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METARHIZIUM ANISOPLIAE AS A SUSTAINABLE BIOCONTROL AGENT FOR EFFECTIVE INSECT PEST MANAGEMENT

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Abstract

Metarhizium anisopliae is a vital fungus employed in microbial pest control to maintain ecological balance. As a non-toxic, eco-friendly alternative to chemical pesticides, it plays a significant role in integrated pest management. This fungus is highly effective against a wide range of insect pests, including beetles, weevils and other agricultural pests, making it an essential tool for crop protection. The mode of action involves fungal spores attaching to the insect cuticle, germinating and penetrating to cause systemic infections. This leads to the eventual death of the pest while minimizing harm to non-target organisms and beneficial species. It has been applied successfully in various crops, such as sugarcane, cotton and vegetables, demonstrating notable efficacy against pests like root weevils, aphids and caterpillars. Additionally, M. anisopliae has the ability to persist in the soil and colonize plant roots, further enhancing its biocontrol potential. This persistence contributes to long-term pest suppression and reduces the need for repeated applications. Its safety profile for beneficial organisms and the environment highlights its role in reducing pesticide resistance, environmental contamination and adverse effects on non-target species. It aims to enhance its commercialization as a biopesticide by identifying specific genes that differentiate it from closely related species. Despite challenges such as potential resistance and environmental variability, M. anisopliae remains a promising alternative to chemical insecticides, supporting the global shift towards eco-friendly pest management solutions.

Keywords: *Metarhizium anisopliae*, Agricultural pests, Insect pest control, Sustainable agriculture and Biopesticides.

INTRODUCTION

In many nations and areas around the world, agricultural pests such as locusts, termites, ticks and grasshoppers have resulted in significant financial losses [1]. Moreover, mosquitoes and other human disease vectors cause roughly a million deaths every year [2]. The most common and extensive method of controlling agricultural pests and disease vectors remains the use of chemical insecticides [3]. However, increasing concerns about environmental contamination, bioaccumulation and insecticide resistance have highlighted the urgent need for sustainable alternatives. Recent advances in waste to value approaches, such as the production of black soldier fly larvae as an alternative to conventional poultry feed and biowaste conversion [4] and the optimisation of vermicompost chemistry through probiotic applications [5], illustrate how sustainable biological strategies can replace chemical intensive practices in agriculture. In line with these developments, biopesticides offer great potential due to their low resistance development, reduced non-target toxicity and environmentally friendly attributes [6,7]. Known as “green pesticides,” entomopathogenic fungi are biological agents that do not harm the environment [8]. Their high host killing efficiency and biodiversity provide a variety of biocontrol options that can help reduce chemical usage and promote sustainable development [9]. Among these, the common insect pathogen *Metarhizium anisopliae* has emerged as a particularly effective candidate [10].

M. anisopliae serves not only as a vector of human disease but also infects some important agricultural pests. Moreover, given the absence of any teleomorphs and with conidia serving as the infectious form, this fungus

is classified as asexual. Spore germination, adhesion, appressorium formation, *in vivo* development, host penetration and host death are all steps in the *M. anisopliae* infection process [11]. *M. anisopliae* kills more slowly than chemical pesticides, taking about five days. This kind of approach to pest control uses agrotoxins with natural agents like pathogens, parasites and predators [12]. A component of biological insect control, microbial control involves the use of pathogens to preserve pest balances in agricultural lands. Fields that have microbial control frequently increases in the number of other natural disasters. As endophytes, saprobes and insect pathogens, these fungi have several functions [13]. Furthermore, more recent research on entomopathogenic fungi as endophytes has been conducted. In order to integrate the endophytism with insect pathogenesis, this study emphasised entomopathogenic fungal–plant interactions [14]. According to the host range of insects, *Metarhizium* species are divided into two groups: specialists with limited host ranges and generalists with wide host ranges [15]. *Metarhizium* can enhance plant growth and fend off plant diseases as symbionts. *Metarhizium* is a bioremediator that can improve plant cadmium capacity and reduce heavy metal pollution of mercury in soil and water. The future potential of *Metarhizium* as a mycoinsecticide and plant bioinoculants and as a biocontrol agent [16].

Biological Safety of *Metarhizium anisopliae*

The use of chemical insecticides to control pests and diseases in agroecosystems is detrimental to the environment and human health. It is crucial to assess the effects of biopesticides in the field application [17]. The entomopathogenic fungus *M. anisopliae* has been found to be biologically safe and is not harmful to vertebrates or the environment [18]. Numerous governments and international organisations have pesticide registration that covers toxicity, bio-efficacy, residue analysis, product analysis, impact on non-target organisms and the environment [19] (Figure 1).

Mechanism of Infection of *Metarhizium anisopliae*

Upon penetrating the cuticle of an insect or mite, fungal hyphae trigger the production of phenoloxidases and haemocyte activation, resulting in the production of bioactive compounds that trigger phagocytosis, encapsulation, or nodulation [20]. Fungal PAMPs, including mannans and fungal β-glucans, interact with peptidoglycans, β-glucan-binding proteins and Pathogen Recognition Receptors (PRRs) to trigger defensive responses [21]. Yeast like blastospores take the place of hyphae once they enter the host. As blastospores proliferate in the host's hemocoel, the fungus keeps consuming nutrients. The primary sugar in insect hemolymph is hydrolysed by the acid trehalase produced by *Metarhizium* [22].

In addition to primary metabolites, certain strains of *Metarhizium* also produce secondary metabolites called Destruxins, which aid in pathogenesis and cause Paralysis by altering the cellular structure of the middle intestine and Malpighian tubules and by blocking H^+ channels in the muscles [23]. Although Destruxin A may function as an immune modulator, reducing the immune responses of insects, it is insufficient to eradicate them. Destruxins may be able to lessen the host insect's immune response to their presence because they are immunomodulators. As the cellular mass increases, this process continues until the insect is completely covered in mycelia [24].

Pathogenesis of *Metarhizium anisopliae* on Insects

M. anisopliae invades its host primarily through direct penetration of the cuticle [25]. The infection cycle generally involves several stages: attachment of conidia to the host surface, germination and hyphal growth, appressorium development, entry and proliferation within the hemolymph, followed by external emergence and sporulation.

Conidia adhesion

Conidia adhere after depositing on the host's cuticle during the initial stage of infection [26]. Conidia outer layer contains hydrophobic proteins that help the hydrophobic epidermis and conidia adhere to one another [27]. Exogenous lectins are also present in the cell walls of *M. anisopliae* conidia. These lectins form a specific bond with the host's epidermal glycoprotein and aid in host identification. The term "adhesion" describes the hydrophobic interactions between spore surface proteins and the lipid layers that cover arthropod cutin [28]. The lipid components of the cuticular layer function as the primary defensive barrier of arthropods against microbial invasion, underscoring the critical role of lipolytic enzymes during the initial stages of infection. In M. anisopliae, pre-penetration growth on the host cuticle is closely associated with the breakdown of these lipid constituents. Identification of vulnerable hosts and the synthesis of the initial nutrient molecules supporting conidia germination depend heavily on the breakdown of the host lipid layer [29].

Conidia Germination and Development

Conidia begin to germinate and produce varying lengths of germ tubes when they adhere to the host cuticle [30]. Trehalose, which is prevalent in host hemolymph, is used by trehalase, which is visible in the early stages of germination. Previous studies states that Trehalase activity may supply glucose for the synthesis of energy [31]. After germination, spores enlarge and form germ tubes that develop into appressorium [32].

The hyphal tip secretes mucilaginous substances that promote germ tube adhesion to the host epidermis, with its growth directed preferentially toward the cuticular surface. A variety of general nutrients, including proteins, sugars, lipids and amino acids can help *M. anisopliae* conidia germinate. Mad1 and Mad2, two genes that encode adhesin, are linked to the pathophysiology of insects and plant root colonisation, respectively. While Mad2 protein

is only expressed after fungal hyphae have emerged and conidiated on the insect cadaver, Mad1 protein is expressed during the early stages of insect infection [33].

Appressorium Formation

Before penetrating the host epidermis, the germ tube differentiates into an appressorium [34], a specialized infection structure enriched with organelles such as mitochondria, Golgi bodies, endoplasmic reticulum and ribosomes. The appressorium is encased in a thick mucilaginous layer and displays diverse morphologies ranging from elliptical to irregular, often resembling a mulberry due to mucus accumulation. Appressorium development is regulated by several genes, including ODC1 (ornithine decarboxylase), which is upregulated during conidial germination and germ tube differentiation and MPL1 (Metarhizium perilipin like protein), predominantly expressed during lipid accumulation [35,36]. Furthermore, Li et al. reported that inhibition of protein kinase A delays both appressorium formation and the expression of cuticle-degrading enzymes, underscoring the role of signaling pathways in fungal pathogenicity [37].

Cuticle Penetration

Physical pressure and cuticle deterioration are two important elements in the penetration process. Insect cuticles contain essential components such as protein, chitin and wax. The primary factor influencing *M. anisopliae* capacity to infect is the activity of protease, which is crucial to the breakdown of the host epidermis. In order to break down the protein-rich plasma membrane of arthropods, *M. anisopliae* produces a variety of catalytic enzymes, including carboxypeptidase, chymotrypsin, acid protease, trypsin-like enzyme (PR2) and subtilisin-like enzyme (PR1) [38].

Because *M. anisopliae* is specific to each host, it can infect a wide variety of hosts. Only certain hosts, like cockroaches and beetles, produce trypsins [39]. Chitin degradation products, or the induction inhibition mechanism, control chitinase activity. The chitinase activity that follows can be increased by pre-treating the insect epidermis with PR1, which is linked to the pathophysiology of *M. anisopliae*. Furthermore, epidermal degradation enzymes can use host proteins as nutrients in addition to destroying host antifungal proteins that prevent pathogen invasion, release amino acids and produce amines to control pH. Consequently, the infected epidermis alkalinity serves as a physiological indicator of toxicity factors. Moreover, exogenous carbon and nitrogen sources inhibited PR1 production [40]. The PR3 is a low isoelectric point, acidic protease. Its makeup and mode of action remain unknown at this time. Additionally, chitinase is the primary factor that determines pathogenicity. The rate and severity of infection may be influenced by carbon competition between hosts and pathogens [41]. Together, protease, lipase and chitinase break down the cuticle, allowing nutrients to enter the host's hemocoel and be used effectively for an infection. Furthermore, when *M. anisopliae* is present, the pH of the surrounding environment shifts, facilitating the synthesis of extracellular enzymes and their functions. Toxic gene expression is also regulated by environmental pH [42].

Colonization of Hemolymph

After the fungus penetrates the lower epidermis and the cuticular layer, it begins to infiltrate and multiply in the hemolymph that remain until the host dies. *M. anisopliae* produces a family of cyclic peptide toxins known as destruxins (DTXs) both *in vivo* and in the culture of infected insects [43]. Catalase and peroxidases are also present on the surface of conidia to shield them from UV light and reactive oxygen species produced at high temperatures. Additionally, the Mad1 protein triggers the expression of genes related to the cell cycle, which allows hyphae to quickly multiply and differentiate in the host's hemolymph. During the cell cycle, these proteins control cell division by targeting the cytoskeleton [44].

Extrusion and Sporulation

As host colonisation progresses, the fungus takes up its nutrients and creates hyphae, which then emerge and produce conidia on the dead host's surface [45]. *M. anisopliae* develops a denser network of green spores on the cadavers of infected hosts.

Toxins in *Metarhizium anisopliae*

Numerous fungal secondary metabolites, such as DTXs, are produced by *M. anisopliae*. These metabolites cause membrane depolarisation by opening Ca_2^+ channels, which paralyses and kills the host insects. The most extensively researched toxins of the entomopathogenic fungi are called DTXs and they belong to a class of insecticidal, phytotoxic and antiviral cyclic peptide insect-borne fungal toxins [46]. These compounds are cyclic hexadepsipeptides made up of five amino acids and an α-hydroxy acid. Chemically, DTXs can be categorised into five basic groups, denoted by the letters A through E. Significant insecticidal activity is demonstrated by Destruxins A, E and B [47]. Additionally, these toxins play a major part in impairing the host's immune system that hinders feeding, excretion and mobility. In order to prevent the growth of the infected microbes, infected insects to increase their body temperature [48]. In order to weaken behaviour defence mechanisms, DTXs can decrease host mobility [49]. Apart from its potential for therapeutic use, Swainsonine is frequently employed as a biochemical tool in research on the characteristics and biological functions of alpha mannosidases and N linked oligosaccharides.

***Metarhizium anisopliae* as a Biological Control Agent**

Human disease and death are caused by a variety of diseases spread by mosquitoes, including dengue virus and Plasmodium. A genetic modification strategy can be used to enhance the virulence of *M. anisopliae* against mosquitoes or to block pathogen development within the host. Ticks are also major vectors of animal diseases and are second only to mosquitoes in transmitting infections to humans. They are globally distributed and capable of spreading a wide range of pathogens, including viruses, bacteria, protozoa and fungi. According to Alkhaibari study indicates that *M. anisopliae* may serve as an effective biocontrol agent for vector borne diseases. Moreover, this fungus shows considerable promise for managing both agricultural pests and human disease vectors [50] (Figure 2).

Formulations of *Metarhizium anisopliae*

Formulations can significantly increase the effectiveness of biological pesticides in addition to strain selection and genetic modification. An optimal formulation minimises the nontarget organisms coming into contact with fungal spores and aids in the application of biopesticides. Formulations of dry, synthetic and aqueous *M. anisopliae* spores for the management of Anopheles larvae. Synthetic oil is one of these formulations that enhances persistence and is easily miscible and appropriate for water surfaces [51]. Both dry and water based formulations of *M. anisopliae* spores showed a rapid decline in pathogenic activity. Compared to applying, when conidia were delivered using oil carriers such as sunflower, peanut, soybean, canola, mineral, Ondina, or cornflour oil, the inoculum was more effectively transported to insect body regions that support better germination.

CONCLUSION

M. anisopliae is an environmentally friendly biological control agent that uses natural processes to efficiently target insect pests. It minimises non-target effects on beneficial organisms, targets particular pest populations and is safe for the environment. It works well with traps, crop rotation and natural predators, among other integrated pest management techniques. Depending on the pests being targeted, *M. anisopliae* can be applied as soil treatments or foliar sprays. To target pests like termites and white grubs, the fungal formulation is often mixed with water and sprayed on crops or mixed into soil. Its effectiveness has been proven in a number of agricultural domains, improving crop productivity and health. As a biocontrol agent in agriculture, *M. anisopliae* provides a practical and sustainable way to manage insect pests.

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Figures

Figure 1: Insect affected by the Entomopathogenic Fungi *Metarhizium anisopliae*

Figure 2: *Metarhizium anisopliae* for the control of Vector-borne disease