

REVIEW ARTICLE

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Fungi against insects and contrariwise as biological control models

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Abstract

Background: Biological control of insects is the current goal of modern researches to avoid using the harmful chemicals. Some fungi are capable of infecting and killing insects and, hence, are commonly known as entomopathogenic fungi (EPF). On the other hand, some insects can kill harmful fungal strains using their products such as peptides. Hence, the aim of this review article is to highlight the use of EPF as biocontrol tools against each other.

Results: EPF are generally characterized by having a wide range of hosts which made them the perfect candidate for biological control missions. They are existing in abundance in the environment and involved in plenty of environmental interactions. They have prestigious enzymatic machinery and toxins that contribute as killing tools. Moreover, after penetrating the insect, the expanded vegetative growth of hyphal bodies enabling the invasion of the fungi throughout the entire tissues of host insect cause phytic, histolytic, and pathologic changes ultimately leading to the death of the host insect. On the other hand, some insects can kill harmful fungal strains using their secreted products such as peptides.

Conclusion: In this review, the use of fungi and insects as biological control agents against each other was described. Furthermore, the history of using EPF for this purpose, their killing mechanism, host range, and the factors affecting EPF virulence were highlighted. Moreover, the role of insect's immunology and some insect's products as antifungal agents was presented focusing on peptides with biological activities against fungi. Finally, future prospects concerning the use of insects and fungi in biological control process were discussed.

Keywords: Insect pests, Entomopathogenic fungi, Biological control, Antifungal peptides

Background

Insect pests cause enormous damage to different agricultural crops. Synthetic chemical pesticides have been used for insect pest control for over 50 years. However, development of resistance against insecticides, pest rebirth, and raising concerns about the environmental impacts of agricultural inputs give urgency to screening and investigation for alternative, biologically based forms of pest control. Insects like other living organisms have their enemies in nature such as microorganisms, especially some fungal species, which can parasitize insects

and cause severe epizootics than what bacteria and viruses can do. During the late nineteenth and early twentieth centuries, many entomopathogenic fungi (EPF) have been examined as possible control agents for various insect pests. About 750 species of EPF were reported to infect insects or mites (Sujeetha and Sahayaraj 2014). The most important groups belong to the class Hyphomycetes, within genera like *Beauveria*, *Metarhizium*, *Verticillium*, *Paecilomyces*, *Nomuraea*, and *Hirsutella* (Butt 2002). Also, the sexual (teleomorph) state (e.g., *Cordyceps*, *Entomophthora*, *Zoophthora*, *Pandora*, *Entomophaga*) belongs to the order Entomophthorales. Most of the EPF are found within the deuteromycetes and entomophthorales. EPF such as *Metarhizium anisopliae* and *Beauveria bassiana* are well characterized in respect

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to pathogenicity to several insects, and they have been used as agents for the biological control of agriculture pests worldwide. The EPF can be collected from naturally infested dead cadavers and also from the soil (Sahayaraj and Karthick Raja 2011). The use of EPF as potential candidates for insect's biological control is based on the fact that they are an important and widespread component of most terrestrial ecosystems. There are about 1.5 million types of fungi, of which nearly 400 species can infect animals and less than 400 species can infect humans. Nevertheless, some fungal diseases can result from opportunistic fungi. In general, a fungi cell wall is made up of chitin, 1,3- β - and 1,6- β -glucans, and proteins, together with other polymers. The cell wall composition is characterized by being so flexible and changes at regular basis during the cell separation. It was reported that the cell wall is associated with several hydrolytic enzymes, which are responsible for maintaining the cell wall flexibility beside their importance for crosslinking of polymers as well as cell division. However, fungi are eukaryotes, which mean that there are many common features in the structure of their cells together with those of humans. There are four types of antifungal agents that are commercially available: azoles, echinocandins, polenes, and pyrimidine analogs (Tawara et al. 2000).

Continuous approaches have been developed to improve biological control as safe alternative to the use of fungicidal agents. Researchers found that many insects produce different compounds, which have antifungal activity. Numerous biologically active peptides have been produced by many insects and interestingly these peptides show wide biological activities as promising antibacterial, antifungal, and antiviral agents (Mishra and Wang 2012). Peptides showing promising antifungal activities include drosomycin produced by the common fruit fly *Drosophila melanogaster* (Da Silva et al. 2003), termicin produced by termites (Khaleel et al. 2013), heliomycin produced by the tobacco budworm *Heliothis virescens* (Fehlbaum et al. 1994), gallerimycin isolated from the greater wax moth "*Galleria mellonella*" larvae (González-Santoyo and Córdoba-Aguilar 2012), and cecropins A and B from the giant silk moth *Hyalopora cecropia* (Schuhmann et al. 2003).

In this review, the potential use of fungi and insects as biological control agents against each other was highlighted. Describing the history of using EPF, their killing mode, host range, and the factors affecting EPF virulence were studied. Moreover, the role of some insect's products as antifungal agents was presented focusing on peptides with biological activities against fungi. Finally, future prospects concerning the use of those organism's products in biological control process were discussed.

Main text

Fungi as antiinsect

Enormous application of pesticides not only excesses the cost of pest control, but also results in environmental hazards and pollution; also, arthropod pests are known to develop resistance to chemical pesticides; researchers have often resort to incorporate alternative control conductance to minimize injuries caused by them. In the previous 50 years, control of pest insects using EPF been received much attention from researchers and a large number of commercial products came into sight (Faria and Wraight 2007). Fungal pathogens play a vital role in suppressing insect population dynamics. Microbial control has been used as a part of IPM programs in many countries, including the African countries with a long history of projects, for example, the expansion of "Green Muscle" was the first procedural for the application of mycoinsecticides in Africa to control insect pests (Maina et al. 2018).

Interestingly, many of the potent EPF are insect generalists (Moonjely et al. 2016). Till the first decade of the second millennium, more than 110 commercial products based on EPF were developed in different multinational agricultural chemical companies, such as Bayer, BASF, Monsanto, DuPont, and Arysta (Ravensberg 2015). Majority of those products was based on the 2 fungal strains, *B. bassiana* and *M. anisopliae sensu lato* (Faria and Wraight 2007). The remaining products are incorporating the fungal species, *B. brongniartii*, *Isaria farinosus*, *I. fumosorosea*, *Lecanicillium muscarium*, *L. lecanii*, and *L. longisporum* (Jaronski and Mascarín 2017). The potent fungus, *B. bassiana*, has been extensively used in fighting harmful insects attacking economically important crops such as cotton, maize, and wheat (Lopez et al. 2014). Also, it is used against insects invading crops of poppy, banana, and white jute (Biswas et al. 2013).

History of using EPF

Accentuation for the history of using organisms in the field is comparatively elusive, but it seems that the first earliest demonstration of the EPF was done by Agostino Bassi (1773–1856) who noticed that the larvae of the silkworm moth, *Bombyx mori* (Linn.), suffered from a disease. According to the color of the conidial layer protrudes from insect cuticle, he named it the white muscardine (Zimmermann 2007). Further studies were then effectuated by the naturalist Balsamo-Crivelli, who described it as *Botrytis bassiana*, later changed to *Beauveria bassiana* (Rehner and Buckley 2005). This was the first microorganism recognized as animal pathogen; thereafter, many researchers had proofed that fungi could be used against pest insects (Audoin 1837; Pasteur 1874). However, Elie Metchnikoff (1845–1916), in Russia discovered the green muscardine when he investigated

the wheat cockchafers and identified it as *Entomophthora anisopliae*, which changed subsequent to *Metarhizium anisopliae* (Vega et al. 2009).

Main text

Fungi infection and mode of action

Infection process and mode of action of the EPF have been precisely defined in a considerable number of publications. Researchers unanimously documented 2 ways of spores' mobility to infect their host insect, (Akbari et al. 2014) as a result of its small size, the conidia's powdery clusters are easy to transport by air (Nolard 2004) or water (Hageskal et al. 2006) till meet its host, and (Almeida and Pokorny 2012) insect infected with fungus itself is considered to be a mechanical carrier that can easily transmit fungi to the intact individuals by direct friction (Ambethgar 2009) or by the excretion of viable conidia in their fecal droppings (Bruck and Lewis 2002). EPF percutaneously attack their hosts; hence, the infection pathway comprises the following 6 stages: adhesion of the spores; germination; penetration through integument, wounds, or trachea; hemolymph colonization, in the meantime, fungus attempts to overcome the host immune reactions; hyphal formation and proliferation; and sporulation and new conidia outgrowth (Leao et al. 2015).

Fungus penetrates cuticle through non-sclerotized areas, wounds, and trachea or via mouthparts. Penetration process accomplishes by mechanical and chemical means including several enzymes. Some fungi have become known what types of enzymes that they produce, e.g., *B. bassiana* is known to produce chitinases, proteases, and lipases (Zimmermann 2007), while others like *M. acridium*, for example, are still vague. The host insect exhibits humoral and cellular immune reactions in order to withstand fungi penetration such as production of phenoloxidase, which leads to pathogens melanization (Amparyup et al. 2013), hemocytes (Lavine and Strand 2002), encapsulation, excretion of antimicrobial peptides, phagocytosis, nodule formation (Hajdušek et al. 2013), and antifungal compounds (Zimmermann 2007). On the other side, fungi produce a set of enzymes and toxins to degrade the insect cuticle (Santi et al. 2010) in a collision, which will determine the successfulness of penetration process. After successful penetration process, hyphae exist in the haemolymph forming **asexual fungal spore**, i.e., blastoconidia. An expanded vegetative growth of hyphal bodies is enabling the invasion of the fungi throughout the entire tissues of host insect causing physis, histolytic, and pathologic changes ultimately leading to the death of the host insect after 3–7 days post infection (Zimmermann 2007; Shahid et al. 2012).

Host range

According to the number and diversity of infectious insect hosts, host range of EPF can be determined.

Scholars defined 2 types of host ranges; first is the ecological host range that refers to the number of insect species that pathogen could successfully infect under field conditions, while the second is the physiological host range, in which an EPF is able to infect under laboratory condition (Hajek and Goettel 2007). The ecological host range is more trustable as it conflicts the realistic risk for the environment. EPF have diverse host ranges as many insect orders can be infected by them; however, Lepidoptera, Diptera, Orthoptera, Coleoptera, Hymenoptera, and Hemiptera are the most common ones (Ramanujam et al. 2014). Most of them are capable of infecting a wide range of insect hosts; however, a few have an exiguous host range (Faria and Wraight 2007). Those who have a narrow physiological or ecological range of host insects are usually strenuous to mass produce (Gryganskyi et al. 2013). For example, EPF belong to the order Entomophthorales, which includes 4 families, Ancylistaceae, Completoriaceae, Entomophthoraceae, and Meristacraceae, which are capable of infecting a few hosts. While the fungus that belongs to order Hypocreales has 8 families and has a broad range of host insects (Faria and Wraight 2007). For example, the EPF *B. bassiana* (Hypocreales: Cordycipitaceae) has an exceedingly considerable host list of more than 700 insect species from different orders (Table 1) (Goettel et al. 2000; Zimmermann 2007; Meyling et al. 2009).

Factors affecting EPF virulence

EPF are involved in plenty of environmental interactions that affect it in multiple manners. The prosperity of EPF in the environment relies on conidial viability and to produce a suitable propagule (Olivera and Neves 2004). This ability contingent on many factors, the species and age of the arthropod host in this regard, is a key consideration in fungal success (Alves da Silva et al. 2015). Furthermore, the difference in host plant species may modulate the susceptibility of insect pest towards EPF (Ocampo-Hernández et al. 2019). The role of insect host species in inhibiting or stimulating the efficiency of EPF is due to the numerous defensive antimicrobial compounds within the cuticle of host insect that fungi have to overcome, in order to a successful virulence (Amparyup et al. 2013; Pedrini et al. 2013). Thus, EPF virulence is markedly in a relation with rapid germination on host insect cuticle. In order to have a successful germination after the attachment of fungi with the insect cuticle, it is essential for the fungi to confront with its favorable conditions of temperature and humidity. Environmental factors, i.e. temperature, sunlight, and humidity, are among the most important abiotic factors, which profound influence on the growth and virulence of a pathogen. It is well known that temperature and relative humidity significantly influence the survival,

Table 1 Examples of insect pest species successfully controlled by the use of *B. bassiana* and *M. anisopliae*

Fungus	Host insect	Host order	References
<i>Beauveria bassiana</i>	Fire ants, <i>Solenopsis invicta</i>	Hymenoptera	Uma Devi et al. (2008)
	Weaver ant, <i>Oecophylla smaragdina</i>		
	Armyworm, <i>Spodoptera litura</i>	Lepidoptera	Ullah et al. (2019)
	European corn borer moth, <i>Ostrinia nubilalis</i>		Cagán and Uhlík (1999)
	Diamondback moth <i>Plutella xylostella</i>		Correa-Cuadros et al. (2014)
	Maize Stem Borer, <i>Chilo partellus</i>		Sufyan et al. (2019)
	Silkworm, <i>Bombyx mori</i>		Hou et al. (2013)
	Sugar cane borer, <i>Diatraea saccharalis</i>		Maurer et al. (1997)
	Potato beetle, <i>Leptinotarsa decemlineata</i>	Coleoptera	Klinger et al. (2006)
	Squash beetle, <i>Epilachna vigintioctopunctata</i>		Hassan et al. (2019)
	Yellow fever mosquito, <i>Aedes aegypti</i>	Diptera	Devi et al. (2006)
	Banded blister beetle, <i>Mylabris pustulata</i>	Homoptera	Uma Devi et al. (2008)
	Bird cherry-oat aphid, <i>Rhopalosiphum padi</i>		Hesketh et al. (2008)
	Cowpea aphid, <i>Aphis craccivora</i>		Mweke et al. (2018)
	Mango scale, <i>Aulacaspis tubercularis</i>		Sayed and Dunlap (2019)
	Mealy bug, <i>Maconellicoccus hirsutus</i>		Uma Devi et al. (2008)
	Mustard aphid, <i>Lipaphis erysimi</i>		Sajid et al. (2017)
	Cabbage aphid, <i>Brevicoryne brassicae</i>		Akbari et al. (2014)
	English Grain Aphid, <i>Sitobion avenae</i>		Hesketh et al. (2008)
	Rose-grain aphid, <i>Metopolophium dirhodum</i>		Hesketh et al. (2008)
	Seychelles scale, <i>Icerya seychellarum</i>		Sayed and Dunlap (2019)
	Wheat aphid, <i>Schizaphis graminum</i>		Haron et al. (2020)
<i>Metarhizium anisopliae</i>	Corn earworm, <i>Helicoverpa armigera</i>	Lepidoptera	Fite et al. (2019)
	Diamondback moth, <i>Plutella xylostella</i>		Correa-Cuadros et al. (2014)
	Coconut beetle, <i>Brontispa longissima</i>	Coleoptera	Hassan et al. (2019)
	Yellow fever mosquito, <i>Aedes aegypti</i>	Diptera	Paula et al. (2011)
	Bird cherry-oat aphid, <i>Rhopalosiphum padi</i>	Homoptera	Hesketh et al. (2008)
	Cowpea aphid, <i>Aphis craccivora</i>		Mweke et al. (2018)
	Mango scale, <i>Aulacaspis tubercularis</i>		Sayed and Dunlap (2019)
	Mustard aphid, <i>Lipaphis erysimi</i>		Sajid et al. (2017)
	Pea aphid, <i>Acyrtosiphon pisum</i>		Hesketh et al. (2008)
	Seychelles scale, <i>Icerya seychellarum</i>		Sayed and Dunlap (2019)
	English grain aphid, <i>Sitobion avenae</i>		Hesketh et al. (2008)
	Rose-grain aphid, <i>Metopolophium dirhodum</i>		Hesketh et al. (2008)

germination, growth, and virulence of EPF (Bugeme et al. 2008; Mishra et al. 2015).

Soil plays a key role in forming insect populations hence the inhabiting EPF. The communities of EPF differ from one location to another, for example, populations of EPF in the arable soils seem to be different than those in barren lands (Devi et al. 2006; Garrido-Jurado et al. 2011). Quesada-Moraga et al. (2007) detected EPF populations in a wide area of Spain, the EPF were isolated from 175 soil samples out of the 244, and only 2 species were found, *B. bassiana* and *M. anisopliae*. Clay

content and pH degree were the 2 predictive factors for the prevailing of *B. bassiana*, while the content of organic matter was the influencing factor for the occurrence of *M. anisopliae*. The alkaline sandy soils found to be empty of any fungal species, whereas soil samples rich in organic matter with acidity contained a high density of EPF. Thus, various fungi species inhabit the soil for a part of their life cycle as it can provide a suitable shelter can provide protecting from unsuitable conditions (Toledo et al. 2008) in which the fungi producing conidia to build up their populations.

Insects as antifungal

Many peptides that showed antimicrobial activities have been isolated from various sources such as bacteria, fungi, and plants as well as animals. Those antimicrobial peptides (AMPs) vary greatly in their properties. AMPs have different molecular weight that range between 1.3 and 30 kDa. They also showed a variable potency and a biological activity spectrum. Most AMPs are heat stable due to the existence of fewer amino acids (Lavery et al. 2011). Many antimicrobial peptides are cationic, named CAPs. More than 1000 CAPs have been fully characterized (Hale and Hancock 2007; Pasupuleti et al. 2012). Naturally derived CAPs are formed of a positive charge between +2 and +9, due to the presence of a very few acidic residues, like aspartate or glutamate together with many of cationic amino acids including arginine or lysine and/or histidine (Yeung et al. 2011).

The presence of hydrophobic residues, that constitutes about 30–50% of the whole peptide structure (such as tryptophan or branched amino acids such as valine), plays an important role in providing an amphiphilic structure upon the interaction with membranes (Qiu et al. 2018). This amphiphilic property, together with the existence of a large amount of positive charges, results in the effective antimicrobial activities of CAPs. Any change in the ratios of net charge and hydrophobicity will greatly affect the antimicrobial activity as well as the peptide spectrum towards various microorganisms. Increasing the antimicrobial activity could be increased by adjusting the lipophilic: charge as in the case of glycopeptides. Vancomycin is a glycopeptide that is effective against many methicillin-resistant *Staphylococcus aureus* strains. Dalbavancin and oritavancin are vancomycin lipoglycopeptide derivatives that showed increased antimicrobial activity against vancomycin-resistant strains (Zelezetsky et al. 2005). The amino acids constituting the CAPs primary sequence are the main factor that affects the antimicrobial spectrum and broad structural diversity (Thomas et al. 2010).

Although CAPs may have different secondary structures, they still share the same basic properties for developing amphipathic structures and being cationic under certain physiological conditions (Maloy and Kari 1995). The secondary structures of the peptides consist of amphiphilic β -sheet structures with two or three disulfide (stabilizing) bonds, together with an α -helical short segment or/and from 2 to 4 β -strands. The formation of disulfide bridges results from a large amount of cysteine found in the primary sequence. α -Defensin and β -defensin are two examples of naturally derived peptides in mammalian host defense system (Wilson et al. 2009). The structure of these peptides is a point of interest since the majority of hydrophobic moieties are found in one face of the helix structure. However, the polar

amino acids that play an important role in solubilizing the microbial membranes are located in opposite face of the helix (Schmidt and Wong 2013). Amphipathic α -helices are not able to form disulfide bridges due to the absence of cysteine (Shai 2002). Among the peptides found in nature are magainin that is isolated from the skin secretions of certain frog species named *Xenopus laevis* (Schäfer-Korting and Rolff 2018), also mellitin, which is obtained from honeybee venom (Lavery et al. 2011; Cardoso et al. 2018) as well as the cecropins, which is a group of the dipteran defense insect peptides (Almeida and Pokorny 2012). On the other hands, cyclic peptides are uncommon class of CAPs. These cyclic structures contain β -turn affected by just a single disulfide bond such as dodecapeptide obtained from bovine neutrophils (Price et al. 2019).

Antifungal peptide groups

The studies reported some peptides with antifungal activities, as they show their ability to suppress fungal growth or even reproduction. The antifungal peptides are classified on the basis of mechanism of action (Geltar et al. 2013). The first group of fungal peptides is the amphipathic peptides. This group is widely distributed in nature and gains a lot of importance as antifungal compounds. They are membrane lytic peptides that are characterized mainly by the presence of both hydrophilic and hydrophobic residues. It has 2 surfaces, one is positively charged, while the second surface remained neutral (uncharged) (Fosso et al. 2015). Moreover, some of these peptides cause disturbance of the membrane structure without crossing the membrane itself (Leuschner and Hansel 2004). Additionally, the second group of peptides can disturb the synthesis of the cell wall and it also can disturb the glucan or chitin biosynthesis (Fernández-Carneado et al. 2004). The antifungal agents belong to these 2 structural groups of peptides are considered to be very effective and safe for immunocompromised patients (Desbois et al. 2010). The University of Nebraska Medical Center (USA) has developed an interesting antimicrobial peptides data base (APD). Furthermore, the update of this antimicrobial peptide database (UAPD) provides very helpful information about 1228 peptides, among which 327 are considered antifungal agents (Wang et al. 2009).

Examples for antifungal peptides

Various biologically active peptides have been found in many insects (Table 2). Interestingly these peptides showed antibacterial and antifungal, as well as antiviral activities (Mishra and Wang 2012). It was reported that insects produce a huge number of different antifungal proteins to be protected against threatening fungal diseases. Many insects exert high antimicrobial activity

Table 2 Naturally occurring antifungal peptides originated from various insect sources (Schuhmann et al. 2003)

Peptide	Target(s)
Brevinin	Bacteria and yeast
Cecropins	Filamentous fungi and bacteria
Insect defensins	Filamentous fungi, yeast, and some show activity against bacteria
Glycine-rich peptides	Yeast
Temporins	Filamentous fungi, yeast, and bacteria
Thanatin	Filamentous fungi and bacteria
Spinigerin	Filamentous fungi, yeast, and bacteria

towards Gram-positive bacteria; however, lower action was detected towards Gram-negative bacteria, fungi, or yeasts (Fu et al. 2009). So far, very few compounds with antifungal activities have been detected in insects. As examples, drosomycin produced from *D. melanogaster* (Da Silva et al. 2003), gallerimycin isolated from the greater wax moth "*Galleria mellonella*" larvae (González-Santoyo and Córdoba-Aguilar 2012), and termicin produced from termites (Khaleel et al. 2013), as well as heliomycin has been found to be produced from the tobacco budworm *Heliothis virescens* (Fehlbaum et al. 1994).

The studies also showed the production of two types of cecropin from the giant silk moth *Hyalopora cecropia*. These were named Cecropin A and Cecropin B that were found to be lytic linear peptides. These two peptides showed about 95% killing effect towards *Aspergillus fumigatus* and *Fusarium oxysporum* (Schuhmann et al. 2003). Plus, both peptides have shown a great antifungal activity in acidic medium (pH 5–6). However, only cecropin A has exerted antifungal activity at neutral pH. This could be attributed to variation in charge found at the two peptides C-terminus (Pushpanathan et al. 2013). Thanatin and drosomycin are examples of cysteine-rich peptides that are obtained from *Podisus maculiveris* and *Drosophila melanogaster*, respectively. Thanatin is a small non-hemolytic peptide that contains 21 residues. When thanatin is found in water, it constitutes an anti-parallel sheet structure with a disulfide bridge (Lemaitre et al. 1997).

Thanatin showed its ability to inhibit both *A. fumigatus* and *F. oxysporum* growth (Van der Weerden et al. 2013). On the other hands, drosomycin is a peptide formed of 44 amino acids and it has twisted three-stranded sheet structure stabilized by the presence of disulfide bonds. Drosomycin is very effective against *F. oxysporum* (De Lucca and Walsh 2000).

The antimicrobial peptides in response to fungal or bacterial infections are expressed in the insects' fat body (which is equivalent to liver in the higher animals), while the peptides are then secreted into the hemolymph (equivalent to blood) (Chen et al. 1988). *Drosophila* showed 2 different pathways in this respect; first, the

immune-deficiency pathway (IMD) that begins by Gram-negative bacteria, and second, the stimulation of the Toll-receptor path that was achieved by fungi, yeast, and mold as well as Gram-positive bacteria (Cooper and Eleftherianos 2017). Usually, the antimicrobial peptides produced from insects after bacterial threatening and that explains the occurrence of fewer antifungal molecules. In response to both in vitro and in vivo antifungal activity, insects can show high production of peptides (Taylor et al. 2008).

Insect's immunology

The vital mechanisms controlling the insect immune response as well as their consequence on the human immunology have attracted the attention of many scientists recently. For any insect to resist various pathogens infection, innate immunity is required and important. There are many barriers that protect the insects. The insect exoskeleton prevents the trachea membrane and the stomodeum. Moreover, insects produce some antimicrobial peptides, which are secreted into hemolymph (Faye and Hultmark 1993). The *drosophila* is an example that comprises a wide range of potent antifungal and antibacterial peptides including attacin, cecropin, diptericin, drosocin, and drosomycin as well as metchnikowin, where they are originated from the fat body. Additionally, there is a cellular response, characterized by the presence of hemocytes that resulted in the phagocytosis of foreign objects as well as microorganisms and other parasites (Brivio et al. 2010). Finally, this was followed by an activation of a proteolytic cascade in the hemolymph, which in turn resulted in the activation of phenol oxidase, the enzyme responsible for the melanin formation, which is finally deposited on the invading parasites.

Conclusion

The history of using EPF, their killing mechanism, host range, and the factors affecting their virulence were studied to accomplish their use as biocontrol agents. Moreover, highlights on the role of insect's immunology and some insect's products as antifungal agents were

presented focusing on peptides and their biological activities against fungi. Survey work should be undertaken in different geographical regions to isolate and identify virulent fungal pathogens. Antifungal peptides play an important role in protection against fungal infection via an innate defense mechanism. Utilizing different antimicrobial peptide creates a strategy for the production of low-cost antimicrobial agent. Additionally, more detailed studies are required to explain the configuration of these peptides that helps in supplying more information for computer simulation methods to figure out the antifungal mechanism at the atomic level.

Abbreviations

EPF: Entomopathogenic fungi; IPM: Integrated pest management; AMPs: Antimicrobial peptides; CAPs: Cationic antimicrobial peptides; APD: Antimicrobial peptides data base; UAPD: Updated antimicrobial peptide database (UAPD); IMD: Immune-deficiency pathway

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WE and GD have substantially contributed to the conception and design of the article. ME and GD have contributed in writing insect as antifungal section. WE and KM have contributed in writing fungi as antiinsect section. All authors have read, revised, and approved the manuscript.

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