CarakaTani
Journal of Sustainable Agriculture
ISSN 2613-9456 (Print) 2599-2570 (Online)

Caraka Tani: Journal of Sustainable Agriculture, 39(2), 281-296, 2024
URL: https://jurnal.uns.ac.id/carakatani/article/view/83012
DOI: http://dx.doi.org/10.20961/carakatani.v39i2.83012

Hormesis in Pathogenic and Biocontrol Fungi: From Inhibition to Stimulation

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Abstract

Hormesis, a biphasic response where low doses of stressors stimulate growth and high doses inhibit it, has significant implications for agricultural chemical use. This review explores the impact of low-dose fungicides or pesticides on pathogenic and biocontrol fungi. This study highlights how sublethal dose exposure can enhance growth and virulence of fungal pathogens, while also potentially increasing their stress tolerance at higher doses. This phenomenon complicates fungicide resistance management strategies. The review focuses on specific fungicides such as dimethachlone, prochloraz, carbendazim, and others, and their hormetic effects on fungal pathogens. Furthermore, the effects of low-dose pesticides and fungicides on beneficial fungi like entomopathogenic and arbuscular mycorrhizal fungi (AMF) are discussed. Here, low-dose exposure can stimulate the germination of entomopathogenic fungal conidia and enhance AMF root colonization and phosphorus uptake. However, hormesis can have trade-offs, potentially leading to unforeseen consequences for the organism. A thorough understanding of hormesis and dose-dependent fungicide effects is crucial for optimizing disease management and agricultural practices. This knowledge can inform strategies to minimize pathogen resistance and promote sustainable approaches. Implementing integrated disease management that combines fungicides with different modes of action alongside other control methods can be effective. Careful consideration of fungicide doses and potential hormesis effects is paramount for ensuring sustainable plant disease control and food security.

Keywords: biphasic; dose-dependent; entomopathogens; fungicide; mycorrhiza

Cite this as: Dharma, K. S., Suryanti, & Widiastuti, A. (2024). Hormesis in Pathogenic and Biocontrol Fungi: From Inhibition to Stimulation. *Caraka Tani: Journal of Sustainable Agriculture*, *39*(2), 281-296. doi: http://dx.doi.org/10.20961/carakatani.v39i2.83012

INTRODUCTION

Fungicides and other agrochemicals play a vital role in modern agriculture, serving as essential tools in conventional farming and integrated disease management to combat plant-damaging fungi (Agathokleous and Calabrese, 2021). These chemicals are essential for maximizing food production efficiency and significantly impact agricultural productivity. However, the application of fungicides at sublethal concentrations can result in an unexpected phenomenon called hormesis, where plant pathogens are stimulated instead of being controlled (Flores and Garzón, 2013).

Hormesis, a dose-dependent response observed across various biological models, has important implications for fungicide application and agricultural practices (Agathokleous and Calabrese, 2021). It refers to the biphasic dose-response relationship exhibited by organisms, where low doses of certain substances elicit stimulatory effects, while high doses have adverse effects (Agathokleous et al., 2022). Fungicide-

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* *Received for publication January 7, 2024*
Accepted after corrections May 8, 2024

induced hormesis in plant pathogens must be carefully considered in scientific evaluations and agricultural strategies. Treating with lower-than-recommended doses may increase pathogenicity and worsen the situation for farmers. This phenomenon is analogous to the enhancement of tumor growth by low doses of specific cancer drugs (Agathokleous and Calabrese, 2021).

Estimating the frequency of hormesis is challenging due to the complexity of dose-response relationships (Figure 1), the need for multiple experiments, and the wide dosing range required. Nevertheless, hormesis is increasingly recognized as a common phenomenon in toxicology literature, describing the adaptive responses of biological systems to moderate challenges that enhance functionality and tolerance to more severe stressors (Calabrese and Mattson, 2017).

Accidental exposure of pathogens to sublethal concentrations of fungicides can occur in ornamental facilities that utilize recirculating watering systems, where fungicides can leach out of pots and enter holding tanks (Garzon et al., 2011). Despite the recommendation against fungicide application through such systems, farmers sometimes apply reduced doses to minimize expenses, inadvertently exposing resistant isolates to sublethal levels (Garzon et al., 2011).

Hormesis has been observed not only with fungicides but also with a range of stress-inducing substances, including insecticides, herbicides, heavy metals, antibiotics, drugs, disinfectants, nanoparticles, and microplastics. It has been documented in various microorganisms, such as fungal pathogens, plant root symbionts like mycorrhizae, and other plant soil microorganisms (Agathokleous et al., 2022).

Hormesis research is experiencing a period of rapid growth, according to a new bibliometric analysis by Agathokleous and Calabrese (2024). The study found a significant increase in publications, particularly within the last 2 to 4 years. Interestingly, the focus of hormesis research has broadened in recent years. While traditionally concentrated on animal and medical research areas like aging and antioxidants, the field now embraces disciplines like plant science, agriculture, entomology, and environmental health.

The landscape of hormesis research is also shifting geographically. The United States held a dominant position in citations until the early 2010s. However, the citation network has become more diverse, with new countries emerging as

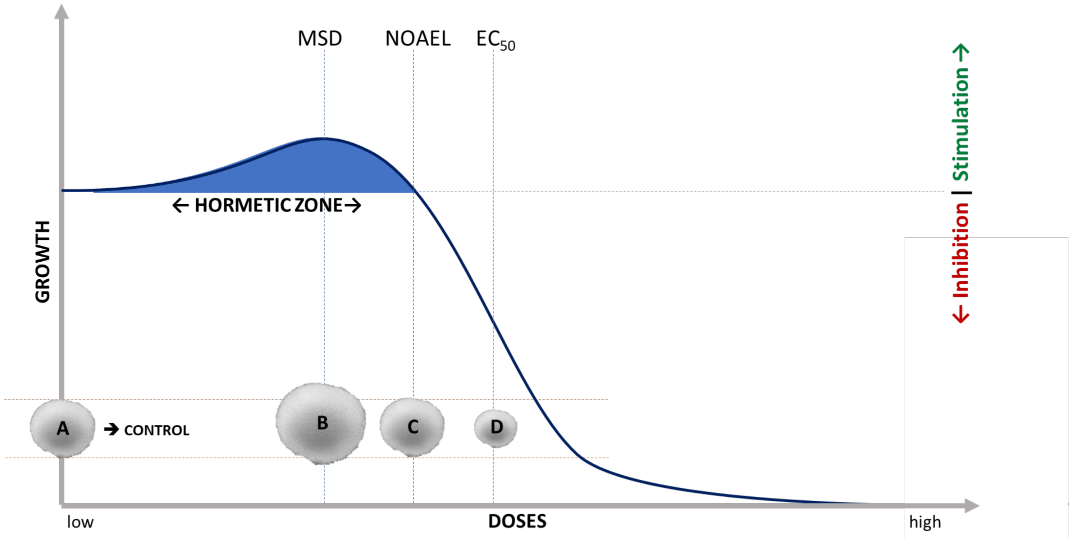

Figure 1. A modeled hormetic (biphasic) dose-response curve on a fungal pathogen treated with a low-dose fungicide

Note: MSD = the maximum stimulation dose, NOAEL (No-observable adverse effect level) = the highest dose with no significant difference from the control group (Agathokleous, 2022), EC_{50} = the concentration of the fungicide inhibiting the growth of a fungal pathogen by 50% (modified from Calabrese and Mattson (2011); Garzón and Flores (2013)). A, B, C, and D illustrate the growth of pathogenic fungal mycelium. A = the control treatment, with growth not significantly different from C (NOAEL). B = the fungal mycelium experiencing maximum growth stimulation at the MSD, while D = the fungal mycelium inhibited by 50% at the EC_{50}

influential contributors. China, in particular, has established itself as a leader in hormesis research over the past 5 years (Agathokleous and Calabrese, 2024).

Research on fungicide-induced hormesis can significantly benefit sustainable practices. By pinpointing the hormesis threshold for specific fungicide-pathogen combinations, we can develop targeted application strategies. This would involve using precise doses to maximize fungicidal effect while minimizing the risk of stimulating pathogens. Furthermore, studying hormesis can encourage the development of alternative disease management methods like biocontrol agents (Ons et al., 2020) and resistant crops (Panth et al., 2020), ultimately reducing reliance on fungicides altogether.

This review investigates the phenomenon of hormesis in pathogenic and biocontrol fungi exposed to low doses of fungicides or pesticides. It explores the transition from inhibition of fungal growth at higher doses to stimulation at lower doses and the implications for agricultural management practices. Understanding hormesis can contribute to the design of Integrated Pest Management (IPM) programs. IPM programs combine various disease control strategies, reducing reliance on any single method, including fungicides, and promoting long-term sustainability (Jacquet et al., 2022; Scortichini, 2022).

MATERIALS AND METHOD

This review paper examines current research on hormesis in various fungi, including pathogenic fungi, entomopathogenic fungi, and arbuscular mycorrhizal fungi (AMF). The authors conducted a comprehensive review of relevant articles from journals, conference proceedings, theses, and online sources. The focus was on investigating the impact of low doses of fungicide or pesticide-active ingredients on fungus development. After collecting the data, the authors synthesized the information and provided a summary. The discussion includes key insights, additional knowledge, and references, offering valuable recommendations for the judicious use of fungicides to combat pathogens without adversely affecting beneficial fungi.

RESULTS AND DISCUSSION

Hormesis in fungal pathogens

Recent studies have brought to light the phenomenon of hormesis in fungal pathogens and its impact on their growth and virulence in the presence of various fungicides. Hormesis refers to a response where low doses of fungicides stimulate the growth and virulence of these pathogens. Several species, including *Botrytis cinerea*, *Fusarium virguliforme*, *Globisporangium ultimum*, *G. irregulare*, *Lasiodiplodia theobromae*, *Magnaporthe oryzae*, *Sclerotinia sclerotiorum*, *S. homoeocarpa*, and *Pythium aphanidermatum*, have been observed to exhibit hormetic responses. Researchers have investigated the effects of specific fungicides such as boscalid, carbendazim, cyazofamid, dimethachlone, fluopyram, iprodione, prochloraz, propamocarb, mefenoxam, and thiophanate-methyl on these fungal pathogens (Table 1).

In a study by Zhang et al. (2019) on dimethachlone-resistant *S. sclerotiorum*, the combined effects of dimethachlone and prochloraz were examined. The researchers discovered that within the concentration range of 1 to 100 $\mu g\ ml^{-1}$, dimethachlone stimulated mycelial growth. Similarly, prochloraz exhibited the highest stimulation at concentrations of 0.0003 and 0.002 $\mu g\ ml^{-1}$. Interestingly, the mycelia treated with these fungicides displayed increased growth and virulence on both culture media and rapeseed leaves. Moreover, the combination of dimethachlone and prochloraz enhanced mycelial tolerance to hydrogen peroxide (H_2O_2).

In another investigation by Song et al. (2022), the effects of low doses of the fungicide carbendazim on *M. oryzae*, the causal agent of rice blast, were explored. It was found that these low doses stimulated the growth and aggressiveness of the fungus on detached rice leaves. Interestingly, a higher dose of carbendazim inhibited growth but increased the fungus's tolerance to H_2O_2. This increased tolerance to H_2O_2 with the higher dose of carbendazim contributed to the fungus's enhanced aggressiveness on detached leaves.

Examining the interaction between fungicides, Cong et al. (2018) studied the hormetic effects of mixtures of carbendazim and iprodione on carbendazim-resistant *B. cinerea* isolates. They observed that spraying carbendazim or iprodione alone had hormetic effects on virulence. However, when combined, the mixture exhibited higher stimulation of virulence than either fungicide alone. This study suggested that the interaction between carbendazim and iprodione had dose-additive effects on virulence. Additionally, the mixtures showed increased tolerance to H_2O_2, which partially explained the stimulatory effects on *B. cinerea* virulence.

Similarly, Flores and Garzon (2013) observed a biphasic response in *P. aphanidermatum* treated with cyazofamid and propamocarb. These fungicides stimulated fungal growth by up to 6% at specific low concentrations. Furthermore, Wang et al. (2017) reported hormetic effects of fluopyram, a fungicide used against *F. virguliforme*. Sublethal doses of fluopyram worsened disease symptoms in a significant portion (22%) of the fungal isolates. This highlights the importance of applying fluopyram at concentrations exceeding 1 µg ml^{-1} for effective control. Dilution in soil or plant tissue might also contribute to unintended hormetic effects with this fungicide.

Pradhan et al. (2019) investigated the response of *S. homoeocarpa* isolates to the fungicide thiophanate-methyl. They observed that highly sensitive and thiophanate-methyl-tolerant isolates showed no stimulation at low doses. However, preconditioned thiophanate-methyl-tolerant isolates exhibited significant growth stimulation. This study was the first to report fungicide hormesis in multiple isolates of *S. homoeocarpa* with varying sensitivity levels, suggesting that fungicide tolerance may trigger stress-response mechanisms resulting in hormesis.

The effects of mefenoxam concentrations on two species of *Globisporangium* (syn. *Pythium*) were examined by Pradhan et al. (2017). Statistically significant stimulatory effects were observed on the growth of both species. *G. ultimum* exhibited a maximum stimulation dose (MSD) of 10.708 µg ml^{-1} in terms of mycelial growth area, while *G. irregulare* showed an MSD of 8.65 µg ml^{-1}.

Da Silva et al. (2022) studied the sensitivity of thiophanate-methyl-resistant *L. theobromae* isolates, a pathogen causing Peduncular rot in papaya crops. They discovered that exposure to subinhibitory doses of thiophanate-methyl stimulated mycelial growth in the resistant isolates and increased their virulence. Furthermore, all isolates showed stimulation when grown on PDA containing 1 µg ml^{-1} of thiophanate-methyl.

Lu et al. (2018) demonstrated that preconditioning phytopathogenic fungi with the fungicide flusilazole stimulated their virulence. Spraying flusilazole at a low dose increased the growth and disease-causing ability of *S. sclerotiorum*. Preconditioning with flusilazole also enhanced growth when exposed to fungicides with the same mode of action, highlighting the need for higher fungicide doses for effective control and caution against consecutive use of fungicides with the same mode of action to avoid preconditioning hormesis.

In the study by Santika et al. (2023), *Phytopythium vexans* displayed resistance to dimethomorph but sensitivity to mancozeb, a mixture of mancozeb and mefenoxam, and a mixture of oxathiapiprolin and famoxadone. Surprisingly, sublethal treatment with mancozeb not only caused resistance to mancozeb itself but also cross-resistance to dimethomorph and the mixture of oxathiapiprolin and famoxadone. Additionally, the resistant isolate of *P. vexans* was capable of producing sporangia and chlamydospores. This phenomenon can be likened to hormesis, where low doses of a stressor or toxic agent stimulate a beneficial response in an organism.

While fungicide resistance is a growing concern, research is exploring alternative control methods. Habibullah et al. (2020) investigated the use of non-fungicide chemicals for disease resistance. Their study demonstrated that applying benzoic acid to maize seeds significantly reduced downy mildew incidence and severity compared to untreated controls. This suggests that non-toxic compounds can activate plant defense mechanisms, offering an eco-friendly approach to disease management.

These studies collectively demonstrate that fungicides can have dose-dependent effects on fungal pathogens. In some cases, low doses of fungicides stimulate mycelial growth, increase virulence, and enhance tolerance to H_2O_2. H_2O_2 plays a multifaceted role in plant defense against pathogens, including direct microbicidal activity, cell wall reinforcement, phytoalexin synthesis, hypersensitive response, systemic acquired resistance, and defense gene induction (Kuźniak and Urbanek, 2000).

The phenomenon of hormesis in fungal pathogens poses challenges in developing effective fungicide strategies. Low-dose exposure can trigger unexpected outcomes, including increased resistance to multiple fungicides. This necessitates careful consideration of fungicide concentrations and combinations to avoid these undesirable consequences. Furthermore, research is exploring alternative approaches like botanical extracts with antifungal properties. Widiastuti et al. (2020) investigated galangal extract as a potential fungicide against grape leaf rust. Their findings showed promise, with the extract

Table 1. Hormetic responses of fungal pathogens to various fungicides

No.	Fungicide active ingredients	Mode of actions	Tested pathogenic fungus	Methods	EC_{50}	NOAEL	Stimulatory doses	References
1.	Boscalid	Systemic, broad-spectrum	*S. sclerotiorum*	*In vitro*	N/A	N/A	0.0005 to 0.002 µg ml^{-1} (mycelial growth stimulation); 0.0001 to 0.1 µg ml^{-1} (virulence stimulation on detached leaves)	Hu et al. (2020)
2.	Carbendazim	Systemic, broad-spectrum	*B. cinerea*	*In vitro*, in planta	0.05 and 0.07 µg ml^{-1} (mycelial growth inhibition for 2 different isolates)	N/A	0.001 and 0.005 µg ml^{-1} (conidia germination percentages increased significantly *in vitro*); 0.001 to 0.03 µg ml^{-1} (virulence stimulation in planta)	Cong et al. (2019)
			M. oryzae	*In vitro*	0.31, 0.38 and 0.37 µg ml^{-1} (mycelial growth inhibition for 3 different isolates)	N/A	0.003 to 0.1 µg ml^{-1} (mycelial growth stimulation); 0.03 µg ml^{-1} (virulence stimulation on detached leaves)	Song et al. (2022)
3.	Carbendazim + iprodione mixtures	Systemic, broad-spectrum	*B. cinerea*	*In vitro*	> 1,000 µg ml^{-1} (mycelial growth inhibition)	N/A	3 to 800 µg ml^{-1} (carbendazim alone, virulence stimulation on detached leaves); 0.0001 to 0.0625 µg ml^{-1} (iprodione alone); 10 and	Cong et al. (2018)

Table 1. Hormetic responses of fungal pathogens to various fungicides (*Continue*)

No.	Fungicide active ingredients	Mode of actions	Tested pathogenic fungus	Methods	EC_{50}	NOAEL	Stimulatory doses	References
							0.0005 µg ml^{-1} (maximum stimulation for carbendazim + iprodione mix)	
4.	Cyazofamid	Protectant	*P. aphanidermatum*	*In vitro*	1.06 ppb	0.26 ppb	0.11 ppb (MSD)	Flores and Garzon (2013)
5.	Dimethachlone + prochloraz mixtures	Protectant	*S. sclerotiorum*	*In vitro*	327.8 and 194.2 µg ml^{-1} (mycelial growth inhibition of dimethachlone for 2 isolates); 0.063 and 0.066 µg ml^{-1} (prochloraz)	N/A	1 to 600 µg ml^{-1} (dimethachlone-treated isolate: increased virulence on detached leaves); 0.0003 to 0.18 µg ml^{-1} (prochloraz)	Zhang et al. (2019)
6.	Fluopyram	Systemic, broad-spectrum	*F. virguliforme*	*In vitro*	< 5 µg ml^{-1} with a mean EC_{50} of 3.35 µg ml^{-1} (mycelial growth inhibition assay) and 2.28 µg ml^{-1} (conidia germination assay)	N/A	1 µg ml^{-1} induced mycelial growth stimulation in 22% of the isolates	Wang et al. (2017)
7.	Flusilazole	Systemic, broad-spectrum	*S. sclerotiorum*	*In vitro*, in planta	0.085 and 0.104 µg ml^{-1} (mycelial growth inhibition for 2 different isolates)	N/A	0.005 to 0.16 µg ml^{-1} (preconditioning flusilazole with growth stimulations *in vitro*); 0.1 µg ml^{-1} (virulence stimulation in planta)	Lu et al. (2018)

Table 1. Hormetic responses of fungal pathogens to various fungicides (*Continue*)

No.	Fungicide active ingredients	Mode of actions	Tested pathogenic fungus	Methods	EC$_{50}$	NOAEL	Stimulatory doses	References
8.	Mefenoxam	Systemic, broad-spectrum	*Globisporangium* spp. *(syn. Pythium)*	*In vitro*	95.104 µg ml^{-1} (*G. ultimum* on mycelial growth area); 103.4 µg ml^{-1} (*G. irregulare*)	25.597 µg ml^{-1} (*G. ultimum* on mycelial growth area); 23.601 µg ml^{-1} (*G. irregulare*)	10.708 µg ml^{-1} (*G. ultimum* MSD); 8.65 µg ml^{-1} (*G. irregulare* MSD)	Pradhan et al. (2017)
			P. aphanidermatum	*In vitro*; in planta	N/A	N/A	1×10^{-4} to 1×10^{-10} µg ml^{-1} (virulence stimulation in planta); *in vitro* radial growth showed varied stimulation with sublethal doses, but the increase was not significant	Garzón et al. (2011)
9.	Propamocarb	Systemic	*P. aphanidermatum*	*In vitro*	2 to 3 ppm	1.77 ppm	0.64 ppm (MSD)	Flores and Garzon (2013)
10.	Thiophanate-Methyl	Systemic fungicide with protective and curative action, broad-spectrum	*S. homoeocarpa*	*In vitro*	Varied from 3 to 1500 µg l^{-1} (for 17 preconditioned isolates with T-methyl)	Varied from 26 to 270 µg l^{-1} (for 17 preconditioned isolates with T-methyl)	MSD ranged from 1 to 79 µg l^{-1} (for 17 preconditioned isolates with T-methyl)	Pradhan et al. (2019)
			L. theobromae	*In vitro*	1,000 µg ml^{-1} (resistant isolates); 0.01 to 1.6 µg ml^{-1} (sensitive isolates)	N/A	1 µg ml^{-1} (mycelial growth stimulation for all isolates)	da Silva et al. (2022)

Note: EC$_{50}$ = concentration of the fungicide that inhibited the growth of a fungal pathogen by 50%, NOAEL = the highest dose of a substance that does not cause any observable adverse effects in a test population, MSD = maximum stimulation dose, N/A = not available inhibiting fungal spore germination. While the long-term effects of these natural alternatives are still being explored, they offer the potential to diversify fungicide use.

Implementing IPM strategies that combine various control methods may also help suppress the development of hormesis in fungal pathogens. By diversifying fungicide use with alternative approaches and incorporating non-chemical controls, IPM can potentially mitigate the risks associated with traditional fungicides and suppress the emergence of hormesis.

Hormesis in entomopathogenic fungi

Entomopathogenic fungi are emerging as silent assassins in the fight for sustainable agriculture. These fungi act as natural enemies, infecting and killing a wide range of insect pests. They achieve this through various mechanisms, including breaching the insect’s exoskeleton with enzymes (Mora et al., 2017), producing toxins that disrupt its physiology (Altinok et al., 2019), and absorbing nutrients from the deceased host for reproduction and spread (Qu and Wang, 2018).

Studies have shown success against mealworm beetles (Vivekanandhan et al., 2024a), fall armyworms (Perumal et al., 2024), coffee berry borers (Krutmuang et al., 2023), brown marmorated stink bugs, yellow mealworms, and Japanese beetles (Swathy et al., 2023), demonstrating their effectiveness as a promising alternative to chemical pesticides. Notably, these fungi pose minimal threat to beneficial organisms like earthworms (Perumal et al., 2024).

Field studies further solidify their potential. For instance, Krutmuang et al. (2023) demonstrated that combining *Beauveria bassiana* with tobacco short-stem suspension and lure traps effectively controlled coffee berry borers. Importantly, *B. bassiana* remained effective even when combined with other control methods, showcasing its compatibility.

Intriguingly, hormesis adds another layer to the potential of entomopathogenic fungi. Alves et al. (2011) explored the potential of *Metarhizium anisopliae* as an environmentally friendly alternative for insect-pest control and the compatibility of this entomopathogen with chemical defensives. They conducted a study to assess the impact of lufenuron, an insect development inhibitor pesticide, on the germination speed of *M. anisopliae* conidia. The findings revealed a stimulating effect on conidia germination at 700 µg ml^{-1} lufenuron concentration but an inhibitory effect at higher concentrations (2 mg ml^{-1}), suggesting the possibility of hormesis occurrence.

Similarly, the study by Pamphile et al. (2012) aimed to assess the toxicity of the pyrethroid deltamethrin on *M. anisopliae* var. *anisopliae*, focusing on conidia germination speed. The findings indicated that 50 µg ml^{-1} of deltamethrin decreased and delayed conidia germination, while concentrations from 250 to 750 µg ml^{-1} completely inhibited germination. Interestingly, ultra-diluted treatments did not show inhibitory effects, with 31.25 ρg ml^{-1} and 31.25 ηg ml^{-1} of deltamethrin revealing a significant increase in germinated conidia, suggestive of hormesis-biological effects at low-level exposures of these concentrations on *M. anisopliae* conidia germination.

The potential of entomopathogenic fungi extends beyond their direct impact on pests. Scientists are exploring their biochemical properties to develop even more targeted control methods. This includes identifying fungal strains with minimal impact on non-target organisms and isolating specific insecticidal compounds with unique modes of action (Perumal et al., 2023a; 2023b; Vivekanandhan et al., 2024b). The interactions between entomopathogenic fungi and insects can also be surprisingly complex. While high doses typically kill insects, low doses of some fungi might surprisingly enhance their survival, as observed with aphids and *B. bassiana* (Arinanto et al., 2024).

These studies collectively highlight the diverse range of entomopathogenic fungi with potential as eco-friendly alternatives for pest control. Their effectiveness against a variety of insect pests, minimal impact on non-target organisms, and the potential role of hormesis in their interaction with chemical pesticides make them promising candidates for sustainable agricultural practices. Further research is needed to fully understand these complexities and optimize the use of these fungi for a greener future in pest management.

Hormesis in mycorrhiza

AMF symbioses play a crucial role in the relationship between certain fungi residing in plant roots and terrestrial plants, including crops. These symbioses are widely found in both natural ecosystems and agroecosystems, providing essential services such as regulating soil fertility and aiding in the production of plant products. The impact of fungicides on AMF, however, can vary due to their selective targeting of specific fungal groups (Pagano et al., 2023).

Jakobsen et al. (2021) investigated the effects of low doses of carbendazim and mancozeb on AMF in symbiosis with pea plants. They focused on three specific AMF species: *Claroideoglomus claroideum*, *Funneliformis mosseae,* and *F. caledonium*. They observed biphasic responses in AMF root colonization and phosphorus uptake. Low doses of fungicides enhanced these factors, while high doses suppressed them. Intriguingly, these responses were observed even in the absence of AMF antagonists, indicating the direct effects of the fungicides on AMF.

The study of Jakobsen et al. (2021) shed light on the occurrence of hormesis in AMF when exposed to mancozeb and carbendazim. The increased root colonization observed in response to a field-equivalent dose of mancozeb was likely attributed to its direct impact on propagule germination, hyphal extension, branching, and the production of AMF myc-factor signals during the early stages of the symbiotic relationship. It should be noted that mancozeb, a contact fungicide, is expected to have minimal influence on AMF growth within the roots. These findings provided valuable insights into the potential hormetic effects of fungicides on AMF and emphasized the need to consider their ecological implications.

The presence of fungicides is not the sole factor that can induce hormesis in AMF. Heavy metals have also been found to have similar effects. A study conducted by Lourdes et al. (2021) explored the hormesis effect of chromium (VI) on root colonization in maize plants associated with AMF. This study found that at low concentrations of chromium (VI) (0.1 and 1 mg l^{-1}), root colonization was stimulated by approximately 55% compared to the control, but inhibited at higher concentrations (10 mg l^{-1}).

Another investigation by da Silva et al. (2021) focused on the effects of cadmium exposure on the growth and enzyme secretion of mycorrhizal fungi. Different fungal species exhibited varying responses to cadmium, including unexpected enzyme activity and potential hormesis effects. *Austroboletus occidentalis* showed increased enzyme activity under cadmium stress, while *Scleroderma* sp. demonstrated enhanced biomass, indicating cadmium-triggered growth.

Research on hormesis is also evident in studies on the biodegradation ability of endophytic fungi towards active pesticide compounds, although it often goes unnoticed by researchers. An example of such research is the study by Fauriah et al. (2021), investigating the potential of endophytic fungi for the biodegradation of chlorpyrifos in shallots. The study reveals the presence of hormesis and identifies *Trichoderma* sp., *Aspergillus* sp., and *Fusarium* sp. as the fungi involved in the degradation process. Some isolates exhibited no growth inhibition in solid media with chlorpyrifos and grew better than the control group at low concentrations of 300 and 150 ppm, highlighting the hormetic effect.

Understanding hormesis is crucial for developing sustainable agricultural practices. It unlocks potential by revealing the intricate interplay between controlled stress and beneficial microbes like AMF. Biocontrol agents offer promising tools for disease management, as demonstrated by studies using *Trichoderma asperellum* to inhibit *Rhizoctonia solani* in rice (Nurhayati et al., 2021) and the combination of *Rhizophagus intraradices* with *Bacillus* strains and silica to reduce shallot diseases (Abdullah et al., 2023; Amalia et al., 2023). However, a cautious approach is necessary. As observed in other organisms (Erofeeva, 2023), hormesis in agriculture might involve trade-offs between benefits and potential negative consequences. Further research is crucial to navigate this complexity and develop sustainable practices that utilize hormesis for plant health and an eco-friendlier future.

Mechanism of hormesis

Studies on hormesis have yet to definitively establish whether the advantages triggered by stress come without accompanying drawbacks or potential adverse effects for organisms. A study by McClure et al. (2014) using fruit flies as a model provided evidence that hormesis, a concept of benefiting from mild stress, has drawbacks, especially related to immunity. This study found that applying dead spores from the *M. robertsii* fungus to fruit flies could extend their lifespan. However, in outbred fly lines, exposure to the fungal pathogen improved survival and reproduction but weakened the flies' ability to defend against live infections.

Erofeeva (2023) proposes two distinct hormesis trade-off scenarios under mild stressors. The first (trade-off 1) involves a situation where stress negatively impacts one aspect of an organism's performance while simultaneously improving other aspects, driven by phenotypic plasticity. The second (trade-off 2) occurs when the mild stressor enhances certain aspects without affecting others. These trade-offs are thought to arise from limited resources available to the organism, leading to a redistribution of energy among its traits (Garland Jr. et al., 2022).

The current literature predominantly highlights trade-offs observed at the cellular, individual, and population levels, with limited exploration of hormetic trade-offs in communities (Erofeeva, 2023). Notably, soil communities of fungi and bacteria exhibited distinct trade-offs in response to cadmium concentrations. For bacteria, cadmium reduced the total count but increased relative abundance and α-diversity (trade-off 1), while for fungi, the diversity remained unchanged, but the total number and relative abundance increased (trade-off 2) (Wang et al., 2021).

Another report indicates that mild stresses, known for inducing hormesis, also extend the lifespan in *Saccharomyces cerevisiae*. Low doses of DNA-damaging stress agents (hydroxyurea, methyl methanesulfonate, 4-nitroquinoline 1-oxide, or Zeocin) extended the chronological lifespan in yeast when exposed during growth but not during the stationary phase. Interestingly, these stressors did not impact mitochondrial activity or increase resistance to various stressors (trade-off 2). Mutant strains lacking genes influencing quiescence prevented this effect, emphasizing the role of quiescence in the observed hormetic response. This suggests that mild DNA damage stress promotes quiescence, leading to lifespan extension in yeast (Ross and Maxwell, 2018).

Hormesis is intricately connected to molecular pathways that interact antagonistically. This interaction allows organisms to dynamically adjust their phenotypes in response to environmental challenges. This evolutionary mechanism likely originated as a response to resource scarcity, facilitating species' adaptation to various stressors and the preservation of community function across a spectrum of stressor levels. Furthermore, hormetic trade-offs within individual organisms in populations can cascade into broader effects on population indicators and alterations in species abundances, ultimately shaping the composition of the entire community (Erofeeva, 2023).

The molecular mechanisms of hormesis remain unclear, especially in fungi. Molecular studies by Cong et al. (2019) demonstrated that sublethal doses of carbendazim had stimulatory effects on the virulence of *B. cinerea*, but did not elevate the expression levels of various pathogenicity-related genes. These genes play roles in processes like cell wall degradation (pectin methylesterase and endopolygalacturonase), cutin degradation (cutinase), and other enzymatic activities.

Hu et al. (2020) reported that boscalid, at stimulatory concentrations, had no significant impact on the expression of three virulence-associated genes in *S. sclerotiorum*. These genes encode enzymes involved in cutin degradation (cutinase), pectin degradation (polygalacturonase), and metabolic processes (oxaloacetate acetylhydrolase). Interestingly, these low doses may even enhance specific aspects of fungal behavior, such as virulence, without substantially affecting the expression of genes associated with pathogenicity.

Another crucial factor often neglected is the role of a microbe's energy source (substrate) in shaping the hormesis effect. Tang et al. (2022) emphasize that variations in the energy source types, concentrations, and compositions significantly impact how microbes respond to stress, influencing their metabolism, population density, and communication pathways. Essentially, the energy source dictates their survival strategy and can determine whether hormesis occurs.

Hormesis presents a complex interplay between stress, adaptation, and trade-offs. While the benefits of hormesis are evident, there is still much to learn about the underlying mechanisms, particularly at the molecular level. Further research into these areas will help us gain a deeper understanding of this intriguing phenomenon.

Hormesis and Shelford's law of tolerance

Organisms face a constant barrage of environmental fluctuations. Two key frameworks, Shelford's law of tolerance and hormesis, offer valuable insights into how organisms respond to these changes. Shelford's law, visualized as a bell-shaped curve, describes an organism's tolerance for specific environmental factors like temperature or salinity. There is an optimal zone within this curve where the organism thrives. As the factor deviates from this ideal range, performance declines, leading to stress on both sides. Eventually, these extremes reach lethal limits (Erofeeva, 2021).

It is important to note that Shelford's law typically applies to factors like temperature, pH, or salinity, where there can be an optimal range for the organism (Figure 2). Toxins like fungicides differ in this crucial aspect. Unlike these other environmental factors, toxins typically do not have an optimal range for an organism.

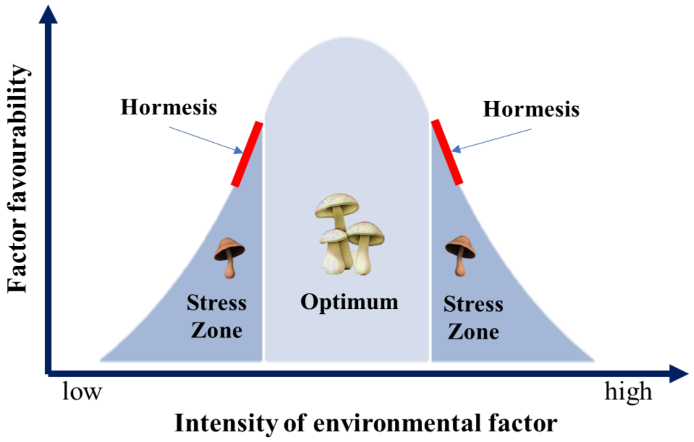

Figure 2. Depiction of hormesis placement on Shelford's tolerance law curve (modified from Erofeeva (2021)). This curve applies to environmental factors like temperature, pH, or salinity, which possess optimal values for an organism (growth, reproduction, etc.). For stressors like toxins (fungicides, pesticides) or pollutants, an optimal range does not exist

Any amount of toxin can potentially cause harm, and there is no real "optimal" range within Shelford's law. While low doses might be beneficial through hormesis, any amount above that can remain harmful.

Previously, scientists assumed stressors always had negative effects. Hormesis challenges this notion. It is a phenomenon where low doses of stressors can stimulate growth and enhance an organism's ability to withstand future challenges. This response is not limited to specific stress types or previously considered "toxic" agents (Agathokleous et al., 2019).

However, it is essential to recognize that hormesis does not contradict the fundamental principle of Shelford's law, particularly for stress induced by environmental factors like temperature, pH, or salinity. By considering both frameworks, we gain a more comprehensive picture of how organisms navigate environmental fluctuations. Shelford's law defines the overall tolerance range, while hormesis provides insights into adaptation and potential benefits from mild stress. This integrated perspective allows us to appreciate the nuanced ways in which organisms respond to environmental challenges (Erofeeva et al., 2023).

Interestingly, hormesis can increase organism tolerance to stressors through preconditioning. Studies on *Sclerotinia homoeocarpa* isolates (Pradhan et al., 2019) showed that preconditioning tolerant isolates with low fungicide doses enhanced their growth, while non-tolerant isolates remained unaffected. Similarly, preconditioning *S. sclerotiorum* with flusilazole increased its virulence (Lu et al., 2018). This highlights how hormesis can induce stress tolerance, potentially rendering fungicide treatments less effective.

Furthermore, the effectiveness of hormesis can vary across species, populations, and even developmental stages (Erofeeva, 2021), emphasizing the need for careful consideration when developing fungicide application strategies. Integrating hormesis into research has the potential to greatly enhance our understanding of environmental biology, ecology, and evolutionary biology.

Implications for agricultural practices

Understanding hormesis in fungal pathogens, biological control agents, and their response to fungicides offers crucial insights for optimizing crop production and sustainability in agriculture. Traditionally, stress was seen solely as detrimental. However, research reveals that low doses can trigger beneficial responses across organisms, suggesting an adaptation mechanism for future challenges. This concept is equally relevant for ecologists, as it sheds light on how organisms adapt to environmental challenges (Erofeeva et al., 2023).

While hormesis does not eliminate the potential harm of toxins like fungicides and pesticides, it allows informed decisions about fungicide application rates. By considering specific doses that stimulate growth and virulence in fungal pathogens, as well as entomopathogenic fungi and mycorrhiza, farmers can optimize disease management. Additionally, the enhanced tolerance to stressors exhibited by pathogens at higher fungicide doses underscores the importance of employing integrated disease management approaches that combine fungicides with other control measures, such as cultural practices and resistant crop varieties (Song et al., 2022).

Careful selection of fungicides and their concentrations, as well as avoiding consecutive use of fungicides with the same mode of action, can help prevent preconditioning hormesis and resistance development (Garzon et al., 2011). These insights contribute to the development of more sustainable and efficient disease management strategies in agriculture and plant pathology. To strengthen disease management and mitigate fungicide hormesis, several strategies can be employed, including threshold-based monitoring, dose optimization, adaptive management, education, and staying current with research and innovations.

The integration of fungicide doses with other control methods, such as host resistance, fungicide mixes, host resistance enhancers, biological control agents, and silicon amendments, has demonstrated promising outcomes in disease management. Rotating fungicides with different modes of action is crucial to prevent the selection of fungicide-resistant strains, which can be stimulated by fungicides even at recommended doses (Garzon et al., 2011). By implementing these strategies in combination, farmers can reduce reliance on fungicides alone, promote a diverse and resilient agroecosystem, and minimize the risk of both pathogenic resistance and biological control agents disruption.

In field conditions, various factors can expose plant pathogens to low fungicide doses, including application drift, rainwater dilution, cost-cutting low-dose applications, and improper fungicide usage. These potential effects, known as fungicide hormesis, pose a serious threat to food security, as they may lead to increased disease incidence and severity, and larger crop losses. Careful consideration of these impacts is essential for effective and sustainable plant disease management (Song et al., 2022). Machine learning and deep learning also offer promising tools to analyze hormesis data in organisms (Rico-Chávez et al., 2022), specifically predicting optimal conditions for biocontrol fungi while also predicting the occurrence of hormesis in fungal pathogens induced by fungicides.

The exploration and benefits of hormesis extend beyond biocontrol fungi to encompass plants. Utilizing biostimulants and elicitors, we can maintain plants within the hormetic zone and even breed future generations for enhanced stress tolerance. This can lead to the cultivation of healthier, more productive, and more resilient crops in a changing climate (Godínez-Mendoza et al., 2023).

CONCLUSIONS

Understanding hormesis in fungi is vital for optimizing agriculture. Recognizing the biphasic dose-response relationship helps minimize pathogen resistance, enhancing sustainable disease management. Integrated approaches like cultural practices and resistant crops show promise and rotating fungicides prevent resistance. Yet, the potential threat of fungicide hormesis must be acknowledged. While low doses may initially benefit pathogens, careful consideration ensures effective disease management for food security. Further research on hormesis in fungal pathogens, entomopathogens, and mycorrhiza is crucial for developing optimal agricultural strategies that balance pathogen control and preserve beneficial functions.

ACKNOWLEDGEMENT

The authors would like to express their gratitude to the Agency for Agricultural Extension and Human Resource Development (BPPSDMP), Ministry of Agriculture (Indonesia) for master student scholarship of the first author. Without their support, this work would not have been possible.

REFERENCES

Abdullah, J. T., Suryanti, S., & Joko, T. (2023). Utilization of arbuscular mycorrhizal fungi and *Bacillus velezensis* inoculation in suppressing twisted disease of shallot. *Jurnal Perlindungan Tanaman Indonesia*, *27*(2), 103–109. https://doi.org/10.22146/jpti.89296

Agathokleous, E. (2022). On the meta-analysis of hormetic effects. *Science of the Total Environment*, *852*, 158273. https://doi.org/10.1016/j.scitotenv.2022.158273

Agathokleous, E., & Calabrese, E. J. (2021). Fungicide-induced hormesis in phytopathogenic fungi: A critical determinant of successful agriculture and environmental sustainability. *Journal of Agricultural and Food Chemistry*, *69*(16), 4561–4563. https://doi.org/10.1021/acs.jafc.1c01824

Agathokleous, E., & Calabrese, E. J. (2024). Evolution of hormesis research: A bibliometric analysis. *Archives of Toxicology*, *98*(2), 577–578. https://doi.org/10.1007/s00204-023-03635-9

Agathokleous, E., Kitao, M., Harayama, H., & Calabrese, E. J. (2019). Temperature-induced hormesis in plants. *Journal of Forestry Research*, *30*, 13–20. https://doi.org/10.1007/s11676-018-0790-7

Agathokleous, E., Wang, Q., Iavicoli, I., & Calabrese, E. J. (2022). The relevance of hormesis at higher levels of biological organization: Hormesis in microorganisms. *Current Opinion in Toxicology*, *29*, 1–9. https://doi.org/10.1016/j.cotox.2021.11.001

Altinok, H. H., Altinok, M. A., & Koca, A. S. (2019). Modes of action of entomopathogenic fungi. *Current Trends in Natural Sciences*, *8*(16), 117–124. Retrieved from https://www.natsci.upit.ro/media/1838/16altinok-et-al.pdf

Alves, M. M. T. A., Orlandelli, R. C., Lourenço, D. A. L., & Pamphile, J. A. (2011). Toxicity of the insect growth regulator lufenuron on the entomopathogenic fungus *Metarhizium anisopliae. African Journal of Biotechnology*, *10*(47), 9668–9672. https://doi.org/10.5897/AJB11.1253

Amallia, R., Suryanti, S., & Joko, T. (2023). The potential of *Rhizophagus intraradices, Bacillus thuringiensis* Bt BMKP and silica for anthracnose disease control in shallot. *Caraka Tani: Journal of Sustainable Agriculture, 38*(2), 433–446. http://dx.doi.org/10.20961/carakatani.v38i2.76536

Arinanto, L. S., Hoffmann, A. A., Ross, P. A., & Gu, X. (2024). Hormetic effect induced by *Beauveria bassiana* in *Myzus persicae. Pest Management Science.* https://doi.org/10.1002/ps.8075

Calabrese, E. J., & Mattson, M. P. (2011). Hormesis provides a generalized quantitative estimate of biological plasticity. *Journal of cell communication and signaling*, *5*, 25–38. https://doi.org/10.1007/s12079-011-0119-1

Calabrese, E. J., & Mattson, M. P. (2017). How does hormesis impact biology, toxicology, and medicine? *NPJ-aging-and-mechanisms-of-disease*, *3*(1), 13. https://doi.org/10.1038/s41514-017-0013-z

Cong, M., He, S., Zhang, J., Luo, C., & Zhu, F. (2018). Hormetic effects of mixtures of carbendazim and iprodione on the virulence of *Botrytis cinerea. Plant Disease*, *103*(1), 95–101. https://doi.org/10.1094/PDIS-05-18-0754-RE

Cong, M., Zhang, B., Zhang, K., Li, G., & Zhu, F. (2019). Stimulatory effects of sublethal doses of carbendazim on the virulence and sclerotial production of *Botrytis cinerea. Plant Disease*, *103*(9), 2385–2391. https://doi.org/10.1094/PDIS-01-19-0153-RE

da Silva, E. L., Garzón, C. D., & Lopes, U. P. (2022). Hormesis effect and management of thiophanate-methyl resistance in *Lasiodiplodia theobromae* isolates. *Research Square*, 1–14. https://doi.org/10.21203/rs.3.rs-1715820/v1

da Silva, G. R. V., De Oliveira, V. H., & Tibbett, M. (2021). Cadmium stress causes differential effects on growth and the secretion of carbon-degrading enzymes in four mycorrhizal basidiomycetes. *Mycoscience*, *62*(2), 132–136. https://doi.org/10.47371/mycosci.2020.12.002

Erofeeva, E. A. (2021). Plant hormesis and Shelford’s tolerance law curve. *Journal of Forestry Research*, *32*(5), 1789–1802. https://doi.org/10.1007/s11676-021-01312-0

Erofeeva, E. A. (2023). Environmental hormesis in living systems: The role of hormetic trade-offs. *Science of the Total Environment*, *901*, 166022. https://doi.org/10.1016/j.scitotenv.2023.166022

Erofeeva, E. A., Gelashvili, D. B., & Rozenberg, G. S. (2023). The modern concept of hormesis: An overview of the issue and its significance for ecology. *Biology Bulletin Reviews*, *13*(Suppl 3), S229–S239. https://doi.org/10.1134/S2079086423090037

Fauriah, R., Amin, N., Daud, I. D., & Harsanti, E. S. (2021). The potential of endophytic fungi as biodegradation of chlorpyrifos in shallots. *IOP Conference Series: Earth and Environmental Science, 807*(3), 032058. https://doi.org/10.1088/1755-1315/807/3/032058

Flores, F. J., & Garzon, C. D. (2013). Detection and assessment of chemical hormesis on the radial growth *in vitro* of oomycetes and fungal plant pathogens. *Dose-Response*, *11*(3), 361–373. https://doi.org/10.2203/dose-response.12-026.Garzon

Garland Jr, T., Downs, C. J., & Ives, A. R. (2022). Trade-offs (and constraints) in organismal biology. *Physiological and biochemical zoology*, *95*(1), 82–112. https://doi.org/10.1086/717897

Garzón, C. D., & Flores, F. J. (2013). *Hormesis: Biphasic dose-responses to fungicides in plant pathogens and their potential threat to agriculture.* Fungicides-Showcases of Integrated Plant Disease Management from Around the World. InTech, Europe, 311–328. https://doi.org/10.5772/55359

Garzón, C. D., Molineros, J. E., Yánez, J. M., Flores, F. J., del Mar Jiménez-Gasco, M., & Moorman, G. W. (2011). Sublethal doses of mefenoxam enhance *Pythium* damping-off of geranium. *Plant Disease*, *95*(10), 1233–1238. https://doi.org/10.1094/PDIS-09-10-0693

Godínez-Mendoza, P. L., Rico-Chávez, A. K., Ferrusquía-Jimenez, N. I., Carbajal-Valenzuela, I. A., Villagómez-Aranda, A. L., Torres-Pacheco, I., & Guevara-González, R. G. (2023). Plant hormesis: Revising of the concepts of biostimulation, elicitation and their application in a sustainable agricultural production. *Science of the Total Environment*, *894*, 164883. https://doi.org/10.1016/j.scitotenv.2023.164883

Habibullah, M., Sumardiyono, C., & Widiastuti, A. (2020). Potency of non-fungicide chemicals for maize inducing resistance against downy mildew. *Jurnal Perlindungan Tanaman Indonesia*, *24*(2), 154. https://doi.org/10.22146/jpti.55057

Hu, S., Xu, Q., Zhang, Y., & Zhu, F. (2020). Stimulatory effects of boscalid on virulence of *Sclerotinia sclerotiorum* indicate hormesis may be masked by inhibitions. *Plant Disease*, *104*(3), 833–840. https://doi.org/10.1094/PDIS-07-19-1421-RE

Jacquet, F., Jeuffroy, M.H., Jouan, J., Le Cadre, E., Litrico, I., Malausa, T., Reboud, X., & Huyghe, C. (2022). Pesticide-free agriculture as a new paradigm for research. *Agronomy for Sustainable Development*, *42*(1), 8. https://doi.org/10.1007/s13593-021-00742-8

Jakobsen, I., Murmann, L. M., & Rosendahl, S. (2021). Hormetic responses in arbuscular mycorrhizal fungi. *Soil Biology and Biochemistry*, *159*, 108299. https://doi.org/10.1016/j.soilbio.2021.108299

Krutmuang, P., Rajula, J., Pittarate, S., Chanbang, Y., Perumal, V., Alford, L., & Thungrabeab, M. (2023). Biocontrol efficacy of *Beauveria bassiana* in combination with tobacco short stem and modified lure traps. *International Journal of Tropical Insect Science*, *43*(5), 1591–1600. https://doi.org/10.1007/s42690-023-01063-x

Kuźniak, E., & Urbanek, H. (2000). The involvement of hydrogen peroxide in plant responses to stresses. *Acta Physiologiae Plantarum*, *22*, 195–203. https://doi.org/10.1007/s11738-000-0076-4

Lourdes, G. C. M., Stéphane, D., & Maryline, C. S. (2021). Impact of increasing chromium (VI) concentrations on growth, phosphorus and chromium uptake of maize plants associated to the mycorrhizal fungus *Rhizophagus irregularis* MUCL 41833. *Heliyon*, *7*(1), e05891. https://doi.org/10.1016/j.heliyon.2020.e05891

Lu, X., He, S., Ma, H., Li, J., & Zhu, F. (2018). Hormetic effects of flusilazole preconditioning on mycelial growth and virulence of *Sclerotinia sclerotiorum. Plant Disease*, *102*(6), 1165–1170. https://doi.org/10.1094/PDIS-10-17-1638-RE

McClure, C. D., Zhong, W., Hunt, V. L., Chapman, F. M., Hill, F. V., & Priest, N. K. (2014). Hormesis results in trade-offs with immunity. *Evolution*, *68*(8), 2225–2233. https://doi.org/10.1111/evo.12453

Mora, M. A. E., Castilho, A. M. C., & Fraga, M. E. (2017). Classification and infection mechanism of entomopathogenic fungi. *Arquivos do Instituto Biológico*, *84*, e0552015. https://doi.org/10.1590/1808-1657000552015

Nurhayati, Y., Suryanti, S., & Wibowo, A. (2021). *In vitro* evaluation of *Trichoderma asperellum* isolate UGM-LHAF against *Rhizoctonia solani* causing sheath blight disease of rice. *Jurnal Perlindungan Tanaman Indonesia*, *25*(1), 64–73. https://doi.org/10.22146/jpti.65290

Ons, L., Bylemans, D., Thevissen, K., & Cammue, B. P. (2020). Combining biocontrol agents with chemical fungicides for integrated plant fungal disease control. *Microorganisms*, *8*(12), 1930. https://doi.org/10.3390/microorganisms8121930

Pagano, M. C., Kyriakides, M., & Kuyper, T. W. (2023). Effects of pesticides on the arbuscular mycorrhizal-symbiosis. *Agrochemicals*, *2*(2), 337–354. https://doi.org/10.3390/agrochemicals2020020

Pamphile, J. A., Tonussi, R. L., Fabrice, C. E. S., Orlandelli, R. C. (2012). Toxicity of the pyrethroid deltamethrin on the entomopathogenic fungus *Metarhizium anisopliae* var. *anisopliae* (Metsch) Sorokin assessed by germination speed parameter. *Annals of Biological Research*, *3*(11), 5028–5033. Retrieved from https://www.scholarsresearchlibrary.com/articles/toxicity-of-the-pyrethroid-deltamethrin-on-the-entomopathogenic-fungus-metarhizium anisopliae-var-anisopliae-metsch-sorok.pdf

Panth, M., Hassler, S. C., & Baysal-Gurel, F. (2020). Methods for management of soilborne diseases in crop production. *Agriculture*, *10*(1), 16. https://doi.org/10.3390/agriculture10010016

Perumal, V., Kannan, S., Alford, L., Pittarate, S., & Krutmuang, P. (2024). Study on the virulence of *Metarhizium anisopliae* against *Spodoptera frugiperda* (JE Smith, 1797). *Journal of Basic Microbiology*, *64*(5), 2300599. https://doi.org/10.1002/jobm.202300599

Perumal, V., Kannan, S., Alford, L., Pittarate, S., Geedi, R., Elangovan, D., Marimuthu, R., & Krutmuang, P. (2023a). First report on the enzymatic and immune response of *Metarhizium majus* bag formulated conidia against *Spodoptera frugiperda*: An ecofriendly microbial insecticide. *Frontiers in Microbiology*, *14*, 1104079. https://doi.org/10.3389/fmicb.2023.1104079

Perumal, V., Kannan, S., Alford, L., Pittarate, S., Mekchay, S., Reddy, G.V., Elangovan, D., Marimuthu, R., & Krutmuang, P. (2023b). Biocontrol effect of entomopathogenic fungi *Metarhizium anisopliae* ethyl acetate-derived chemical molecules: An eco-friendly anti-malarial drug and insecticide. *Archives of Insect Biochemistry and Physiology*, *114*(2), 1–19. https://doi.org/10.1002/arch.22037

Pradhan, S., Flores, F. J., Molineros, J. E., Walker, N. R., Melouk, H., & Garzon, C. D. (2017). Improved assessment of mycelial growth stimulation by low doses of mefenoxam in plant pathogenic *Globisporangium* species. *European Journal of Plant Pathology*, *147*, 477–487. https://doi.org/10.1007/s10658-016-1016-5

Pradhan, S., Miller, L., Marcillo, V., Koch, A. R., Graf Grachet, N., Molineros, J. E., Walker, N.R., Melouk, H., & Garzon, C. D. (2019). Hormetic effects of thiophanate-methyl in multiple isolates of *Sclerotinia homoeocarpa. Plant disease*, *103*(1), 89–94. https://doi.org/10.1094/PDIS-05-18-0872-RE

Qu, S., & Wang, S. (2018). Interaction of entomopathogenic fungi with the host immune system. *Developmental & Comparative Immunology*, *83*, 96–103. https://doi.org/10.1016/j.dci.2018.01.010

Rico-Chávez, A. K., Franco, J. A., Fernandez-Jaramillo, A. A., Contreras-Medina, L. M., Guevara-González, R. G., & Hernandez-Escobedo, Q. (2022). Machine learning for plant stress modeling: A perspective towards hormesis management. *Plants*, *11*, 970. https://doi.org/10.3390/plants11070970

Ross, E. M., & Maxwell, P. H. (2018). Low doses of DNA damaging agents extend *Saccharomyces cerevisiae* chronological lifespan by promoting entry into quiescence. *Experimental gerontology*, *108*, 189–200. https://doi.org/10.1016/j.exger.2018.04.020

Santika, I. A., Wibowo, A., Suryanti, S., Sumardiyono, C., & Widiastuti, A. (2023). *In vitro* evaluation on resistance of *Phytopythium vexans* (NG isolate) cultured from sublethal concentration against several fungicides. *Jurnal Perlindungan Tanaman Indonesia*, *27*(1), 10–17. https://doi.org/10.22146/jpti.73045

Scortichini, M. (2022). Sustainable management of diseases in horticulture: Conventional and new options. *Horticulturae*, *8*(6), 517. https://doi.org/10.3390/horticulturae8060517

Song, J., Han, C., Zhang, S., Wang, Y., Liang, Y., Dai, Q., Huo, Z., & Xu, K. (2022). Hormetic effects of carbendazim on mycelial growth and aggressiveness of *Magnaporthe oryzae. Journal of Fungi*, *8*(10), 1008. https://doi.org/10.3390/jof8101008

Swathy, K., Parmar, M. K., & Vivekanandhan, P. (2023). Biocontrol efficacy of entomopathogenic fungi *Beauveria bassiana* conidia against agricultural insect pests. *Environmental Quality Management*. https://doi.org/10.1002/tqem.22174

Tang, L., Zhou, Y., Zhang, Y., & Sun, H. (2022). The role of energy source or substrate in microbial hormesis. *Current Opinion in Toxicology*, *29*, 10–18. https://doi.org/10.1016/j.cotox.2021.12.001

Vivekanandhan, P., Alahmadi, T. A., & Ansari, M. J. (2024a). Pathogenicity of *Metarhizium rileyi* (Hypocreales: Clavicipitaceae) against *Tenebrio molitor* (Coleoptera: Tenebrionidae). *Journal of Basic Microbiology*, *64*(5), 2300744. https://doi.org/10.1002/jobm.202300744

Vivekanandhan, P., Swathy, K., Alahmadi, T. A., & Ansari, M. J. (2024b). Biocontrol effects of chemical molecules derived from *Beauveria bassiana* against larvae of *Tuta absoluta* (Meyrick) (Lepidoptera: Gelechiidae). *Frontiers in Microbiology*, *15*, 1336334. https://doi.org/10.3389/fmicb.2024.1336334

Vivekanandhan, P., Swathy, K., Bedini, S., & Shivakumar, M. S. (2023). Bioprospecting of *Metarhizium anisopliae* derived crude extract: A ecofriendly insecticide against insect pest. *International Journal of Tropical Insect Science*, *43*(2), 429–440. https://doi.org/10.1007/s42690-022-00935-y

Wang, J., Bradley, C. A., Stenzel, O., Pedersen, D. K., Reuter-Carlson, U., & Chilvers, M. I. (2017). Baseline sensitivity of *Fusarium virguliforme* to fluopyram fungicide. *Plant Disease*, *101*(4), 576–582. https://doi.org/10.1094/PDIS-09-16-1250-RE

Wang, S., Huang, B., Fan, D., Agathokleous, E., Guo, Y., Zhu, Y., & Han, J. (2021). Hormetic responses of soil microbiota to exogenous Cd: A step toward linking community-level hormesis to ecological risk assessment. *Journal of Hazardous Materials*, *416*, 125760. https://doi.org/10.1016/j.jhazmat.2021.125760

Widiastuti, A., Simarmata, R. F., & Sumardiyono, C. (2021). Potency of galangal extract as botanical fungicide to control grape leave rust disease (*Phakopsora euvitis*). *Jurnal Fitopatologi Indonesia*, *16*(3), 135–143. https://doi.org/10.14692/jfi.16.3.135-143

Zhang, R., Zhang, Y., Xu, Q., Li, J., & Zhu, F. (2019). Hormetic effects of mixtures of dimethachlone and prochloraz on *Sclerotinia sclerotiorum*. *Plant Disease*, *103*(3), 546–554. https://doi.org/10.1094/PDIS-06-18-1071-RE