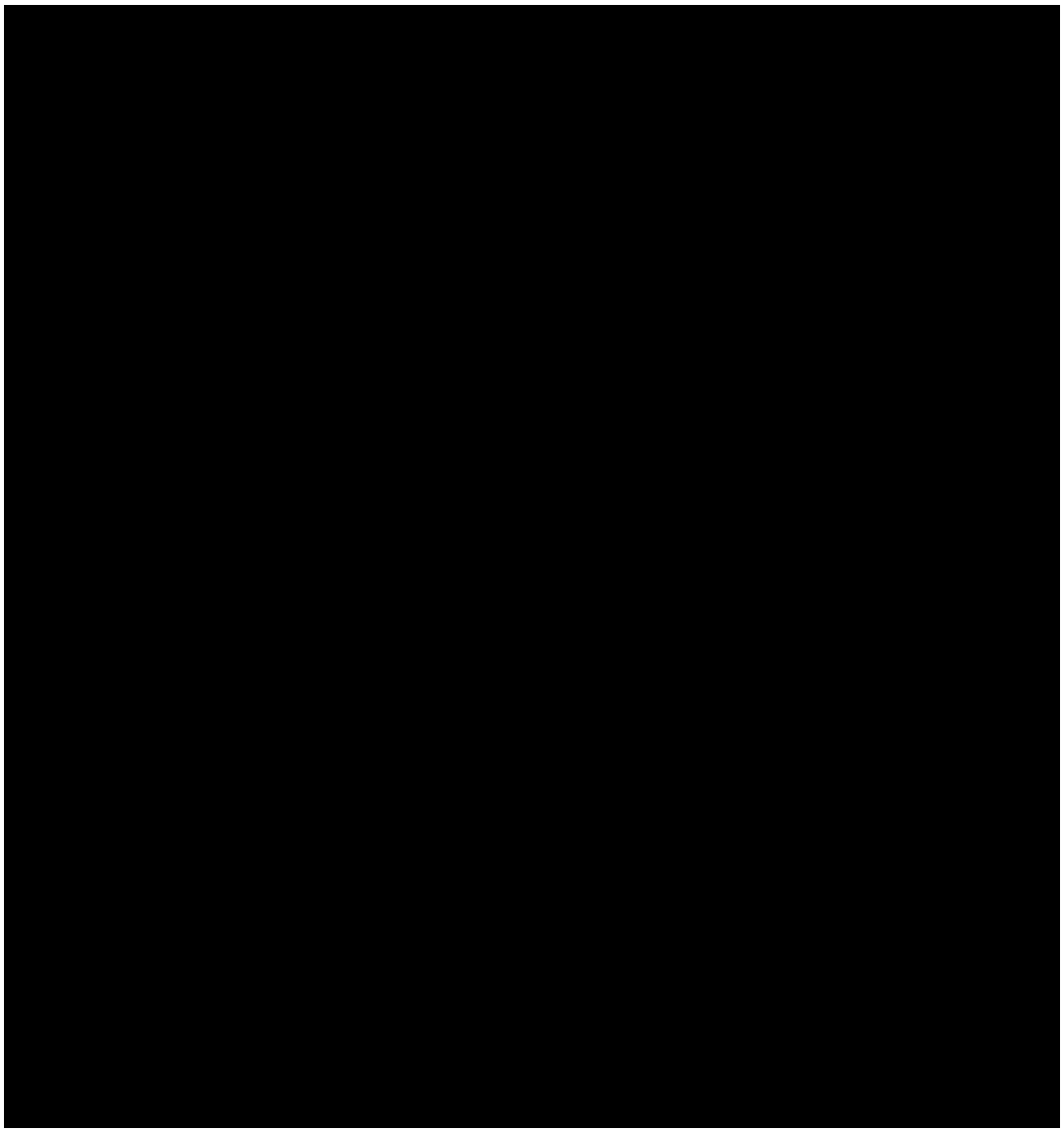

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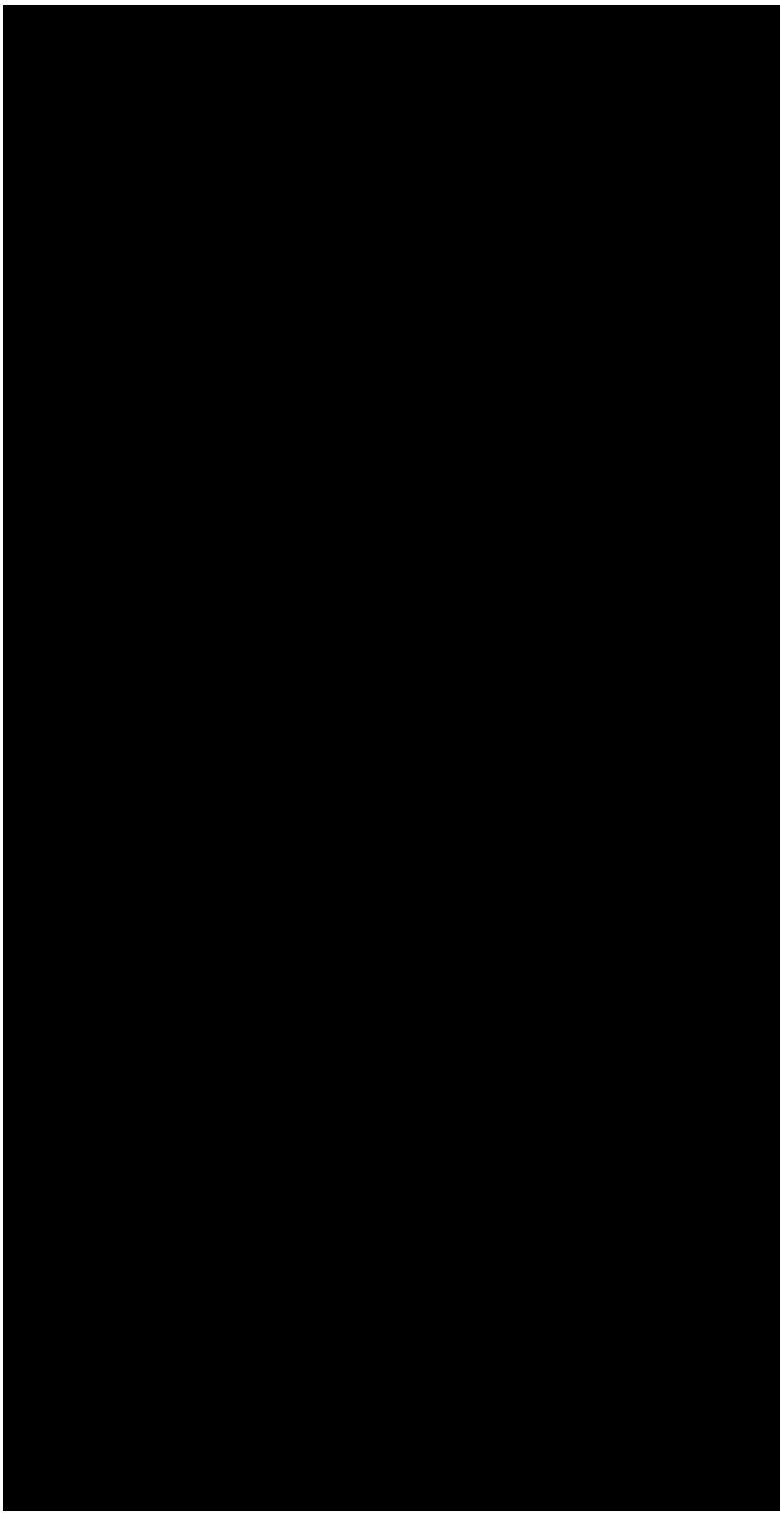
B. bassiana to produce metabolic acids in carbohydrate-supplemented media Bidochka and Khachatourians, 1993). Here, to correlate organic acid production by *B. bassiana* and its ability to antagonize the growth of the fungal plant pathogen *F. oxysporum in vitro*, dual confrontation assays

and media supplemented with pH indicator were used. Only three isolates, *Bb*716, *Bb*672 and *Bb*762, were identified as producing a yellow acidification halo around their colonies when grown on MADM, while all other isolates were not able to lower medium pH even 9 days post inoculation (Fig. 4.1). However, the *B. bassiana* isolates *Bb*709, *Bb*716, *Bb*762, *Bb*672 and *Bb*633 showed higher inhibition of *F. oxysporum* growth, as the interaction Radius (Ri) of *F. oxysporum* colonies grown alone was significantly bigger than that of colonies grown opposite to the above mentioned *B. bassiana* isolates (Fig. 4.2). All other isolates were not capable of significantly inhibiting *F. oxysporum* mycelial growth.

Moreover, all isolates promoted *F. oxysporum* growth distally, as evidenced by measuring the opposite Radius (Ro) of *F. oxysporum* colonies grown in presence of *B. bassiana* as compared to those grown alone (Fig. 4.3).



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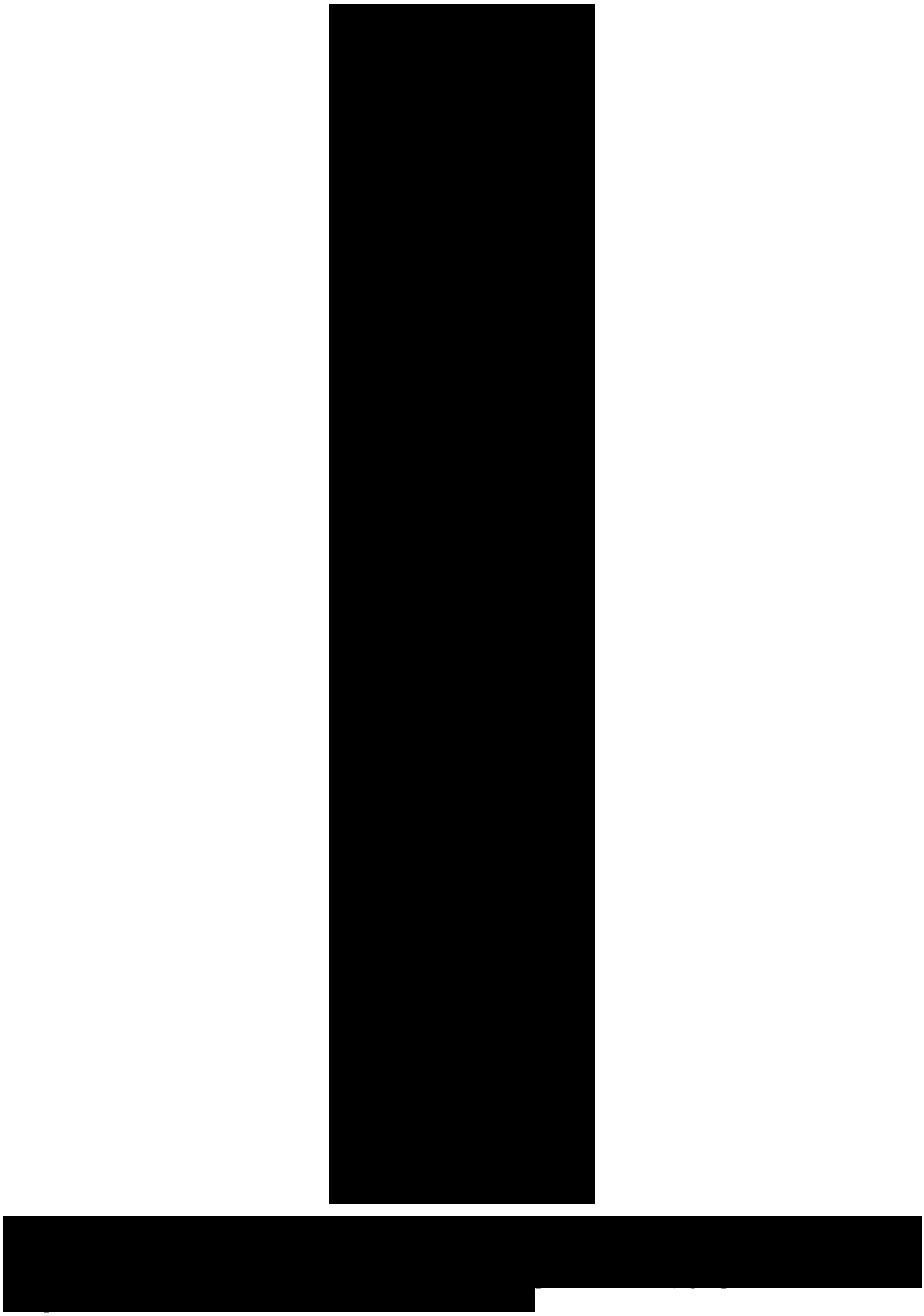

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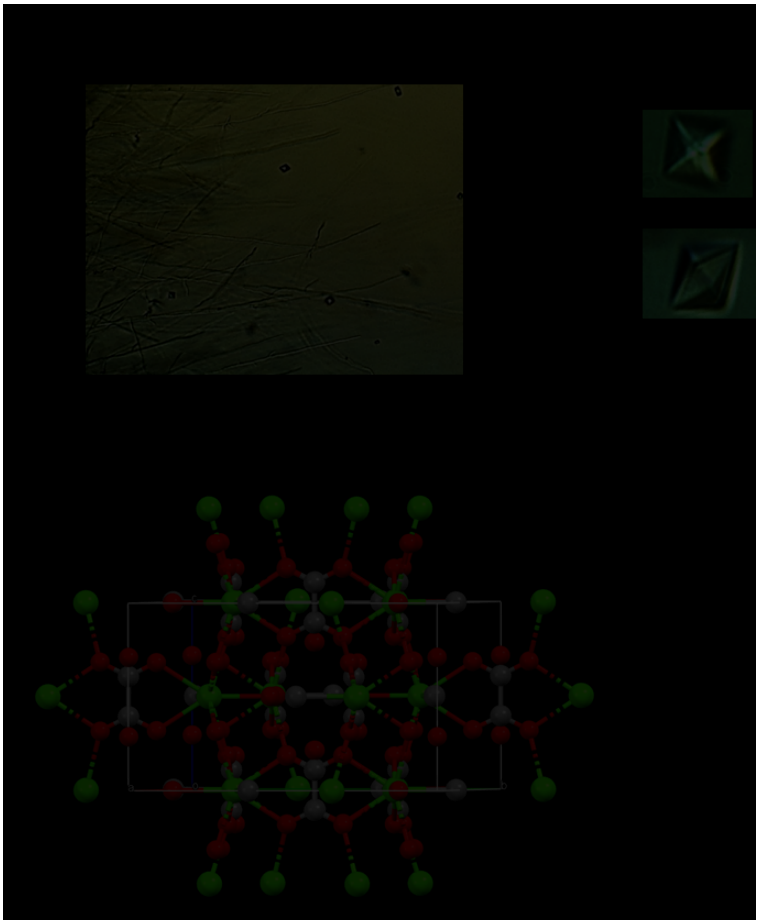

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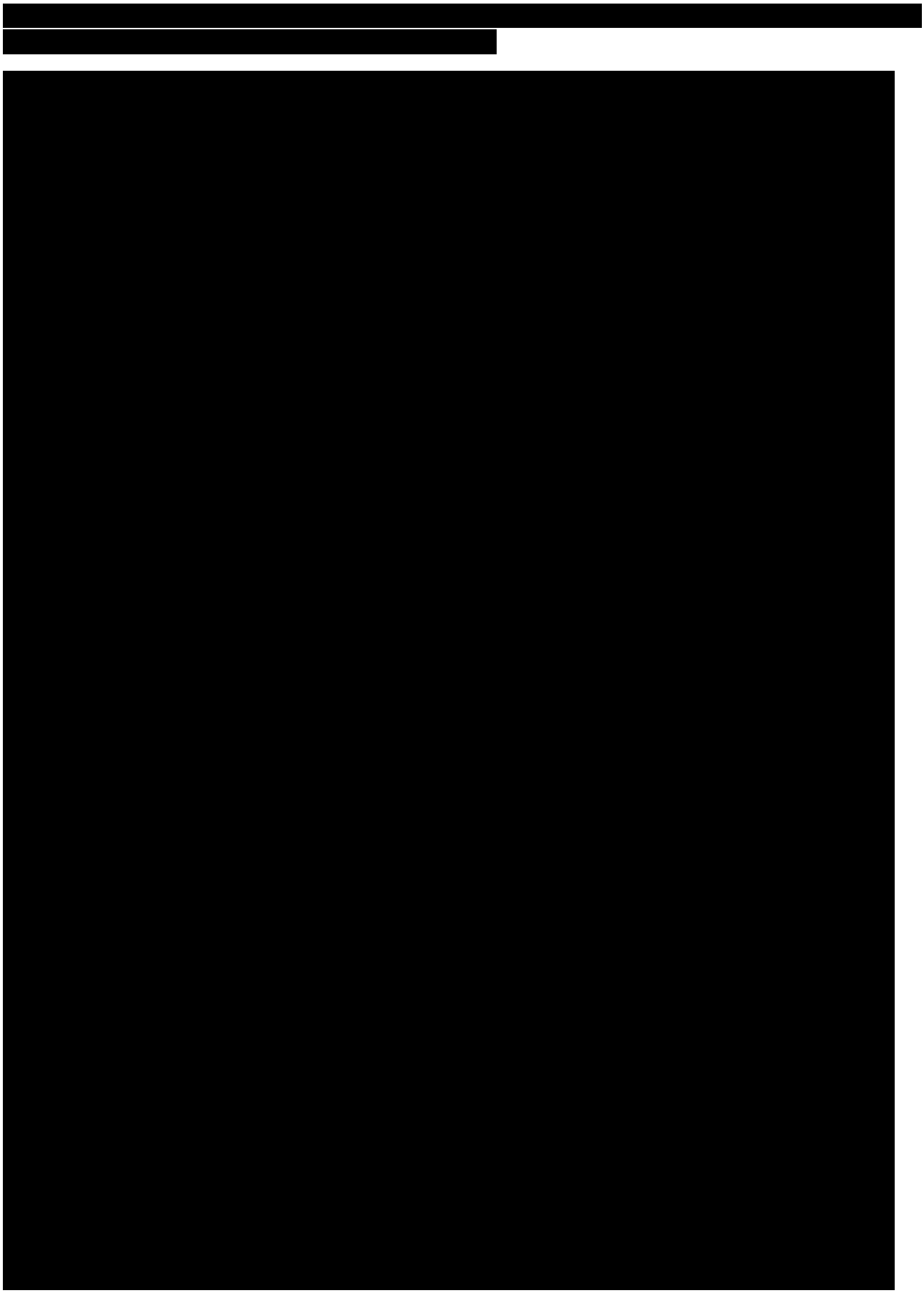
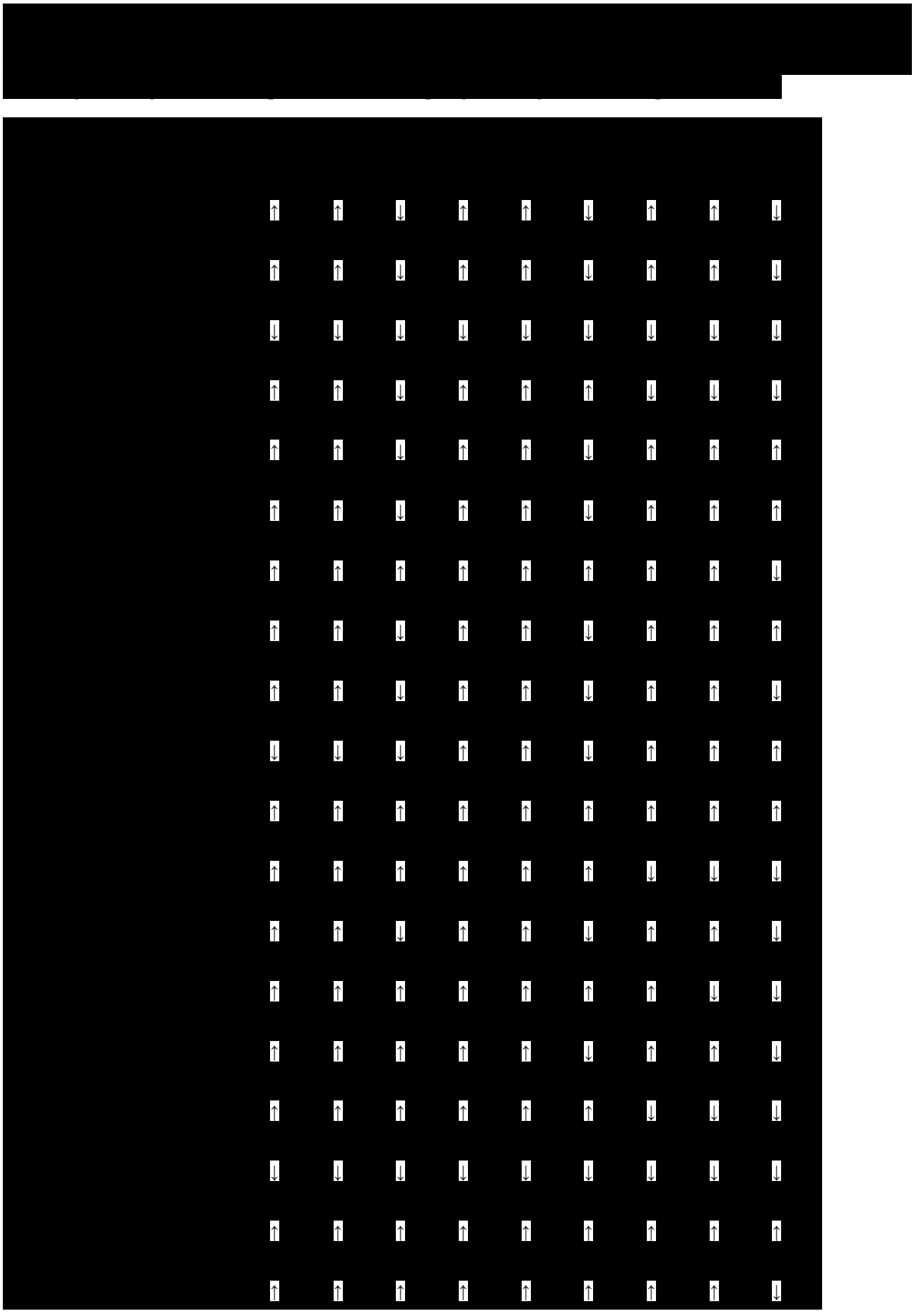
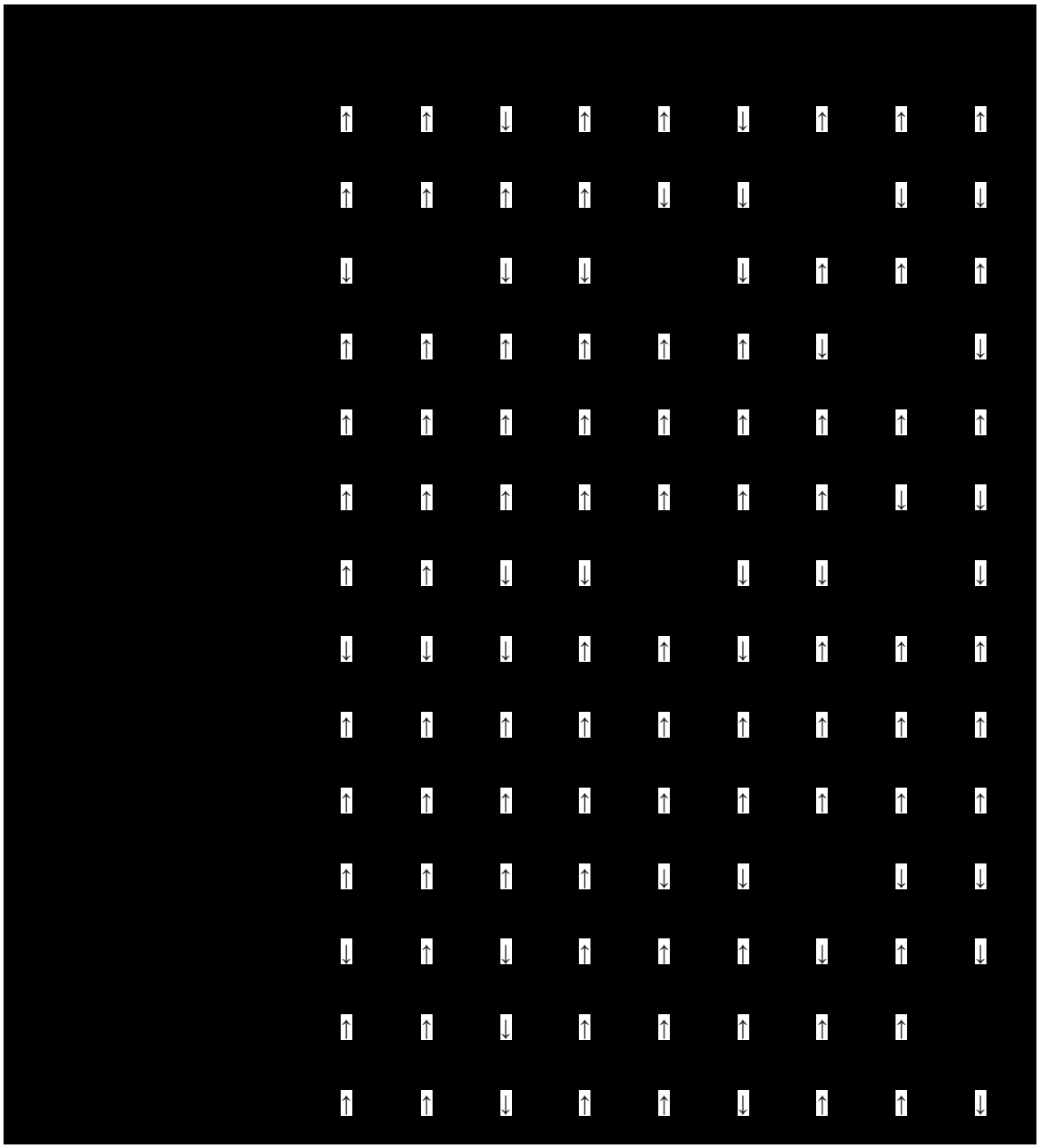
on the right hand-side of the plot. As a result of the multi- and univariate analysis of the GC-MS datasets, it was possible to putatively identify several acids (Table 6.2) apart from additional metabolites (Table 6.3). Oxalic acid, phenylethyl alcohol, glyceric acid, hexanedioic acid, dodecanoic acid, octanedioic acid, pentadecanoic acid, palmitic acid, stearic acid were found to be produced by all the tested isolates. 2,6-Pyridinedicarboxylic acid, citric acid, eicosanoic acid and heneicosanoic acid were instead produced only by the *Bb*716, *Bb*672 and *Bb*762, and myristic acid only from *Bb*632, *Bb*633 and *Bb*758 isolates.







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Conclusions

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Airaudi, D., Marchisio, V. F. (1996). Fungal biodiversity in the air of Turin. *Mycopathologia*, *136*(2), 95-102.

Allegrucci, N., Velazquez, M. S., Russo, M. L., Pérez, M. E., Scorsetti, A. C. (2017). Endophytic colonisation of tomato by the entomopathogenic fungus *Beauveria bassiana*: the use of different inoculation techniques and their effects on the tomato leafminer *Tuta absoluta* (Lepidoptera: Gelechiidae). *Journal of Plant Protection Research*.

Altieri, C., Cardillo, D., Bevilacqua, A., Sinigaglia, M. (2007). Inhibition of Aspergillus spp. and Penicillium spp. by fatty acids and their monoglycerides. *Journal of food protection*, *70*(5), 1206-1212.

Altimira, F., Arias-Aravena, M., Jian, L., Real, N., Correa, P., González, C., Godoy, S., Castro, J.F., Zamora, O., Vergara, C., Nitta, N., Tapia, E. (2022). Genomic and experimental analysis of the insecticidal factors secreted by the entomopathogenic fungus *Beauveria pseudobassiana* RGM 2184. *Journal of Fungi*, *8*(3), 253.

Andersen, M. R., Lehmann, L., & Nielsen, J. (2009). Systemic analysis of the response of Aspergillus nigerto ambient pH. *Genome biology*, *10*(5), 1-14.

Alkan, N., Davydov, O., Sagi, M., Fluhr, R., & Prusky, D. (2009). Ammonium secretion by *Colletotrichum coccodes* activates host NADPH oxidase activity enhancing host cell death and fungal virulence in tomato fruits. *Molecular plant-microbe interactions*, *22*(12), 1484-1491.

Alverson, J. (2003). Effects of mycotoxins, kojic acid and oxalic acid, on biological fitness of *Lygus hesperus* (Heteroptera: Miridae). *Journal of Invertebrate Pathology*, *83*(1), 60-62.

Amin, G. A., Youssef, N. A., Bazaid, S., Saleh, W. D. (2010). Assessment of insecticidal activity of red pigment produced by the fungus *Beauveria bassiana*. *World Journal of Microbiology and Biotechnology*, *26*(12), 2263-2268.

Anderson, R. M., May, R. M. (1981). The population dynamics of microparasites and their invertebrate hosts. *Philosophical Transactions of the Royal Society of London. B, Biological Sciences*, *291*(1054), 451-524.

Arnold, A. E., Lutzoni, F. (2007). Diversity and host range of foliar fungal endophytes: are tropical leaves biodiversity hotspots? *Ecology*, *88*(3), 541-549.

Audenaert, K., Pattery, T., Cornelis, P., Höfte, M. (2002). Induction of systemic resistance to *Botrytis cinerea* in tomato by *Pseudomonas aeruginosa* 7NSK2: role of salicylic acid, pyochelin, and pyocyanin. *Molecular Plant-Microbe Interactions*, *15*(11), 1147-1156.

Ávila-Hernández, J. G., Carrillo-Inungaray, M. L., Cruz-Quiroz, R. D., Wong-Paz, J. E., Muñiz-Márquez, D. B., Parra, R., Aguilar, C.N., Aguilar-Zárate, P. (2020). *Beauveria bassiana* secondary metabolites: a review inside their production systems, biosynthesis, and bioactivities. *Mex. J. Biotechnol*, *5*, 1-33.

Baker, K. F., & Cook, R. J. (1974). *Biological control of plant pathogens*. San Francisco, W.H. Freeman, 443.

Balmforth, A. J., Thomson, A. (1984). Isolation and characterization of glyoxylate dehydrogenase from the fungus *Sclerotium rolfsii*. *Biochemical Journal*, *218*(1), 113.

Bark, Y. G., Lee, D. G., Kang, S. C., Kim, Y. H. (1996). Antibiotic properties of an entomopathogenic fungus, *Beauveria bassiana*, on *Fusarium oxysporum* and *Botrytis cinerea*. *Korean Journal of Plant Pathology (Korea Republic)*.

Barr, D. P., Aust, S. D. (1994). Mechanisms white rot fungi use to degrade pollutants. *Environmental science & technology*, *28*(2), 78A-87A.

Barra-Bucarei, L., France Iglesias, A., Gerding González, M., Silva Aguayo, G., Carrasco-Fernández, J., Castro, J. F., Ortiz Campos, J. (2019). Antifungal activity of *Beauveria bassiana* endophyte against *Botrytis cinerea* in two solanaceae crops. *Microorganisms*, *8*(1), 65.

Barratt, B. I. P., Moran, V. C., Bigler, F., Van Lenteren, J. C. (2018). The status of biological control and recommendations for improving uptake for the future. *BioControl*, *63*(1), 155-167.

Bateman, D. F. and Beer, S.V. (1965). Simultaneous production and synergistic action of oxalic acid and polygalacturonase during pathogenesis by *Sclerotium rolfsii*. *Phytophalology*, *55*, 204-211.

Benton, T. G., Vickery, J. A., Wilson, J. D. (2003). Farmland biodiversity: is habitat heterogeneity the key? *Trends in ecology & evolution*, *18*(4), 182-188.

Bergsson, G., Arnfinnsson, J., Steingrímsson, O., Thormar, H. (2001). In vitro killing of *Candida albicans* by fatty acids and monoglycerides. *Antimicrobial agents and chemotherapy*, *45*(11), 3209-3212.

Bi, F., Barad, S., Ment, D., Luria, N., Dubey, A., Casado, V., Glam, N., Diaz Mínguez, J., Espeso, E.A., Fluhr, R., Prusky, D. (2016). Carbon regulation of environmental pH by secreted small molecules that modulate pathogenicity in phytopathogenic fungi. *Molecular plant pathology*, *17*(8), 1178-1195.

Bidochka, M. J., Pfeifer, T. A., Khachatourians, G. G. (1987). Development of the entomopathogenic fungus *Beauveria bassiana* in liquid cultures. *Mycopathologia*, *99*(2), 77-83.

Bidochka, M. J., Khachatourians, G. G. (1988a). Regulation of extracellular protease in the entomopathogenic fungus *Beauveria bassiana*. *Experimental mycology*, *12*(2), 161-168.

Bidochka, M. J., Khachatourians, G. G. (1991). The implication of metabolic acids produced by *Beauveria bassiana* in pathogenesis of the migratory grasshopper, *Melanoplus sanguinipes*. *Journal of Invertebrate Pathology*, *58*(1), 106-117.

Bidochka, M. J., Khachatourians, G. G. (1993). Oxalic acid hyperproduction in *Beauveria bassiana* mutants is related to a utilizable carbon source but not to virulence. *Journal of Invertebrate Pathology*, *62*(1), 53-57.

Bidochka, M. J., Kasperski, J. E., Wild, G. A. (1998). Occurrence of the entomopathogenic fungi *Metarhizium anisopliae* and *Beauveria bassiana* in soils from temperate and near-northern habitats. *Canadian Journal of Botany*, *76*(7), 1198-1204.

Bills, G. F., Polishook, J. D. (1991). Microfungi from *Carpinus caroliniana*. *Canadian Journal of Botany*, *69*(7), 1477-1482.

Bindi, M., Hacour, A., Vandermeiren, K., Craigon, J., Ojanperä, K., Sellden, G., Fibbi, L. (2002). Chlorophyll concentration of potatoes grown under elevated carbon dioxide and/or ozone concentrations. *European Journal of Agronomy*, *17*(4), 319-335.

Bing, L. A., Lewis, L. C. (1991). Suppression of *Ostrinia nubilalis* (Hübner) (Lepidoptera: Pyralidae) by endophytic *Beauveria bassiana* (Balsamo) Vuillemin. *Environmental entomology*, *20*(4), 1207-1211.

Bing, L. A., Lewis, L. C. (1992). Endophytic *Beauveria bassiana* (Balsamo) Vuillemin in corn: the influence of the plant growth stage and *Ostrinia nubilalis* (Hübner). *Biocontrol Science and Technology*, *2*(1), 39-47.

Bing, L. A., Lewis, L. C. (1993). Occurrence of the entomopathogen *Beauveria bassiana* (Balsamo) Vuillemin in different tillage regimes and in *Zea mays* L. and virulence towards *Ostrinia nubilalis* (Hübner). *Agriculture, ecosystems & environment*, *45*(1-2), 147-156.

Boucias, D. G., Pendland, J. C., Latge, J. (1988). Nonspecific factors involved in attachment of entomopathogenic deuteromycetes to host insect cuticle. *Applied and environmental microbiology*, *54*(7), 1795-1805.

Boucias, D.G., Pendland, J.C. (1991). Attachment of Mycopathogens to Cuticle. In *The Fungal Spore and Disease Initiation in Plants and Animals*. Springer, Boston, MA, *5*, 101-127.

Brewer, D., Jen, W. C., Jones, G. A., Taylor, A. (1984). The antibacterial activity of some naturally occurring 2, 5-dihydroxy-l, 4-benzoquinones. *Canadian journal of microbiology*, *30*(8), 1068-1072.

Bruck, D. J., Lewis, L. C. (2002a). Rainfall and crop residue effects on soil dispersion and *Beauveria bassiana* spread to corn. *Applied Soil Ecology*, *20*(3), 183-190.

Bruck, D. J., Lewis, L. C. (2002b). *Carpophilus freemani* (Coleoptera: Nitidulidae) as a vector of *Beauveria bassiana*. *Journal of Invertebrate Pathology*, *3*(80), 188-190.

Butt, T. M., Ibrahim, L., Clark, S. J., Beckett, A. (1995). The germination behaviour of *Metarhizium anisopliae* on the surface of aphid and flea beetle cuticles. *Mycological Research*, *99*(8), 945-950.

Butt, T. M., Coates, C. J., Dubovskiy, I. M., Ratcliffe, N. A. (2016). Entomopathogenic fungi: new insights into host–pathogen interactions. *Advances in genetics*, *94*, 307-364.

Caddick, M. X., Brownlee, A. G., & Arst, H. N. (1986). Regulation of gene expression by pH of the growth medium in *Aspergillus nidulans*. *Molecular and General Genetics MGG*, *203*(2), 346-353.

Caloni, F., Fossati, P., Anadón, A., Bertero, A. (2020). Beauvericin: The beauty and the beast. *Environmental Toxicology and Pharmacology*, *75*, 103349.

Campbell, R. J., Mobley, K. N., Marini, R. P., Pfeiffer, D. G. (1990). Growing conditions alter the relationship between SPAD-501 values and apple leaf chlorophyll. *HortScience*, *25*(3), 330-331.

Cardinale, B. J., Harvey, C. T., Gross, K., Ives, A. R. (2003). Biodiversity and biocontrol: emergent impacts of a multi-enemy assemblage on pest suppression and crop yield in an agroecosystem. *Ecology letters*, *6*(9), 857-865.

Castlebury, L. A., Sutherland, J. B., Tanner, L. A., Henderson, A. L., Cerniglia, C. E. (1999). Use of a bioassay to evaluate the toxicity of beauvericin to bacteria. *World Journal of Microbiology and Biotechnology*, *15*(1), 119-121.

Cen, K., Li, B., Lu, Y., Zhang, S., Wang, C. (2017). Divergent LysM effectors contribute to the virulence of *Beauveria bassiana* by evasion of insect immune defenses. *PLoS pathogens*, *13*(9), e1006604.

Charnley, A. K., Leger, R. J. S.(1991). The role of cuticle-degrading enzymes in fungal pathogenesis in insects. In *The fungal spore and disease initiation in plants and animals*. Springer, Boston, MA. *12*, 267-286.

Chen, C., & Dickman, M. B. (2005). Proline suppresses apoptosis in the fungal pathogen *Colletotrichum trifolii*. Proceedings of the National Academy of Sciences, *102*(9), 3459-3464.

Chen, X., Zhang, W., Wang, J., Zhu, S., Shen, X., Chen, H., Fan, Y. (2022). Transcription Factors BbPacC and Bbmsn2 Jointly Regulate Oosporein Production in *Beauveria bassiana*. *Microbiology Spectrum*, e03118-22.

Cherry, A. J., Lomer, C. J., Djegui, D., Schulthess, F. (1999). Pathogen incidence and their potential as microbial control agents in IPM of maize stem borers in West Africa. *BioControl*, *44*(3), 301-327.

Cho, E. M., Kirkland, B. H., Holder, D. J., Keyhani, N. O. (2007). Phage display cDNA cloning and expression analysis of hydrophobins from the entomopathogenic fungus *Beauveria* (Cordyceps) *bassiana*. *Microbiology*, *153*(10), 3438-3447.

Clarkson, J. M., Charnley, A. K. (1996). New insights into the mechanisms of fungal pathogenesis in insects. *Trends in microbiology*, *4*(5), 197-203.

Cook, R. J., Baker, K. F. (1983). The nature and practice of biological control of plant pathogens. *American Phytopathological Society*, 539.

Cook, R. J. (1993). Making greater use of introduced microorganisms for biological control of plant pathogens. *Annual review of phytopathology*, *31*(1), 53-80.

de Hoog, G. S. (1972). The genera Beauveria, Isaria, Tritirachium and Acrodontium gen. nov. *Stud. Mycol.*, *1*, 1-41.

De Meyer, G., Höfte, M. (1997). Salicylic acid produced by the rhizobacterium *Pseudomonas aeruginosa* 7NSK2 induces resistance to leaf infection by *Botrytis cinerea* on bean. *Phytopathology*, *87*(6), 588-593.

de Oliveira Mendes, G., Murta, H. M., Valadares, R. V., da Silveira, W. B., da Silva, I. R., Costa, M. D. (2020). Oxalic acid is more efficient than sulfuric acid for rock phosphate solubilization. *Minerals Engineering*, *155*, 106458.

DeBach, P., & Rosen, D. (1991). Biological control by natural enemies. Cambridge University Press.

Delgado-Jarana, J., Sousa, S., Gonzalez, F., Rey, M., Llobell, A. (2006). ThHog1 controls the hyperosmotic stress response in *Trichoderma harzianum*. *Microbiology*, *152*(6), 1687-1700.

Dhokchawle, B. V., Kamble, M. D., Tauro, S. J., Bhandari, A. B. (2014). Synthesis, spectral studies, hydrolysis kinetics and pharmacodynamic profile of mefenamic acid prodrugs. *Der Pharma Chemica*, *6*(3).

Dias, B. A., Neves, P. M. O. J., Furlaneto-Maia, L., Furlaneto, M. C. (2008). Cuticle-degrading proteases produced by the entomopathogenic fungus *Beauveria bassiana* in the presence of coffee berry borer cuticle. *Brazilian Journal of Microbiology*, *39*, 301-306.

Dixon, K. P., Xu, J. R., Smirnoff, N., Talbot, N. J. (1999). Independent signaling pathways regulate cellular turgor during hyperosmotic stress and appressorium-mediated plant infection by *Magnaporthe grisea*. *The Plant Cell*, *11*(10), 2045-2058.

Dromph, K. M., Vestergaard, S. (2002). Pathogenicity and attractiveness of entomopathogenic hyphomycete fungi to collembolans. *Applied Soil Ecology*, *21*(3), 197-210.

Dromph, K. M. (2003). Collembolans as vectors of entomopathogenic fungi. *Pedobiologia*, *47*(3), 245-256.

Eilenberg, J., Hajek, A., Lomer, C. (2001). Suggestions for unifying the terminology in biological control. *BioControl*, *46*(4), 387-400.

Elad, Y., Baker, R. (1985). The role of competition for iron and carbon in suppression of chlamydospore germination of Fusarium spp. by Pseudomonas spp. *Phytopathology*, *75*(9), 1053-1059.

El-Deeb, H. M., Lashin, S. M., Arab, Y. A. S. (2012). Reaction of some tomato cultivars to tomato leaf curl virus and evaluation of the endophytic colonisation with *Beauveria bassiana* on the disease incidence and its vector, *Bemisia tabaci*. *Archives of phytopathology and plant protection*, *45*(13), 1538-1545.

Eley, K. L., Halo, L. M., Song, Z., Powles, H., Cox, R. J., Bailey, A. M., Lazarus, C.M., Simpson, T. J. (2007). Biosynthesis of the 2-pyridone tenellin in the insect pathogenic fungus *Beauveria bassiana*. *ChemBioChem*, *8*(3), 289-297.

Ecology letters 3(3), 228-235.

Esposti, M. D. D., de Siqueira, D. L., Pereira, P. R. G., Venegas, V. H. A., Salomão, L. C. C., Filho, J. A. M. (2003). Assessment of nitrogenized nutrition of citrus rootstocks using chlorophyll concentrations in the leaf. *Journal of Plant nutrition*, *26*(6), 1287-1299.

Fan, Y., Fang, W., Guo, S., Pei, X., Zhang, Y., Xiao, Y., Li, D., Jin, K., Bidochka, M.J., Pei, Y. (2007). Increased insect virulence in *Beauveria bassiana* strains overexpressing an engineered chitinase. *Applied and Environmental Microbiology*, *73*(1), 295-302.

Fan, Y., Ortiz-Urquiza, A., Kudia, R. A., Keyhani, N. O. (2012b). A fungal homologue of neuronal calcium sensor-1, Bbcsa1, regulates extracellular acidification and contributes to virulence in the entomopathogenic fungus *Beauveria bassiana*. *Microbiology*, *158*(7), 1843-1851.

Fan, Y., Ortiz-Urquiza, A., Garrett, T., Pei, Y., Keyhani, N. O. (2015). Involvement of a caleosin in lipid storage, spore dispersal, and virulence in the entomopathogenic filamentous fungus, *B eauveria bassiana*. *Environmental microbiology*, *17*(11), 4600-4614.

Fan, Y., Liu, X., Keyhani, N. O., Tang, G., Pei, Y., Zhang, W., Tong, S. (2017). Regulatory cascade and biological activity of *Beauveria bassiana* oosporein that limits bacterial growth after host death. *Proceedings of the National Academy of Sciences*, *114*(9), E1578-E1586.

Fang, W., Leng, B., Xiao, Y., Jin, K., Ma, J., Fan, Y., Feng, J., Yang, X., Zhang, Y., Pei, Y. (2005). Cloning of *Beauveria bassiana* chitinase gene Bbchit1 and its application to improve fungal strain virulence. *Applied and environmental microbiology*, *71*(1), 363-370.

Fang, W., Feng, J., Fan, Y., Zhang, Y., Bidochka, M. J., Leger, R. J. S., Pei, Y. (2009). Expressing a fusion protein with protease and chitinase activities increases the virulence of the insect pathogen *Beauveria bassiana*. *Journal of invertebrate pathology*, *102*(2), 155-159.

Fargues, J., Goettel, M. S., Smits, N., Ouedraogo, A., Vidal, C., Lacey, L. A., Lomer, C.J., Rougier, M. (1996). Variability in susceptibility to simulated sunlight of conidia among isolates of entomopathogenic Hyphomycetes. *Mycopathologia*, *135*(3), 171-181.

Fargues, J., Goettel, M. S., Smits, N., Ouedraogo, A., Rougier, M. (1997). Effect of temperature on vegetative growth of *Beauveria bassiana* isolates from different origins. *Mycologia*, *89*(3), 383-392.

Feng, M. (1998). Reliability of extracellular protease and lipase activities of *Beauveria bassiana* isolates used as their virulence indices. *Wei Sheng wu xue bao= Acta Microbiologica Sinica*, *38*(6), 461-467.

Feng, M. G., Chen, C., Chen, B. (2004). Wide dispersal of aphid-pathogenic Entomophthorales among aphids relies upon migratory alates. *Environmental Microbiology*, *6*(5), 510-516.

Feng, P., Shang, Y., Cen, K., Wang, C. (2015). Fungal biosynthesis of the bibenzoquinone oosporein to evade insect immunity. *Proceedings of the National Academy of Sciences*, *112*(36), 11365-11370.

Firouzbakht, H., Zibaee, A., Hoda, H., Sohani, M. M. (2015). Virulence determination of *Beauveria bassiana* isolates on a predatory Hemipteran, *Andrallus spinidens* Fabricius (Hemiptera: Pentatomidae). *Acta Phytopathologica et Entomologica Hungarica*, *50*(1), 115-125.

Fornelli, F., Minervini, F., Logrieco, A. (2004). Cytotoxicity of fungal metabolites to lepidopteran (*Spodoptera frugiperda*) cell line (SF-9). *Journal of invertebrate pathology*, *85*(2), 74-79.

Franceschi, V. R., Horner, H. T. (1980). Calcium oxalate crystals in plants. *The Botanical Review*, *46*(4), 361-427.

Galani, G. (1988). Cultivation of some entomopathogenic fungi in liquid media with various initial pH values. *Analel-Institutului-de-Cercetari-pentru-Protecta-Plantelor*, *21*, 54.

Ganassi, S., Moretti, A., Pagliai, A. M. B., Logrieco, A., Sabatini, M. A. (2002). Effects of beauvericin on *Schizaphis graminum* (Aphididae). *Journal of invertebrate pathology*, *80*(2), 90-96.

Garantonakis, N., Pappas, M. L., Varikou, K., Skiada, V., Broufas, G. D., Kavroulakis, N., Papadopoulou, K. K. (2018). Tomato inoculation with the endophytic strain *Fusarium solani* K results in reduced feeding damage by the zoophytophagous predator *Nesidiocoris tenuis*. *Frontiers in Ecology and Evolution*, *6*, 126.

Garcia-Pichel, F., Wingard, C. E., Castenholz, R. W. (1993). Evidence regarding the UV sunscreen role of a mycosporine-like compound in the cyanobacterium Gloeocapsa sp. *Applied and Environmental Microbiology*, *59*(1), 170-176.

Gardarin, A., Garnier, É., Carrère, P., Cruz, P., Andueza, D., Bonis, A., Colace, M.P., Dumont, B., Duru, M., Farruggia, A., Gaucherand, S., Grigulis, K., Kazakou, E. (2014). Plant trait–digestibility relationships across management and climate gradients in permanent grasslands. *Journal of Applied Ecology*, *51*(5), 1207-1217.

Geraldes, V., Pinto, E. (2021). Mycosporine-like amino acids (MAAs): biology, chemistry and identification features. *Pharmaceuticals*, *14*(1), 63.

Gibson, D. M., Donzelli, B. G., Krasnoff, S. B., Keyhani, N. O. (2014). Discovering the secondary metabolite potential encoded within entomopathogenic fungi. *Natural Product Reports*, *31*(10), 1287-1305.

Gottwald, T. R., Tedders, W. L. (1982). Studies on conidia release by the entomogenous fungi *Beauveria bassiana* and *Metarhizium anisopliae* (Deuteromycotina: Hyphomycetes) from adult pecan weevil (Coleoptera: Curculionidae) cadavers. *Environmental entomology*, *11*(6), 1274-1279.

Gray, J. A., Chandry, P. S., Kaur, M., Kocharunchitt, C., Bowman, J. P., Fox, E. M. (2018). Novel biocontrol methods for *Listeria monocytogenes* biofilms in food production facilities. *Frontiers in Microbiology*, *9*, 605.

Gregorc, A., Poklukar, J. (2003). Rotenone and oxalic acid as alternative acaricidal treatments for *Varroa destructor* in honeybee colonies. *Veterinary parasitology*, *111*(4), 351-360.

Groden, E., & Dunn, T. (1996). Germination, host infection and survival of *Beauveria bassiana* conidia in natural soils. *Proceedings of the 3rd International Workshop on Microbial Control of Soil Dwelling Pests. AgResearch, New Zealand*, 137-145.

Groden, E., Lockwood, J. L. (1991). Effects of soil fungistasis on *Beauveria bassiana* and its relationship to disease incidence in the Colorado potato beetle, *Leptinotarsa decemlineata*, in Michigan and Rhode Island soils. *Journal of Invertebrate Pathology*, *57*(1), 7-16.

Grove, J. F., Pople, M. (1980). The insecticidal activity of beauvericin and the enniatin complex. *Mycopathologia*, *70*(2), 103-105.

Güerri-Agulló, B., Gómez-Vidal, S., Asensio, L., Barranco, P., Lopez-Llorca, L. V. (2010). Infection of the red palm weevil (*Rhynchophorus ferrugineus*) by the entomopathogenic fungus *Beauveria bassiana*: a SEM study. *Microscopy research and technique*, *73*(7), 714-725.

Gupta, S., Krasnoff, S. B., Underwood, N. L., Renwick, J. A. A., Roberts, D. W. (1991). Isolation of beauvericin as an insect toxin from *Fusarium semitectum* and *Fusarium moniliforme* var. *subglutinans*. *Mycopathologia*, *115*(3), 185-189.

Gupta, S. C., Leathers, T. D., El-Sayed, G. N., Ignoffo, C. M. (1994). Relationships among enzyme activities and virulence parameters in *Beauveria bassiana* infections of *Galleria mellonella* and *Trichoplusia ni*. *Journal of Invertebrate Pathology*, *64*(1), 13-17.

Gurulingappa, P., Sword, G. A., Murdoch, G., McGee, P. A. (2010). Colonization of crop plants by fungal entomopathogens and their effects on two insect pests when in planta. *Biological control*, *55*(1), 34-41.

Hairston, N. G., Smith, F. E., Slobodkin, L. B. (1960). Community structure, population control, and competition. *The american naturalist*, *94*(879), 421-425.

Hajek, A. E. (1997). Ecology of terrestrial fungal entomopathogens. In *Advances in microbial ecology*. Springer, Boston, MA, *15*, 193-249.

Halouane F. (2008). Basic research on the entomopathogen *Beauveria bassiana* (Bals.-Criv.) Vuill. (Ascomycota: Hypocreales): bioecology, production and application on *Schistocerca gregaria* (Forskål, 1775) and *Locusta migratoria* (Linné, 1758) (Orthoptera, Acrididae).

Hamill, R. L., Higgens, C. E., Boaz, H. E., Gorman, M. (1969). The structure op beauvericin, a new depsipeptide antibiotic toxic to *Artemia salina*. *Tetrahedron Letters*, *10*(49), 4255-4258.

Heimpel, G. E., & Mills, N. J. (2017). *Biological contro: Ecology and Applications*. Cambridge University Press.

Henke, M. O., de Hoog, G. S., Gross, U., Zimmermann, G., Kraemer, D., Weig, M. (2002). Human deep tissue infection with an entomopathogenic Beauveria species. *Journal of clinical microbiology*, *40*(7), 2698-2702.

Hoch, H. C., Staples, R. C., Whitehead, B., Comeau, J., Wolf, E. D. (1987). Signaling for growth orientation and cell differentiation by surface topography in Uromyces. *Science*, *235*(4796), 1659-1662.

Holder, D. J., Keyhani, N. O. (2005). Adhesion of the entomopathogenic fungus *Beauveria* (Cordyceps) *bassiana* to substrata. *Applied and environmental microbiology*, *71*(9), 5260-5266.

Holder, D. J., Kirkland, B. H., Lewis, M. W., Keyhani, N. O. (2007). Surface characteristics of the entomopathogenic fungus *Beauveria* (Cordyceps) *bassiana*. *Microbiology*, *153*(10), 3448-3457.

Howell, C. R., Stipanovic, R. D. (1980). Suppression of *Pythium ultimum*-induced damping-off of cotton seedlings by *Pseudomonas fluorescens* and its antibiotic, pyoluteorin. *Phytopathology*, *70*(8), 712-715.

Howell, C. R. (2003). Mechanisms employed by Trichoderma species in the biological control of plant diseases: the history and evolution of current concepts. *Plant disease*, *87*(1), 4-10.

Hummel, R. L., Walgenbach, J. F., Barbercheck, M. E., Kennedy, G. G., Hoyt, G. D., Arellano, C. (2002). Effects of production practices on soil-borne entomopathogens in western North Carolina vegetable systems. *Environmental Entomology*, *31*(1), 84-91.

Inglis, G. D., Ivie, T. J., Duke, G. M., Goettel, M. S. (2000). Influence of rain and conidial formulation on persistence of *Beauveria bassiana* on potato leaves and Colorado potato beetle larvae. *Biological Control*, *18*(1), 55-64.

Inglis, G.D., Goettel, M.S., Butt, T.M., Strasser, H., Jackson, C.W., & Magan, N. (2001). Use of hyphomycetous fungi for managing insect pests. In: Butt, T.M., Jackson, C., Magan, N. (eds) *Fungi as biocontrol agents: progress problems and potential*. CABI Publisher, Wallingford, UK, 23, 23-69.

Islam, M. T., Hashidoko, Y., Deora, A., Ito, T., Tahara, S. (2005). Suppression of damping-off disease in host plants by the rhizoplane bacterium Lysobacter sp. strain SB-K88 is linked to plant colonization and antibiosis against soilborne Peronosporomycetes. *Applied and Environmental Microbiology*, *71*(7), 3786-3796.

Jaber, L. R., Ownley, B. H. (2018). Can we use entomopathogenic fungi as endophytes for dual biological control of insect pests and plant pathogens? *Biological control*, *116*, 36-45.

Jackson, M. A., Mcguire, M. R., Lacey, L. A., Wraight, S. P. (1997). Liquid culture production of desiccation tolerant blastospores of the bioinsecticidal fungus *Paecilomyces fumosoroseus*. *Mycological Research*, *101*(1), 35-41.

Jaronski, S. (2014). Mass Production of Entomopathogenic Fungi: State of the Art. In: Morales-Ramos, J.A., Guadalupe Rojas, M., Shapiro-Ilan, D.I., (eds) *Mass Production of Beneficial Organisms*. Academic Press. 11, 357-413.

Jeffries, P., & Young, T. W. (1994). *Interfungal parasitic relationships*. Cab International.

Jeffs, L. B., Khachatourians, G. G. (1997). Toxic properties of Beauveria pigments on erythrocyte membranes. *Toxicon*, *35*(8), 1351-1356.

Jernejc, K., & Legiša, M. (2001). Activation of plasma membrane H+-ATPase by ammonium ions in *Aspergillus niger*. *Applied microbiology and biotechnology*, *57*(3), 368-373.

Jirakkakul, J., Cheevadhanarak, S., Punya, J., Chutrakul, C., Senachak, J., Buajarern, T., & Amnuaykanjanasin, A. (2015). Tenellin acts as an iron chelator to prevent iron-generated reactive oxygen species toxicity in the entomopathogenic fungus *Beauveria bassiana*. *FEMS microbiology letters*, *362*(2), 1-8.

Joshi, L., Leger, R.J.S., Bidochka, M. J. (1995). Cloning of a cuticle-degrading protease from the entomopathogenic fungus, *Beauveria bassiana*. *FEMS Microbiology Letters*, *125*(2-3), 211-217.

Kabara, J. J., Swieczkowski, D. M., Conley, A. J., Truant, J. P. (1972). Fatty acids and derivatives as antimicrobial agents. *Antimicrobial agents and chemotherapy*, *2*(1), 23-28.

Kawasaki, L., Sánchez, O., Shiozaki, K., Aguirre, J. (2002). SakA MAP kinase is involved in stress signal transduction, sexual development and spore viability in *Aspergillus nidulans*. *Molecular microbiology*, *45*(4), 1153-1163.

Keel, C., Voisard, C., Berling, C. H., Kahr, G., Defago, G. (1989). Iron sufficiency, a prerequisite for the suppression of tobacco black root rot by *Pseudomonas fluorescens* strain CHA 0 under gnotobiotic conditions. *Phytopathology*, *79*(5), 584-589.

Keller, S., Zimmermann, G. (1989). Mycopathogens of soil insects. In: Wilding, N., Collins, N. M., Hammond, P. M., & Webber, J. F. (eds) *Insect-fungus interactions*. London, Academic press. 239-270.

Keller, S., Kessler, P., Schweizer, C. (2003). Distribution of insect pathogenic soil fungi in Switzerland with special reference to *Beauveria brongniartii* and *Metharhizium anisopliae*. *BioControl*, *48*(3), 307-319.

Kirkland, B. H., Eisa, A., Keyhani, N. O. (2005). Oxalic acid as a fungal acaracidal virulence factor. *Journal of medical entomology*, *42*(3), 346-351.

Kirkland, B. H., Keyhani, N. O. (2011). Expression and purification of a functionally active class I fungal hydrophobin from the entomopathogenic fungus *Beauveria bassiana* in *E. coli*. *Journal of Industrial Microbiology and Biotechnology*, *38*(2), 327-335.

Kisla, T. A., Cu-Unjieng, A., Sigler, L., Sugar, J. (2000). Medical management of *Beauveria bassiana* keratitis. *Cornea*, *19*(3), 405-406.

Klieber, J., Reineke, A. (2016). The entomopathogen *Beauveria bassiana* has epiphytic and endophytic activity against the tomato leaf miner *Tuta absoluta*. *Journal of Applied Entomology*, *140*(8), 580-589.

Klingen, I., Eilenberg, J., Meadow, R. (2002). Effects of farming system, field margins and bait insect on the occurrence of insect pathogenic fungi in soils. *Agriculture, ecosystems & environment*, *91*(1-3), 191-198.

Kloepper, J. W., Leong, J., Teintze, M., Schroth, M. N. (1980). Enhanced plant growth by siderophores produced by plant growth-promoting rhizobacteria. *Nature*, *286*(5776), 885-886.

Kogl, F., & Van Wessem, G. C. (1944). Analysis concerning pigments of fungi XIV: Concerning oosporein, the pigment of *Oospora colorans* van Beyma. *Recl Trav Chim Pays Bas*, *63*, 5-24.

Kojima, K., Takano, Y., Yoshimi, A., Tanaka, C., Kikuchi, T., Okuno, T. (2004). Fungicide activity through activation of a fungal signalling pathway. *Molecular microbiology*, *53*(6), 1785-1796.

Kolattukudy, P. E., Rogers, L. M., Li, D., Hwang, C. S., Flaishman, M. A. (1995). Surface signaling in pathogenesis. *Proceedings of the National Academy of Sciences*, *92*(10), 4080-4087.

Kos, J., Zadrazilova, I., Pesko, M., Keltosova, S., Tengler, J., Gonec, T., Bobal, P., Kauerova, T., Oravec, M., Kollar, P., Cizek, A., Kralova, K., Jampilek, J. (2013). Antibacterial and herbicidal activity of ring-substituted 3-hydroxynaphthalene-2 carboxanilides. *Molecules*, *18*(7), 7977-7997.

Kossowska, B., Lamer-Zarawska, E., Olczak, M., Kątnik-Prastowska, I. (1999). Lectin from *Beauveria bassiana* mycelium recognizes Thomsen–Friedenreich antigen and related structures. *Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology*, *123*(1), 23-31.

Kouri, K., Duchen, M. R., Lemmens-Gruber, R. (2005). Effects of beauvericin on the metabolic state and ionic homeostasis of ventricular myocytes of the guinea pig. *Chemical research in toxicology*, *18*(11), 1661-1668.

Krátký, M., Vinšová, J. (2012). Antifungal activity of salicylanilides and their esters with 4-(trifluoromethyl) benzoic acid. *Molecules*, *17*(8), 9426-9442.

Krieger de Moraes, C., Schrank, A., Vainstein, M. H. (2003). Regulation of extracellular chitinases and proteases in the entomopathogen and acaricide *Metarhizium anisopliae*. *Current Microbiology*, *46*(3), 0205-0210.

Křížová, L., Dadáková, K., Dvořáčková, M., & Kašparovský, T. (2021). Feedborne mycotoxins beauvericin and enniatins and livestock animals. *Toxins*, *13*(1), 32.

Kubicek, C. P. (1987). The role of the citric acid cycle in fungal organic acid fermentations. In *Biochemical Society Symposium, 54*, 113-126.

Kubicek, C. P., Schreferl-Kunar, G., Wöhrer, W., Röhr, M. (1988). Evidence for a cytoplasmic pathway of oxalate biosynthesis in *Aspergillus niger*. *Applied and Environmental Microbiology*, *54*(3), 633-637.

Kubicek, C. P., Mach, R. L., Peterbauer, C. K., Lorito, M. (2001). Trichoderma: from genes to biocontrol. *Journal of Plant Pathology*, 11-23.

Lacey, L. A., Grzywacz, D., Shapiro-Ilan, D. I., Frutos, R., Brownbridge, M., Goettel, M. S. (2015). Insect pathogens as biological control agents: back to the future. *Journal of invertebrate pathology*, *132*, 1-41.

Landraud, P., Chuzeville, S., Billon-Grande, G., Poussereau, N., & Bruel, C. (2013). Adaptation to pH and role of PacC in the rice blast fungus *Magnaporthe oryzae*. *PLoS One*, *8*(7), e69236.

Lee, S. M., Yeo, W. H., Jee, H. J., Shin, S. C., Moon, Y. S. (1999). Effect of entomopathogenic fungi on growth of cucumber and *Rhizoctonia solani*. *Journal of Forest Science*, *62*, 118-125.

Leeman, M., Van Pelt, J. A., Den Ouden, F. M., Heinsbroek, M., Bakker, P. A. H. M., Schippers, B. (1995). Induction of systemic resistance against Fusarium wilt of radish by lipopolysaccharides of *Pseudomonas fluorescens*. *Phytopathology*, *85*(9), 1021-1027.

Leger, R. J. S., Butt, T. M., Staples, R. C., Roberts, D. W. (1989a). Synthesis of proteins including a cuticle-degrading protease during differentiation of the entomopathogenic fungus *Metarhizium anisopliae*. *Experimental Mycology*, *13*(3), 253-262.

Leger, R. J. S., Butt, T. M., Goettel, M. S., Staples, R. C., Roberts, D. W. (1989b). Production *in vitro* of appressoria by the entomopathogenic fungus *Metarhizium anisopliae*. *Experimental mycology*, *13*(3), 274-288.

Leger, R. J.S., Joshi, L., & Roberts, D. (1998). Ambient pH is a major determinant in the expression of cuticle-degrading enzymes and hydrophobin by *Metarhizium anisopliae*. *Applied and Environmental Microbiology*, *64*(2), 709-713.

Leger, R. J. S., Nelson, J. O., & Screen, S. E. (1999). The entomopathogenic fungus Metarhizium anisopliae alters ambient pH, allowing extracellular protease production and activity. *Microbiology*, *145*(10), 2691-2699.

Leland, J. E., McGuire, M. R., Grace, J. A., Jaronski, S. T., Ulloa, M., Park, Y. H., Plattner, R. D. (2005). Strain selection of a fungal entomopathogen, *Beauveria bassiana*, for control of plant bugs (Lygus spp.) (Heteroptera: Miridae). *Biological Control*, *35*(2), 104-114.

Lewis, M. W., Robalino, I. V., Keyhani, N. O. (2009). Uptake of the fluorescent probe FM4-64 by hyphae and haemolymph-derived in vivo hyphal bodies of the entomopathogenic fungus *Beauveria bassiana*. *Microbiology*, *155*(9), 3110-3120.

Lingg, A. J., Donaldson, M. D. (1981). Biotic and abiotic factors affecting stability of *Beauveria bassiana* conidia in soil. *Journal of Invertebrate Pathology*, *38*(2), 191-200.

Lipa JJ. (1975). White muscardine (*Beauveria* sp.). In: Lipa JJ, editor. *An outline of insect pathology*. Warsaw: Foreign Sciences Publications, 139–42.

Liu, S., Ruan, W., Li, J., Xu, H., Wang, J., Gao, Y., Wang, J. (2008). Biological control of phytopathogenic fungi by fatty acids. *Mycopathologia*, *166*(2), 93-102.

Logrieco, A., Moretti, A., Castella, G., Kostecki, M., Golinski, P., Ritieni, A., Chelkowski, J. (1998). Beauvericin production by Fusarium species. *Applied and Environmental Microbiology*, *64*(8), 3084-3088.

Loper, J. E., Buyer, J. S. (1991). Siderophores in microbial interactions on plant surfaces. *Mol. Plant-Microbe Interact*, *4*(1), 5-13.

Lu, H. L., Leger, R.J.S. (2016). Insect immunity to entomopathogenic fungi. *Advances in genetics*, *94*, 251-285.

Magnuson, J. K., & Lasure, L. L. (2004). Organic acid production by filamentous fungi. *Advances in fungal biotechnology for industry, agriculture, and medicine*. Springer, Boston, MA, *12*, 307-340.

Magro, P., Marciano, P., Di Lenna, P. (1984). Oxalic acid production and its role in pathogenesis of *Sclerotinia sclerotiorum*. *FEMS Microbiology Letters*, *24*(1), 9-12.

Markesteijn, L., Poorter, L., Paz, H., Sack, L., Bongers, F. (2011). Ecological differentiation in xylem cavitation resistance is associated with stem and leaf structural traits. *Plant, Cell & Environment*, *34*(1), 137-148.

Marshall, E. J. P., Moonen, A. C. (2002). Field margins in northern Europe: their functions and interactions with agriculture. *Agriculture, Ecosystems & Environment*, *89*(1-2), 5-21.

Mascarin, G. M., Jaronski, S. T. (2016). The production and uses of *Beauveria bassiana* as a microbial insecticide. *World Journal of Microbiology and Biotechnology*, *32*(11), 1-26.

Maudsley, M., Seeley, B., Lewis, O. (2002). Spatial distribution patterns of predatory arthropods within an English hedgerow in early winter in relation to habitat variables. *Agriculture, Ecosystems & Environment*, *89*(1-2), 77-89.

Maxwell, D. P., Bateman, D. F. (1968). Influence of carbon source and pH on oxalate accumulation in culture filtrates of *Sclerotium rolfsii*. *Phytopathology*, *58*(10), 1351.

McConn, M. M., Nakata, P. A. (2002). Calcium oxalate crystal morphology mutants from *Medicago truncatula*. *Planta*, *215*(3), 380-386.

McCullough, W., Roberts, C. F., Osmani, S. A., & Scrutton, M. C. (1986). Regulation of carbon metabolism in filamentous fungi. *Carbohydrate metabolism in cultured cells*, 287-355.

McKinnon, A. C., Saari, S., Moran-Diez, M. E., Meyling, N. V., Raad, M., Glare, T. R. (2017). *Beauveria bassiana* as an endophyte: a critical review on associated methodology and biocontrol potential. *BioControl*, *62*(1), 1-17.

Meca, G., Sospedra, I., Soriano, J. M., Ritieni, A., Moretti, A., Manes, J. (2010). Antibacterial effect of the bioactive compound beauvericin produced by *Fusarium proliferatum* on solid medium of wheat. *Toxicon*, *56*(3), 349-354.

Meikle, W. G., Jaronski, S. T., Mercadier, G., Quimby, P. C. (2003). A distributed delay routine-based simulation model of *Beauveria bassiana* conidial stability in response to environmental stressors. *BioControl*, *48*(5), 561-578.

Mekalanos, J. J. (1992). Environmental signals controlling expression of virulence determinants in bacteria. *Journal of bacteriology*, *174*(1), 1-7.

Menjivar, R. D., Cabrera, J. A., Kranz, J., Sikora, R. A. (2012). Induction of metabolite organic compounds by mutualistic endophytic fungi to reduce the greenhouse whitefly *Trialeurodes vaporariorum* (Westwood) infection on tomato. *Plant and soil*, *352*(1), 233-241.

Meyling, N. V. (2005). *Population ecology and genetic diversity of entomopathogenic fungi (Ascomycota: Hypocreales) in agroecosystems and field margins*. Ph.D. Thesis. Center for Skov, Landskab og Planlægning/Københavns Universitet.

Meyling, N. V., Eilenberg, J. (2006a). Isolation and characterisation of *Beauveria bassiana* isolates from phylloplanes of hedgerow vegetation. *Mycological research*, *110*(2), 188-195.

Meyling, N. V., Eilenberg, J. (2006b). Occurrence and distribution of soil borne entomopathogenic fungi within a single organic agroecosystem. *Agriculture, ecosystems & environment*, *113*(1-4), 336-341.

Meyling, N. V., Pell, J. K., Eilenberg, J. (2006). Dispersal of *Beauveria bassiana* by the activity of nettle insects. *Journal of invertebrate pathology*, *93*(2), 121-126.

Moino Jr, A., Alves, S. B., Lopes, R. B., Neves, P. M. O. J., Pereira, R. M., Vieira, S. A. (2002). External development of the entomopathogenic fungi *Beauveria bassiana* and *Metarhizium anisopliae* in the subterranean termite *Heterotermes tenuis*. *Scientia agricola*, *59*, 267-273.

Molnár, I., Gibson, D. M., Krasnoff, S. B. (2010). Secondary metabolites from entomopathogenic Hypocrealean fungi. *Natural product reports*, *27*(9), 1241-1275.

Munir, E., Yoon, J. J., Tokimatsu, T., Hattori, T., Shimada, M. (2001). A physiological role for oxalic acid biosynthesis in the wood-rotting basidiomycete *Fomitopsis palustris*. *Proceedings of the National Academy of Sciences*, *98*(20), 11126-11130.

Murphy, R. J., Levy, J. F. (1983). Production of copper oxalate by some copper tolerant fungi. *Transactions of the British Mycological Society*, *81*(1), 165-168.

Naglik, J. R., Challacombe, S. J., & Hube, B. (2003). *Candida albicans* secreted aspartyl proteinases in virulence and pathogenesis. *Microbiology and molecular biology reviews*, *67*(3), 400-428.

Neufeld, H. S., Chappelka, A. H., Somers, G. L., Burkey, K. O., Davison, A. W., Finkelstein, P. L. (2006). Visible foliar injury caused by ozone alters the relationship between SPAD meter readings and chlorophyll concentrations in cutleaf coneflower. *Photosynthesis Research*, *87*(3), 281-286.

Nicoletti, R., Becchimanzi, A. (2020). Endophytism of Lecanicillium and Akanthomyces. *Agriculture*, *10*(6), 205.

Nilanonta, C., Isaka, M., Kittakoop, P., Palittapongarnpim, P., Kamchonwongpaisan, S., Pittayakhajonwut, D., Tanticharoen, M., Thebtaranonth, Y. (2000). Antimycobacterial and antiplasmodial cyclodepsipeptides from the insect pathogenic fungus *Paecilomyces tenuipes* BCC 1614. *Planta medica*, *66*(08), 756-758.

Noodén, L. D., Guiamét, J. J., John, I. (1997). Senescence mechanisms. *Physiologia plantarum*, *101*(4), 746-753.

Oke, O. L. (1969). Oxalic acid in plants and in nutrition. *World Review of Nutrition and Dietetics*. Basel, Karger, *10*, 262-303.

Onoda, Y., Westoby, M., Adler, P. B., Choong, A. M., Clissold, F. J., Cornelissen, J. H.C., Dìaz, S., Dominy, N.J., Elgart, A., Enrico, L., Fine, P.V.A., Howard, J.J., Jalili, A., Kitajima, K., Kurokawa, H., McArthur, C., Lucas, P.W., Markesteijn, L., Pérez-Harguindeguy, N., Poorter, L., Richards, L., Santiago, L.S., Sosinski Jr, E.E, Van Bael, S.A., Warton, D.I., Wright, I.J., Wright, S.J., Yamashita, N. (2011). Global patterns of leaf mechanical properties. *Ecology letters*, *14*(3), 301-312.

Oren, A. (1997). Mycosporine-like amino acids as osmotic solutes in a community of halophilic cyanobacteria. *Geomicrobiology Journal*, *14*(3), 231-240.

Orole, O. O., Adejumo, T. O. (2009). Activity of fungal endophytes against four maize wilt pathogens. *Afr. J. Microbiol. Res*, *3*(12), 969-973.

Ortiz-Urquiza, A., Luo, Z., Keyhani, N. O. (2015). Improving mycoinsecticides for insect biological control. *Applied microbiology and biotechnology*, *99*(3), 1057-1068.

Ortiz-Urquiza, A., Fan, Y., Garrett, T., Keyhani, N. O. (2016). Growth substrates and caleosin-mediated functions affect conidial virulence in the insect pathogenic fungus *Beauveria bassiana*. *Microbiology*, *162*(11), 1913-1921.

Ortiz-Urquiza, A. (2021). The split personality of *Beauveria bassiana*: understanding the molecular basis of fungal parasitism and mutualism. *Msystems*, *6*(4), e00766-21.

Paciolla, C., Dipierro, N., Mule, G., Logrieco, A., Dipierro, S. (2004). The mycotoxins beauvericin and T-2 induce cell death and alteration to the ascorbate metabolism in tomato protoplasts. *Physiological and Molecular Plant Pathology*, *65*(1), 49-56.

Pal, K. K., Gardener, B. M. (2006). Biological control of plant pathogens.

Palmieri, D., Vitullo, D., De Curtis, F., Lima, G. (2017). A microbial consortium in the rhizosphere as a new biocontrol approach against fusarium decline of chickpea. *Plant Soil*, 412, 425–439.

Palmieri, D., Vitale, S., Lima, G., Di Pietro, A., Turrà, D. (2020). A bacterial endophyte exploits chemotropism of a fungal pathogen for plant colonization. *Nat Commun* 11, 5264.

Papagianni, M. (2007). Advances in citric acid fermentation by *Aspergillus niger*: biochemical aspects, membrane transport and modeling. *Biotechnology advances*, *25*(3), 244-263.

Patocka, J. (2016). Bioactive metabolites of entomopathogenic fungi *Beauveria bassiana*. *Mil. Med. Sci. Lett*, *85*(2), 80.

Pedrini, N. (2018). Molecular interactions between entomopathogenic fungi (Hypocreales) and their insect host: Perspectives from stressful cuticle and hemolymph battlefields and the potential of dual RNA sequencing for future studies. *Fungal Biology*, *122*(6).

Peng, Y. J., Ding, J. L., Lin, H. Y., Feng, M. G., Ying, S. H. (2021). A virulence-related lectin traffics into eisosome and contributes to functionality of cytomembrane and cell-wall in the insect-pathogenic fungus *Beauveria bassiana*. *Fungal Biology*, *125*(11), 914-922.

Peñalva, M. A., Tilburn, J., Bignell, E., & Arst Jr, H. N. (2008). Ambient pH gene regulation in fungi: making connections. *Trends in microbiology*, *16*(6), 291-300.

Pereira, C. B., de Sá, N. P., Borelli, B. M., Rosa, C. A., Barbeira, P. J. S., Cota, B. B., Johann, S. (2016). Antifungal activity of eicosanoic acids isolated from the endophytic fungus Mycosphaerella sp. against *Cryptococcus neoformans* and *C. gattii*. *Microbial pathogenesis*, *100*, 205-212.

Pimentel, I. C., Glienke-Blanco, C., Gabardo, J., Stuart, R. M., Azevedo, J. L. (2006). Identification and colonization of endophytic fungi from soybean (*Glycine max* (L.) Merril) under different environmental conditions. *Brazilian archives of biology and technology*, *49*, 705-711.

Poorter, H., Evans, J. R. (1998). Photosynthetic nitrogen-use efficiency of species that differ inherently in specific leaf area. *Oecologia*, *116*(1), 26-37.

Portwich, A., Garcia-Pichel, F. (1999). Ultraviolet and osmotic stresses induce and regulate the synthesis of mycosporines in the cyanobacterium Chlorogloeopsis PCC 6912. *Archives of microbiology*, *172*(4), 187-192.

Posada, F., Vega, F. E. (2005). Establishment of the fungal entomopathogen *Beauveria bassiana* (Ascomycota: Hypocreales) as an endophyte in cocoa seedlings (*Theobroma cacao*). *Mycologia*, *97*(6), 1195-1200.

Prabhukarthikeyan, S. R., Keerthana, U., Archana, S., Raguchander, T. (2017). Induced resistance in tomato plants to *Helicoverpa armigera* by mixed formulation of *Bacillus subtilis* and *Beauveria bassiana*. *Research Journal of Biotechnology*, *12*(10), 53-59.

Prusky, D., McEvoy, J. L., Leverentz, B., & Conway, W. S. (2001). Local modulation of host pH by Colletotrichum species as a mechanism to increase virulence. *Molecular Plant-Microbe Interactions*, *14*(9), 1105-1113.

Pywell, R. F., James, K. L., Herbert, I., Meek, W. R., Carvell, C., Bell, D., Sparks, T. H. (2005). Determinants of overwintering habitat quality for beetles and spiders on arable farmland. *Biological Conservation*, *123*(1), 79-90.

Qayyum, M. A., Wakil, W., Arif, M. J., Sahi, S. T., Dunlap, C. A. (2015). Infection of *Helicoverpa armigera* by endophytic *Beauveria bassiana* colonizing tomato plants. *Biological Control*, *90*, 200-207.

Quesada-Moraga, E., Landa, B. B., Muñoz-Ledesma, J., Jiménez-Diáz, R. M., Santiago-Alvarez, C. (2006). Endophytic colonisation of opium poppy, *P. somniferum*, by an entomopathogenic *Beauveria bassiana* strain. *Mycopathologia*, *161*(5), 323-329.

Quesada-Moraga, E., Ruiz-García, A., Santiago-Alvarez, C. (2006). Laboratory evaluation of entomopathogenic fungi *Beauveria bassiana* and *Metarhizium anisopliae* against puparia and adults of *Ceratitis capitata* (Diptera: Tephritidae). *Journal of Economic Entomology*, *99*(6), 1955-1966.

Quesada-Moraga, E., López-Díaz, C., Landa, B. B. (2014). The hidden habit of the entomopathogenic fungus *Beauveria bassiana*: first demonstration of vertical plant transmission. *PLoS One*, *9*(2), e89278.

Rawat, P., Das, S., Shankhdhar, D., Shankhdhar, S. C. (2020). Phosphate-solubilizing microorganisms: mechanism and their role in phosphate solubilization and uptake. *Journal of Soil Science and Plant Nutrition*, *21*(1), 49-68.

Rehner, S. A., Minnis, A. M., Sung, G. H., Luangsa-ard, J. J., Devotto, L., Humber, R. A. (2011). Phylogeny and systematics of the anamorphic, entomopathogenic genus Beauveria. *Mycologia*, *103*(5), 1055-1073.

Reisenzein, H., Tiefenbrunner, W. (1997). Growth inhibiting effect of different isolates of the entomopathogenic fungus *Beauveria bassiana* (Bals.) Vuill. to the plant parasitic fungi of the genera Fusarium, Armillaria and Rosselinia. *Pflanzenschutz Berichte*, *57*, 15-24.

Renwick, A., Campbell, R., Coe, S. (1991). Assessment of in vivo screening systems for potential biocontrol agents of *Gaeumannomyces graminis*. *Plant Pathology*, *40*(4), 524-532.

Resquín-Romero, G., Garrido-Jurado, I., Delso, C., Ríos-Moreno, A., Quesada-Moraga, E. (2016). Transient endophytic colonizations of plants improve the outcome of foliar applications of mycoinsecticides against chewing insects. *Journal of invertebrate pathology*, *136*, 23-31.

Říháková, Z., Plocková, M., Filip, V., Šmidrkal, J. (2001). Antifungal activity of lauric acid derivatives against *Aspergillus niger*. *European Food Research and Technology*, *213*(6), 488-490.

Safavi, S. A. (2013). In vitro and in vivo induction, and characterization of beauvericin isolated from *Beauveria bassiana* and its bioassay on *Galleria mellonella* larvae. *Journal of Agricultural Science and Technology*, *15*(1), 1-10.

Saikkonen, K., Wäli, P., Helander, M., Faeth, S. H. (2004). Evolution of endophyte–plant symbioses. *Trends in plant science*, *9*(6), 275-280.

San José, C., Monge, R. A., Perez-Diaz, R., Pla, J., Nombela, C. (1996). The mitogen-activated protein kinase homolog HOG1 gene controls glycerol accumulation in the pathogenic fungus *Candida albicans*. *Journal of Bacteriology*, *178*(19), 5850-5852.

Santos, A., Navascués, E., Bravo, E., Marquina, D. (2011). *Ustilago maydis* killer toxin as a new tool for the biocontrol of the wine spoilage yeast *Brettanomyces bruxellensis*. *International journal of food microbiology*, *145*(1), 147-154.

Sasan, R. K., Bidochka, M. J. (2012). The insect-pathogenic fungus *Metarhizium robertsii* (Clavicipitaceae) is also an endophyte that stimulates plant root development. *American journal of botany*, *99*(1), 101-107.

Schardl, C. L., Grossman, R. B., Nagabhyru, P., Faulkner, J. R., Mallik, U. P. (2007). Loline alkaloids: currencies of mutualism. *Phytochemistry*, *68*(7), 980-996.

Schroeckh, V., Scherlach, K., Nützmann, H. W., Shelest, E., Schmidt-Heck, W., Schuemann, J., Martin, K., Hertweck, C., Brakhage, A. A. (2009). Intimate bacterial–fungal interaction triggers biosynthesis of archetypal polyketides in *Aspergillus nidulans*. *Proceedings of the National Academy of Sciences*, *106*(34), 14558-14563.

Schultz, J. C., & Lechowicz, M. J. (1986). Hostplant, larval age, and feeding behavior influence midgut pH in the gypsy moth (*Lymantria dispar*). *Oecologia*, *71*, 133-137.

Seger, C., Erlebach, D., Stuppner, H., Griesser, U. J., Strasser, H. (2005). Physicochemical properties of oosporein, the major secreted metabolite of the entomopathogenic fungus *Beauveria brongniartii*. *Helvetica chimica acta*, *88*(4), 802-810.

Sensagent. Online encyclopedia, dictionary Parisien. Paris: Sensagent; 2000-2016.

Senthilraja, G., Anand, T., Durairaj, C., Kennedy, J. S., Suresh, S., Raguchander, T., & Samiyappan, R. (2010). A new microbial consortia containing entomopathogenic fungus, *Beauveria bassiana* and plant growth promoting rhizobacteria, *Pseudomonas fluorescens* for simultaneous management of leafminers and collar rot disease in groundnut. *Biocontrol Science and Technology*, *20*(5), 449-464.

Shah, P. A., Pell, J. K. (2003). Entomopathogenic fungi as biological control agents. *Applied microbiology and biotechnology*, *61*(5), 413-423.

Shanahan, P., O'Sullivan, D. J., Simpson, P., Glennon, J. D., O'Gara, F. (1992). Isolation of 2, 4-diacetylphloroglucinol from a fluorescent pseudomonad and investigation of physiological parameters influencing its production. *Applied and environmental microbiology*, *58*(1), 353-358.

Sharma, P., Meena, N., Aggarwal, M., Mondal, A. K. (2005). *Debaryomyces hansenii*, a highly osmo-tolerant and halo-tolerant yeast, maintains activated Dhog1p in the cytoplasm during its growth under severe osmotic stress. *Current genetics*, *48*(3), 162-170.

Shimazu, M., Sato, H., & Maehara, N. (2002). Density of the entomopathogenic fungus, *Beauveria bassiana* Vuillemin (Deuteromycotina: Hyphomycetes) in forest air and soil. *Applied entomology and zoology*, *37*(1), 19-26.

Shnaiderman, C., Miyara, I., Kobiler, I., Sherman, A., & Prusky, D. (2013). Differential activation of ammonium transporters during the accumulation of ammonia by *Colletotrichum gloeosporioides* and its effect on appressoria formation and pathogenicity. *Molecular Plant-Microbe Interactions*, *26*(3), 345-355.

Sinno, M., Ranesi, M., Di Lelio, I., Iacomino, G., Becchimanzi, A., Barra, E., Molisso, D., Pennacchio, F., Digilio, M.C., Vitale, S., Turrà, D., Harizanova, V., Lorito, M., Woo, S. L. (2021). Selection of endophytic *Beauveria bassiana* as a dual biocontrol agent of tomato pathogens and pests. *Pathogens*, *10*(10), 1242.

Slayman, C. L., Kaminski, P., & Stetson, D. (1990). Structure and function of fungal plasma-membrane ATPases. *Biochemistry of cell walls and membranes in fungi*. Springer, Berlin, Heidelberg, *19*, 299-316.

Smith, R. J., & Grula, E. A. (1982). Toxic components on the larval surface of the corn earworm (*Heliothis zea*) and their effects on germination and growth of *Beauveria bassiana*. *Journal of Invertebrate Pathology*, *39*(1), 15-22.

Sood, S., Sandhu, S. S., Mukherjee, T. K. (2017). Pharmacological and therapeutic potential of beauvericin: a short review. *J. Proteom. Bioinform*, *10*, 18-23.

Sosa-Gomez, D. R., Moscardi, F. (1994). Effect of till and no-till soybean cultivation on dynamics of entomopathogenic fungi in the soil. *Florida Entomologist*, *77*, 284-284.

Steenberg, T. (1995). Natural occurrence of *Beauveria bassiana* (Bals.) Vuill. with focus on infectivity to Sitona species and other insects in lucerne.

Steinhaus, E. (1956). Microbial control—the emergence of an idea. A brief history of insect pathology through the nineteenth century. *Hilgardia*, *26*(2), 107-160.

Sterling, C. (1965). Crystal structure analysis of weddellite, . *Acta Crystallographica*, *18*(5), 917-921.

Sung, J. M., Lee, J. O., Humber, R. A., Sung, G. H., & Shrestha, B. (2006). *Cordyceps bassiana* and production of stromata in vitro showing Beauveria anamorph in Korea. *Mycobiology*, *34*(1), 1-6.

Tall, S., & Meyling, N. V. (2018). Probiotics for plants? Growth promotion by the entomopathogenic fungus Beauveria bassiana depends on nutrient availability. *Microbial ecology*, *76*(4), 1002-1008.

Terry, B. J., Liu, W. C., Cianci, C. W., Proszynski, E., Fernandes, P., Bush, K., & Meyers, E. (1992). Inhibition of *Herpes implex* Virus Type 1 Dna Polymerase by the natural product oosporein. *The Journal Of Antibiotics*, *45*(2), 286-288.

Tomoda, H., Huang, X. H., Caoa, J., Nishida, H., Nagao, R., Okuda, S., Tanaka, H., Omura, S., Arai, H., Inoue, K. (1992). Inhibition of acyl-CoA: cholesterol acyltransferase activity by cyclodepsipeptide antibiotics. *The Journal of antibiotics*, *45*(10), 1626-1632.

Tong, Y., Liu, M., Zhang, Y., Liu, X., Huang, R., Song, F., Zhang, L. (2016). Beauvericin counteracted multi-drug resistant *Candida albicans* by blocking ABC transporters. *Synthetic and systems biotechnology*, *1*(3), 158-168.

Trinchant, J. C., Guerin, V., Rigaud, J. (1994). Acetylene reduction by symbiosomes and free bacteroids from broad bean (*Vicia faba* L.) nodules (role of oxalate). *Plant Physiology*, *105*(2), 555-561.

Tscharntke, T., Klein, A. M., Kruess, A., Steffan-Dewenter, I., Thies, C. (2005). Landscape perspectives on agricultural intensification and biodiversity–ecosystem service management. *Ecology letters*, *8*(8), 857-874.

Tsunoda, K., Nagashima, K., Takahashi, M. (1997). High tolerance of wood-destroying brown-rot fungi to copper-based fungicides. *Material und Organismen (Germany)*.

Tucker, D. L., Beresford, C. H., Sigler, L., Rogers, K. (2004). Disseminated *Beauveria bassiana* infection in a patient with acute lymphoblastic leukemia. *Journal of clinical microbiology*, *42*(11), 5412-5414.

Turrà, D., El Ghalid, M., Rossi, F., & Di Pietro, A. (2015). Fungal pathogen uses sex pheromone receptor for chemotropic sensing of host plant signals. *Nature*, *527*(7579), 521-524.

Vänninen, I. (1996). Distribution and occurrence of four entomopathogenic fungi in Finland: effect of geographical location, habitat type and soil type. *Mycological Research*, *100*(1), 93-101.

Varrot, A., Basheer, S. M., Imberty, A. (2013). Fungal lectins: structure, function and potential applications. *Current Opinion in Structural Biology*, *23*(5), 678-685.

Vega, F. E. (2008). Insect pathology and fungal endophytes. *Journal of invertebrate pathology*, *98*(3), 277-279.

Vega, F. E. (2018). The use of fungal entomopathogens as endophytes in biological control: a review. *Mycologia*, *110*(1), 4-30.

Veselý, D., Koubova, D. (1994). In vitro effect of entomopathogenic fungi *Beauveria bassiana* (Bals.-Criv.) Vuill. and *Beauveria brongniartii* (Sacc.) Petch on phytopathogenic fungi. *Ochrana Rostlin*, *30*(2), 113-120.

von Döhren, H. (2004). Biochemistry and general genetics of nonribosomal peptide synthetases in fungi. *Molecular Biotechnolgy of Fungal beta-Lactam Antibiotics and Related Peptide Synthetases*, 217-264.

Wainwright, M., Betts, R. P., Teale, D. M. (1986). Antibiotic activity of oosporein from *Verticillium psalliotae*. *Transactions of the British Mycological Society*, *86*(1), 168-170.

Walters, D. R., Walker, R. L., Walker, K. C. (2003). Lauric acid exhibits antifungal activity against plant pathogenic fungi. *Journal of Phytopathology*, *151*(4), 228-230.

Walters, D., Raynor, L., Mitchell, A., Walker, R., Walker, K. (2004). Antifungal activities of four fatty acids against plant pathogenic fungi. *Mycopathologia*, *157*(1), 87-90.

Wanchoo, A., Lewis, M. W., Keyhani, N. O. (2009). Lectin mapping reveals stage-specific display of surface carbohydrates in in vitro and haemolymph-derived cells of the entomopathogenic fungus *Beauveria bassiana*. *Microbiology*, *155*(9), 3121-3133.

Wang, C., Leger, R.J.S. (2007). The MAD1 adhesin of *Metarhizium anisopliae* links adhesion with blastospore production and virulence to insects, and the MAD2 adhesin enables attachment to plants. *Eukaryotic cell*, *6*(5), 808-816.

Wang, H., Peng, H., Li, W., Cheng, P., & Gong, M. (2021). The Toxins of *Beauveria bassiana* and the Strategies to Improve Their Virulence to Insects. *Frontiers in microbiology*, *12*, 705343.

Wei, Q. Y., Li, Y. Y., Xu, C., Wu, Y. X., Zhang, Y. R., Liu, H. (2020). Endophytic colonization by *Beauveria bassiana* increases the resistance of tomatoes against *Bemisia tabaci*. *Arthropod-plant interactions*, *14*(3), 289-300.

Weibull, A. C., Östman, Ö. (2003). Species composition in agroecosystems: the effect of landscape, habitat, and farm management. *Basic and Applied Ecology*, *4*(4), 349-361.

White Jr, J. F., Belanger, F., Meyer, W., Sullivan, R. F., Bischoff, J. F., & Lewis, E. A. (2002). Minireview article: Clavicipitalean Fungal Epibionts and Endophytes-Development of Symbiotic Interactions with Plants. *Symbiosis*, *33*(3), 201.

Wilby, A., Thomas, M. B. (2002). Natural enemy diversity and pest control: patterns of pest emergence with agricultural intensification. *Ecology letters*, *5*(3), 353-360.

Wilson, P. J., Thompson, K. E. N., Hodgson, J. G. (1999). Specific leaf area and leaf dry matter content as alternative predictors of plant strategies. *The New Phytologist*, *143*(1), 155-162.

Wraight, S. P., Roberts, D. W. (1987). Insect control efforts with fungi. *Developments in industrial microbiology*, *28*, 77-87.

Wu, Q., Patocka, J., Nepovimova, E., & Kuca, K. (2018). A review on the synthesis and bioactivity aspects of beauvericin, a Fusarium mycotoxin. *Frontiers in pharmacology*, *9*, 1338.

Xavier-Santos, S., Magalhães, B., Lima, E. A. (1999). Differentiation of the entomopathogenic fungus *Metarhizium flavoviride* (Hyphomycetes). *Revista de microbiologia*, *30*, 47-51.

Xiao, G., Ying, S. H., Zheng, P., Wang, Z. L., Zhang, S., Xie, X. Q., Shang, Y., Leger, R.J.S., Zhao, G.P., Wang, C., Feng, M. G. (2012). Genomic perspectives on the evolution of fungal entomopathogenicity in *Beauveria bassiana*. *Scientific reports*, *2*(1), 1-10.

Xu, L., Wang, J., Zhao, J., Li, P., Shan, T., Wang, J., Zhou, L. (2010). Beauvericin from the endophytic fungus, *Fusarium redolens*, isolated from *Dioscorea zingiberensis* and its antibacterial activity. *Natural product communications*, *5*(5), 811–814.

Ying, S. H., & Feng, M. G. (2004). Relationship between thermotolerance and hydrophobin-like proteins in aerial conidia of *Beauveria bassiana* and *Paecilomyces fumosoroseus* as fungal biocontrol agents. *Journal of Applied Microbiology*, *97*(2), 323-331.

Zeilinger, S., Gupta, V. K., Dahms, T. E., Silva, R. N., Singh, H. B., Upadhyay, R. S., Gomes, E.V., Kin-Ming Tsui, C., Nayak S, C. (2016). Friends or foes? Emerging insights from fungal interactions with plants. *FEMS microbiology reviews*, *40*(2), 182-207.

Zhan, J., Burns, A. M., Liu, M. X., Faeth, S. H., Gunatilaka, A. L. (2007). Search for cell motility and angiogenesis inhibitors with potential anticancer activity: beauvericin and other constituents of two endophytic strains of *Fusarium oxysporum*. *Journal of natural products*, *70*(2), 227-232.

Zhang, L., Yan, K., Zhang, Y., Huang, R., Bian, J., Zheng, C., Sun, H., Chen, Z., Sun, N., An, R., Min, F., Zhao, W., Zhuo, Y., You, J., Song, Y., Yu, Z., Liu, Z., Yang, K., Gao, H., Dai, H., Zhang, Z., Wang, J., Fu, C., Pei, G., Liu, J., Zhang, S., Goodfellow, M., Jiang, Y., Kuai, J., Zhou, G., Chen, X. (2007). High-throughput synergy screening identifies microbial metabolites as combination agents for the treatment of fungal infections. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(11), 4606-4611.

Zhang, S., Xia, Y. X., Kim, B., & Keyhani, N. O. (2011). Two hydrophobins are involved in fungal spore coat rodlet layer assembly and each play distinct roles in surface interactions, development and pathogenesis in the entomopathogenic fungus, *Beauveria bassiana*. *Molecular microbiology*, *80*(3), 811-826.

Zhang, Y., Lamm, R., Pillonel, C., Lam, S., Xu, J. R. (2002). Osmoregulation and fungicide resistance: the *Neurospora crassa* os-2 gene encodes a HOG1 mitogen-activated protein kinase homologue. *Applied and Environmental Microbiology*, *68*(2), 532-538.

Zhang, Y., Zhao, J., Fang, W., Zhang, J., Luo, Z., Zhang, M., Fan, Y., Pei, Y. (2009). Mitogen-activated protein kinase hog1 in the entomopathogenic fungus *Beauveria bassiana* regulates environmental stress responses and virulence to insects. *Applied and environmental microbiology*, *75*(11), 3787-3795.

Zhang, Y., Zhang, J., Jiang, X., Wang, G., Luo, Z., Fan, Y., Wu, Z., Pei, Y. (2010). Requirement of a mitogen-activated protein kinase for appressorium formation and penetration of insect cuticle by the entomopathogenic fungus *Beauveria bassiana*. *Applied and environmental microbiology*, *76*(7), 2262-2270.

Zhang, L., Fasoyin, O. E., Molnár, I., Xu, Y. (2020). Secondary metabolites from hypocrealean entomopathogenic fungi: Novel bioactive compounds. *Natural product reports*, *37*(9), 1181-1206.

Zhou, Y. H., Hou, L., Zhang, Y. J., Fan, Y. H., Luo, Z. B., Jin, D., Zhou, Q. S., Li, Y.J., Wang, Y., & Pei, Y. (2014). Expression and promoter characterization of BbPacC, a pH response transcription factor gene of the entomopathogenic fungus *Beauveria bassiana*. *Microbiology*, *160*(2), 353-361.

Zhou, Q., Yu, L., Ying, S. H., Feng, M. G. (2021). Comparative roles of three adhesin genes (adh1–3) in insect-pathogenic lifecycle of *Beauveria bassiana*. *Applied Microbiology and Biotechnology*, *105*(13), 5491-5502.