AN OVERVIEW OF THE POTENTIAL APPLICATION OF PRODIGIOSIN IN CONTROL OF PLANT PATHOGENIC ORGANISMS

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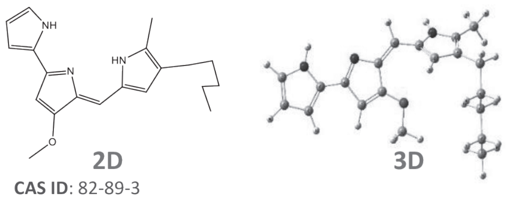
ABSTRACT

Prodigiosin (PG) is a red pigment mainly biosynthesized by *Serratia marcescens*. This pigment compound possesses potential applications in various fields. Due to showing various bioactivities, PG has received much attention for study. Numerous review papers concerning the production and applications of PG were reported. However, almost all previous reviews focus on its potential application in medicine. To date, PG has been widely investigated for its application in agriculture with plant anti-pathogenic potent against nematodes, fungi, and bacteria. To highlight the novel and promising utilization of PG in agriculture, this review extensively presented and discussed the applications of PG in agriculture via in vitro tests, greenhouse tests, and field studies. The mechanism action of PG was also presented in this paper.

Keywords: *Bactericidal effect, fungicidal effect, nematicidal effect, prodigiosin, S. marcescens.*

1. INTRODUCTION

PG, a red pigment compound, is a prodigionine compound with a pyrrolylpyrromethane skeleton (Darshan N., *et al*., 2015). The structure and some basic physicochemical properties of PG are presented in Figure 1. PG was biosynthesized by various microbial strains, of these, *S. marcescens* was reported as a major PG-producing strain (Wang S.L. *et al*., 2020). This bacterial pigment compound has been reported to show potential applications in various fields, including medicine, food, industry, environment, and agriculture (Wang S.L. *et al*., 2020; Shaikh Z., 2016; Islan G.A. et al., 2022). In addition, the safety of PG was also confirmed previously (Li X. *et al*., 2021; Nguyen V.B. *et al*., 2020; Siew W.S. *et al*., 2016; Suryawanshi R.K. *et al*., 2014; Guryanova I.D. *et al*., 2013; Tomas R.P. *et al.,* 2010).



CAS ID: 82-89-3
Molecular formula: $C_{20}H_{25}N_{3}O$
Molecular weight: 232.44 Da
Melting point: 151-152°
Boiling point: 554.3 ± 50.0 °C
Soluble solvent: Well soluble in non-polar solvents, partially soluble in alcohol and ether

Figure 1. The structure and basic physico-chemical properties of PG

Recently, the studies on PG have increased dramatically due to its numerous benefits (Nguyen V.B. et al., 2020). This compound was extensively studied for its biosynthesis using various substrates, including commercial broth, agro-products, agro by-products, as well as organic wastes (Wang S.L. et al., 2020). The condition fermentation, and additive agents for enhancing PG productivity via fermentation were studied (Han R. *et al*., 2021). For scaling-up of PG productivity, bioreactor systems with various working volumes were also investigated. Until now, there have been many overview works on PG. However, almost focus on its potential applications in medicines (Wang S.L. *et al*., 2020; Islan G.A. *et al*., 2022; Han R. *et al*., 2021; Rafael G.A. *et al.,* 2022; Mnif S. *et al*., 2022), several review papers focused on some aspects such as the general biosynthesis pathway of PG and physical-chemical characteristics (Han R. *et al*., 2021; Rafael G.A. *et al*., 2022; Anita K. *et al*., 2006), or high-level PG biosynthesis (Wang S.L. et al., 2020; Islan G.A. *et al*., 2022; Han R. *et al*., 2021; Rafael G.A. *et al*., 2022; Mnif S. *et al*., 2022). To highlight the novel and promising utilization of PG in agriculture, this review extensively presented and discussed the applications of PG in controlling major plant pathogenic organisms, including nematodes, insects, bacteria, and fungi. The mechanism action of PG for medical effects has been investigated in many reports. However, the mechanism action of PG for bioactivities in controlling major plant pathogenic organisms were just reported in several

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works. Concerning the mechanism action of PG on nematodes was investigated by Roser F. *et al*. (2007), Nguyen, T.H., *et al*. (2024), Nguyen, T.H., *et al*. (2024). The mechanism action of PG against fungi was reported by Hazarika D.J. *et al*. (2020), Nguyen, V.B. *et al*. (2023), and Nguyen, T.H. *et al*. (2024). Several reports also proposed the possible mechanism action of PG against bacteria (Danevcic T. *et al*., 2016; Kimyon, O. *et al*. 2016; Danevčič T. *et al.,* 2016; Yip C.H. *et al.,* 2021). To highlight this issue needs to be further investigated, the mechanism action of PG was also presented and discussed in this paper.

Up to now, several derives of PG were also found to be produced by bacteria (Eckelmann D. et al., 2018; Klein A.S. et al. 2017&2018) or obtained from chemoenzymatic synthesis (Tim M.W. et al., 2023). These PG derives showed some bioactivities, including good effects against Nematodes and Fungi. However, investigations of PG derives is still rare. Thus in this paper, we focused on presenting and discussing the application of PG.

2. NEMATICIDAL EFFECT OF PG

Up to date, PG has been found as a nematicidal compound against several nematodes, including *Radopholus similis*, *Meloidogyne javanica* (Rahul S. *et al*., 2014), *Caenorhabditis elegans*, *Heterodera schachtii* (Samer S.H. *et al*., 2020), *Meloidogyne incognita* (Omnia M.M. *et al*., 2020), and Black pepper *Meloidogyne* spp. (Nguyen T.H. *et al*., 2022; Nguyen T.H. *et al.*, 2024) (Table 1).

The first study evaluating the nematicidal effect of PG was reported by Rahul, S., *et al*. (2014), in this work, PG was found to potentially inhibiting against *R. similis* and *M. javanica* with low IC_{50} values of 0.083 and 0.079 mg/ml, respectively. PG demonstrated even higher activity compared to a positive control - copper sulphate (IC_{50} value of 0.38 and 0.23 mg/ml, respectively). In 2020, PG was evidenced as the most active compound among the prodigiosin structures in nematicidal effect against *C. elegans* and *H. schachtii* (Samer S.H. *et al*., 2020). PG showed a potential effect on *C. elegans* and moderate activity against *H. schachtii* with IC_{50} values of 0.127 and 13.3 μM, respectively.

Recently, PG was also found as a novel nematicidal compound of root-knot nematodes (Omnia M.M. *et al*., 2020; Nguyen T.H. *et al.*, 2022; Nguyen T.H. *et al*., 2024). This pigment showed a moderate effect against *M. incognita* with the highest inhibition (84%) at the tested concentration of 100 mg/ml, and the IC_{50} value was recorded at 31.9 mg/ml. Nearby, PG was produced at a high-level yield and found as an effective nematicidal agent against black pepper *Meloidogyne* spp.

This purified pigment effectively inhibited J2 nematode *Meloidogyne* spp. and egg-hatching with max values of 96.7 and 87%, with low IC_{50} values of 0.2 and 0.32 mg/ml, respectively. PG was further nanozationized to enhance nematicidal effect and stability (Nguyen T.H. *et al.*, 2024). The result showed that nano/micro-PG demonstrated a strong effect on both eggs and *J2* nematodes with IC_{50} values of 0.85 and 0.38 mg/ml, respectively, besides, the nematicidal effect of nano/micro-PG was improved by about 4-folds compared with pure PG.

Several studies were conducted in greenhouses and in the fields for investigation of the effect of PG on preventing plant pathogenic diseases and showed its plant-promoting effect and got positive results. In the work of Samer, S.H., *et al*. (2020), PG reduced approximately 50% of the total number of individual *H. schachtii* development in the *Arabidopsis thaliana* plant and also promoted the growth of the plant depending on treatment concentration. Some studies also assessed the role of PG on root-knot nematode in the greenhouse condition. Omnia, M.M., et al. (2020) used the culture broth and culture filtrate of *S. marcescens* for testing the effect against *Meloidogyne incognita* inhibition in-vivo on tomato seedlings and found that all the treatments showed a significant decrease in the nematode population, in soil and tomato root. The shoot and root lengths and plant biomass were found to increase significantly in comparison to that in the untreated plants. In the study conducted by Nguyen, D.N., *et al*. (2020), the fermented culture broth of *S. marcescens* TNU02 with high PG content (at the treatment dose of 80 mL) was used for testing the nematicidal effect against *M. incognita* on the black pepper plant model in greenhouse conditions and showed potential effect against nematodes in soil and pepper root with mortality rates of 85% and 70%, respectively. Forty mL and 80 mL of the fermented culture broth had a more potent plant-promoting effect than other treatments at other concentrations. Recently, purified PG was assessed for its effect on orange orchards Asian *Citrus psyllid* (Wei H. *et al*., 2021) and reported that at 10% emulsifiable concentration demonstrated more effectiveness with inhibition values up to 70-100% than other concentrations. The potency recorded in July and

August was better than that recorded in October.

3. INSECTICIDAL EFFECT OF PG

In the aspect of insect management, PG was reported inhibition against some insects such as *Plutella xylostella*, *Spodoptera litura, Adoxophyes honmai* (Asano S. *et al*., 1999; Wang S.L. *et al*., 2012), *Drosophila* (Wang S.L. *et al*., 2012; Liang T.W. *et al*., 2013), *Diaphorina citri* (Wei H. *et al*., 2021), *Spodoptera litura* and *Helicoverpa armigera* (Patil N.G. *et al*., 2013).

Table 1. Nematicidal and Insecticidal effect of PG

Pathogenic strains	Activity unit	Value	Reference
	Nematicidal effect		
Radopholus similis	Anti - *J2* nematode, IC_{50}, mg/ml	0.083	Rahul, S., *et al*. 2014
Meloidogyne javanica	Anti - *J2* nematode, IC_{50}, mg/ml	0.079	Rahul, S., *et al*. 2014
Caenorhabditis elegans	Anti – *J1* nematode, IC_{50} (μM)	0.127	Samer, S.H., *et al*. 2020
Heterodera schachtii	Anti – *J2* nematode, IC_{50} (μM)	13.3	Samer, S.H., *et al*. 2020
Meloidogyne incognita	Anti - *J2* nematode - % (at 100 mg/ml)	84	Omnia, M.M., *et al*. 2020
Meloidogyne incognita	Anti - *J2* nematode, IC_{50}, mg/ml	31.9	Omnia, M.M., *et al*. 2020
Meloidogyne spp.	Anti - *J2* nematode, IC_{50}, mg/ml	0.2	Nguyen, T.H., *et al.* 2022
Meloidogyne spp.	Anti - *J2* nematode, % (at 0.5mg/ml)	96.7	Nguyen, T.H., *et al.* 2022
Meloidogyne spp.	Anti egg-hatching (IC_{50}, mg/mL)	0.32	Nguyen, T.H., *et al.* 2022
Meloidogyne spp.	Anti egg-hatching (%, at mg/ml)	87	Nguyen, T.H., *et al.* 2022
Black pepper *Meloidogyne* spp.	Anti - *J2* nematode, IC_{50}, mg/ml	0.018 0.004*	Nguyen, T.H., *et al.* 2024
Black pepper *Meloidogyne* spp.	Anti egg-hatching (IC_{50}, mg/mL)	0.013 0.003*	Nguyen, T.H., *et al.* 2024
	Insecticidal effect		
Plutella xylostella	The mortality, %, at 8 μg/g diet	100	Asano, S., *et al.* 1999
Spodoptera litura	The mortality, %, at 8μg/g diet	34	Asano, S., *et al.* 1999
Adoxophyes honmai	The mortality, %, at 8μg/g diet	12	Asano, S., *et al.* 1999
Drosophila	Survival rate, %, at 1.2μg/ml	0	Wang, S.L., *et al.* 2012
Drosophila	Anti larval, IC_{50}, (g/L^{-1})	0.23	Wang, S.L., *et al.* 2012
Drosophila	Anti larval, IC_{50}, ppm	230	Liang, T.W., *et al*. 2013
Diaphorina citri	Inhibitory rate of oviposition (%), at 40mg/L	42	Wei, H., *et al*. 2021
Diaphorina citri	Inhibitory rate of egg hatch (%), at at 40mg/L	26	Wei, H., *et al.* 2021
Spodoptera litura	Larval mortality rate (%), at 30mg/ml	100	Patil, N.G., *et al.* 2023
Helicoverpa armigera	Larval mortality rate (%), at 20g/ml	70	Patil, N.G., *et al*. 2023

*Note: * the activity of nano/micro-prodigiosin.*

PG was early evaluated in its effect on several insect species, including *Plutella xylostella*, *Spodoptera litura, Adoxophyes honmai* by Asano, S., *et al*. (1999). Of these PG effectively inhibited *Plutella xylostella* with a great mortality rate of 100% at a tested concentration of 8 μg/g diet, while it showed moderate and low effect against *Spodoptera litura, Adoxophyes honmai* with a mortality rate of 34% and 12%, respectively at the same tested concentration. In the year 2012, Wang, S.L., *et al*. conducted a study concerning the enhanced production of insecticidal prodigiosin from *S. marcescens* TKU011 in media containing squid pens and reporting its potential insecticidal effect against *Drosophila*. The record result indicated that PG showed a high effect on *Drosophila* with a survival rate of 0 % at the tested concentration of 1.2 μg/ml, and the anti *Drosophila* larval effect was recorded with a low IC_{50} value of 0.23 g/L.

Recently, Wei, H. et al. (2021) tested the potential use of PG for the management of *Asian Citrus Psyllid*. The toxicity of PG against nymphs depends on temperature and the most suitable temperature was 30°C based on tested results. This pigment compound was found effective against *Diaphorina citri* and moderate anti-egg hatching with an inhibitory rate of 42% and 26%, respectively. In addition, the treatments with IC_{20} and IC_{50} solution of purified PG at 30°C against adult hoppers were recorded to excrete less honeydew compared with the control. Most recently, Patil, N.G., *et al*. 2023 reported the potential effect of PG against two species of insects, including *Spodoptera litura* and *Helicoverpa armigera* with potential Larval mortality rate of 100% and 70% at the tested concentration of 30 mg/ml and 20 mg/ml, respectively. Though PG was confirmed as an agent having potential in the management of some insects, a few studies on the greenhouse and field conditions were conducted to evaluate the applicability of PG.

4. ANTI PATHOGENIC MICROBES

4.1. Bactericidal effect of PG

Up to date, PG has been reported to be a potential bactericidal agent against numerous pathogenic bacterial strains, such as inhibiting against *P. aeruginosa* (Ma Z. *et al.,* 2024), *E. coli* NCIM 2065, *K. pneumoniae* NCIM 2706, *P. aeruginosa* NCIM 2036, *B. subtilis* NCIM 2545, MRSA ATCC 43300 (Arivuselvam R. *et al*., 2023), *Listeria monocytogenes, Bacillus cereus, Pseudomonas aeruginosa, Salmonella typhimurium, Staphylococcus aureus*, and *Vibrio parahaemolyticus* (Ji K. *et al*., 2019), *Pseudomonas aeruginosa, Staphylococcus aureus* and *Chromobacterium violaceum* (Gohil N. *et al*., 2020), *S. aureus, E. coli and E. faecalis* (Yip C.H. *et al*., 2021). However, almost all previous works evaluated the effect of PG against bacterial strains infected to humans. Few studies assessed the potential application of PG in inhibiting plant pathogenic bacteria. Only one study conducted by Hiroshi, O. *et al.* (1998) tested the potential effect of PG against some plant pathogenic bacteria. In this early report, PG was found most effect against *Clavibacter michiganensis* subsp. *michiganensis* with the maximal allowable concentration (MAC) of 6.3 µg/ml, high inhibition against *Erwinia carotovora* subsp. *carotovora*, *Xanthomonas campetris* pv. *campestris* and *X. campetris* pv. *oryzae* with MAC values in the range of 25-25.5 µg/ml, while it showed moderate inhibition against *Acidovonax avenae, Agrobacterium tumefaciens, E. herbicola*, and *X. campetris* pv. *carotae* with MAC values of 50 µg/ml, and showed a weak effect against other tested bacterial strains with MAC higher than 100 µg/ml (Hiroshi, O. *et al.,* 1998).

4.2. Fungicidal effect of PG

Among bioactivities of PG concerning the application in agriculture, the fungicidal effect was the most widely investigated. To date, PG has been reported for its fungicidal effect against numerous fungi causing harm to many crops (Suryawanshi R.K. *et al*., 2014; Samer S.H. *et al*., 2020; Hiroshi, O. *et al*., 1998; Nobutaka S. *et al*., 2001; Parani K. *et al*., 2008; Duzhak A.B. *et al*., 2012; Sumathi C. *et al*., 2014; Ingrid G.R.M. *et al*., 2015; Jimtha J.C. *et al*., 2017; Alijani Z. *et al*., 2022; Sagar B.S.V. *et al.,* 2019; Nguyen V.B. *et al*., 2023; Nguyen T.H. *et al.,* 2024). The detailed activity against tested fungal strains was summarized in Table 2. The first study evaluating the fungicidal effect of PG was conducted by Hiroshi, O., *et al*. (1998). In this early work, PG was assessed for its effect on 20 pathogenic fungal strains belonging to 6 genera. At the tested concentration of 10 µg/ml, PG showed positive inhibition against all the fungal strains. Of those it highly inhibited some fungi, including *Phytophthora melonis, Phytophthora cactorum, Phytophthora citrophthora, Cochliobolus miyabeanus, Phytophthora infestans* sp. with great growth inhibition values in the range of 83.2-93%, and moderately inhibited *Pythium spinosum, Phytophthora capsici, Rhizoctonia solani* sp., and *Pythium ultimum* with growth inhibition values ranging from 42.2% to 66.4%. The crude PG extracted from *S. marcescens* SR1 tested anti-fungal activity against some fungi using the well-diffusion method and showed good effect on *Helminthosporium sativum, Curvularia lunata*, and *Alternaria alternate* with maximum inhibitory zone of more than 40 nm.

Further studies proved that PG may be a potential fungicide for management some pathogenic fungal strains, including *Didymella applanata* (Duzhak, A.B., *et al*. 2012), *Aspergillus flavus, Fusarium oxysporum* (Suryawanshi, R.K., *et al*. 2014), *Pythium myriotylum, Rhizoctonia solani (*Jimtha, J.C., *et al*. 2017), *Fusarium solani* F04 (Nguyen, V.B., *et al.* 2023), and *C. gloeosporioides* F05 (Nguyen, T.H., *et al*. 2024). Of these, PG showed great inhibition against *Fusarium solani* F04 and *C. gloeosporioides* F05 with maximum inhibition value up to 100%.

The effect of PG on fungal spore germination was also performed in several works. Nobutaka, S., et al. 2001 reported the potent anti-spore germination of PG against *Botrytis cinerea* with an inhibition value of 80%. PG was also found to be highly inhibiting germination of *Colletotrichum nymphaeae* spore up to 100% in the study by Alijani, Z., *et al*. (2017). Recently, PG was also evaluated for its effect on the fungal spore germination of *Fusarium solani* F04 (Nguyen, V.B., *et al*. 2023) and *C. gloeosporioides* F05 (Nguyen, T.H., *et al*. 2024) and showing moderate inhibition values of 50% and 60%, respectively.

For further evaluating the potential application of PG, several studies were conducted in the conditions of greenhouses and the fields (Alijani, Z., *et al*., 2022; Roberts, D.P. *et al*., 2021). Alijani, Z., *et al*. (2022) conducted the study using, a culture fluid containing PG for the management of *Colletotrichum nymphaeae* causing Strawberry anthracnose and found that the culture fluid significantly reduced the fruit decay with an efficacy value of 48.60%. Among the treatment methods, plant spraying of culture fluid was found better method than the drenching soil method with recorded biocontrol efficacy percentages of 72.22% and 44.44%, respectively. In another study by Roberts, D.P. *et al*. (2021), purified PG was used for controlling the damping-off of cucumber caused by *Pythium ultimum.* The cucumber seeds treated by PG generated the plants with greater development compared to the nontreated and control groups. Though the fungicidal effect of PG was widely investigated in invitro conditions, the evaluation in greenhouses and the fields is quite limited. Thus, for applications of PG in agriculture, more studies on the conditions of greenhouses and in the fields should be further conducted.

Table 2. Fungicidal effectof PG

Pathogenic strains	Activity unit	Value	Reference
Phytophthora melonis	Growth inhibition (%)	93.0	Hiroshi, O., *et al.* 1998
Phytophthora cactorum	Growth inhibition (%)	89.7	Hiroshi, O., *et al.* 1998
Phytophthora citrophthora	Growth inhibition (%)	85.1	Hiroshi, O., *et al.* 1998
Cochliobolus miyabeanus	Growth inhibition (%)	83.3	Hiroshi, O., *et al.* 1998
Phytophthora infestans sp.	Growth inhibition (%)	83.2	Hiroshi, O., *et a*l. 1998
Pythium spinosum	Growth inhibition (%)	66.4	Hiroshi, O., *et al.* 1998
Phytophthora capsici	Growth inhibition (%)	63.5	Hiroshi, O., *et al.* 1998
Rhizoctonia solani sp.	Growth inhibition (%)	52.9	Hiroshi, O., *et al.* 1998
Pythium ultimum	Growth inhibition (%)	44.2	Hiroshi, O., *et al.* 1998
Pyricularia oryzae	Growth inhibition (%)	28.8	Hiroshi, O., *et al*. 1998
Fusarium oxysporum f. sp.*cucumerinum*	Growth inhibition (%)	23.5	Hiroshi, O., *et al.* 1998
Fusarium oxysporum f. sp. *cepae*	Growth inhibition (%)	17.8	Hiroshi, O., *et al*. 1998
Fusarium oxysporum f .sp. *allii*	Growth inhibition (%)	17.6	Hiroshi, O., *et al.* 1998
Phytophthora castaneae	Growth inhibition (%)	74.5	Hiroshi, O., *et al*. 1998
Fusarium oxysporum f. sp.*raphani*	Growth inhibition (%)	16.3	Hiroshi, O., *et al*. 1998
Fusarium solani var. Coeruleum	Growth inhibition (%)	14.3	Hiroshi, O., *et al*. 1998
Fusarium ventricosum	Growth inhibition (%)	11.1	Hiroshi, O., *et al.* 1998
Fusarium moniliforme	Growth inhibition (%)	5.9	Hiroshi, O., *et al.* 1998
Fusarium roseum	Growth inhibition (%)	5.8	Hiroshi, O., *et al.* 1998
Fusarium oxysporum f. sp. *spinaciae*	Growth inhibition (%)	1.2	Hiroshi, O., *et al.* 1998
Botrytis cinerea	Anti-spore germination (%)	80	*Nobutaka*, S., *et al.* 2001
Helminthosporium sativum	Diameter of inhibition zone (mm)	42	Parani, K., *et al.* 2008
Curvularia lunata	Diameter of inhibition zone (mm)	40	Parani, K., *et al*. 2008

Pathogenic strains	Activity unit	Value	Reference
Alternaria alternate	Diameter of inhibition zone (mm)	40	Parani, K., *et al*. 2008
Fusarium oxysporum	Diameter of inhibition zone (mm)	30	Parani, K., *et al*. 2008
Cercospora apii	Diameter of inhibition zone (mm)	24	Parani, K., *et al*. 2008
Rhizoctonia solani	Diameter of inhibition zone (mm)	11	Parani, K., *et al*. 2008
Didymella applanata	IC_{50} - nmol/mL	2.5	Duzhak, A.B., *et al*. 2012
Aspergillus flavus	MIC-µg/mL	10	Suryawanshi, R.K., *et al*. 2014
Fusarium oxysporum	MIC-µg/mL	8	Suryawanshi, R.K., *et al*. 2014
Aspergillus niger	MIC-µg/mL	230	Sumathi, C., *et al*. 2014
Fusarium moniliforme	MIC-µg/mL	210	Sumathi, C., *et al*. 2014
Mycosphaerella fijiensis	IC_{50} - µg/mL)	996	Ingrid, G.R.M., *et al*. 2015
Mycosphaerella fijiensis	Inhibits growing germ tubes (%)	63	Ingrid, G.R.M., *et al*. 2015
Pythium myriotylum	Growth inhibition (%)	71.33	Jimtha, J.C., *et al*. 2017
Rhizoctonia solani	Growth inhibition (%)	61.33	Jimtha, J.C., *et al*. 2017
Sclerotium rolfsii	Growth inhibition (%)	49.33	Jimtha, J.C., *et al*. 2017
Phytophthora infestans	Growth inhibition (%)	48.66	Jimtha, J.C., *et al*. 2017
Fusarium oxysporum	Growth inhibition (%)	31	Jimtha, J.C., *et al*. 2017
Colletotrichum nymphaeae	Inhibits germination (%)	100	Alijani, Z., *et al*. 2017
Alternaria sp.	MIC-µg/mL	80	Sagar, B.S.V., *et al*. 2019
Fusarium sp.	MIC-µg/mL	160	Sagar, B.S.V., *et al*. 2019
Phoma lingam	Hyphal growth diameter (%)	25	Samer, S.H., *et al*. 2020
Sclerotinia sclerotiorum	Hyphal growth diameter (%)	60	Samer, S.H., *et al*. 2020
Fusarium solani F04	Mycelial growth inhibition (%)	100	Nguyen, V.B., *et al*. 2023
Fusarium solani F04	Spore germination inhibition (%)	50	Nguyen, V.B., *et al*. 2023
G. butleri F07	Mycelial growth inhibition (%)	8.55	Nguyen, V.B., *et al*. 2023
P.mangiferae F08	Mycelial growth inhibition (%)	3.05	Nguyen, V.B., *et al*. 2023
Fusarium oxysporum F10	Mycelial growth inhibition (%)	19.69	Nguyen, V.B., *et al*. 2023
Fusarium incarnatum F15	Mycelial growth inhibition (%)	6.97	Nguyen, V.B., *et al*. 2023
P.lilacinum F01	Mycelial growth inhibition (%)	10	Nguyen, T.H., *et al*. 2024
Fusarium solani F02	Mycelial growth inhibition (%)	5	Nguyen, T.H., *et al*. 2024

Pathogenic strains	Activity unit	Value	Reference
C. gloeosporioides F05	Mycelial growth inhibition (%)	100	Nguyen, T.H., *et al*. 2024
C. gloeosporioides F05	Spore germination inhibition (%)	60	Nguyen, T.H., *et al*. 2024
Fusarium incarnatum F06	Mycelial growth inhibition (%)	7	Nguyen, T.H., *et al*. 2024
Pestalotiopsis mangiferae F08	Mycelial growth inhibition (%)	5	Nguyen, T.H., *et al*. 2024

5. THE MECHANISMS ACTION OF PG

Concerning the mechanism action of PG on nematodes, it was suggested by Roser F. *et al*. (2007) that the mode of action of PG may be due to its possessing proton sequestering ability (Roser *et al*., 2007) which affects intracellular pH gradient. Prodigiosin also affects mitochondrial ATP synthesis; it causes a reduction in ATP production without decreasing oxygen consumption. Recently, the molecular docking and enzyme inhibition assays conducted by Nguyen, T.H., *et al*. 2024 suggested the possible pathway of the nematicidal effect of PG via inhibition of acetylcholinesterase. In an earlier report by Nguyen, V.B., *et al*. (2021), PG showed effective inhibition against this enzyme via experimental study.

It was evidenced that the inhibition effect of *Serratia marcescens* on zygomycetes and ascomycetes fungi via the role of PG. This compound was found to increase the permeability of cell membranes, then *Serratia marcescens* may be easily infiltrated inside fungal hyphae (Hazarika D.J. *et al*., 2020). Some recent virtual studies were conducted for an inside understanding of the molecular mechanism action of PG against some pathogenic fungal strains (Nguyen V.B. *et al*., 2023; Nguyen T.H. *et al*., 2024). The molecular docking result indicated that PG possibly inhibited *F. solani* via effective binding to the protein 3QPC targeting anti-*F. solani* with good binding energy (DS, -9.2 kcal/mol) and an acceptable RMSD value (0.94 Å) (Nguyen, V.B. *et al.* 2023). In recent work, PG was found highly interacted with multiple target proteins (CDC42, CYP51, CAS2, Pectate lyase B, and Beta tubulin) targeting inhibition against *C. gloeosporioides* via docking simulation (Nguyen, T.H., *et al.* 2024).

The antibacterial effect of PG against various bacterial strains has been reported, and antibacterial mechanisms such as induction of autolysin in *Bacillus* species and formation of ROS in *Pseudomonas aeruginosa* have been suggested (Danevcic T. *et al*., 2016; Kimyon, O. *et al*. 2016). In PG-treated bacterial cells, the outer membrane, however, becomes leaky. Cells had severely decreased respiration activity. In PG-treated cells protein and RNA synthesis were inhibited, and cells were elongated but could not divide (Danevčič T. *et al*., 2016). Recently, in a report by Yip C.H. *et al*. (2021), PG was found to be a potent bactericidal agent with higher selectivity towards gram-positive bacteria, and the possible mechanisms of action of PG were also proposed. These mechanisms may include higher prodigiosin cell permeability through interaction with the peptidoglycan structure of gram-positive bacteria, disruption of bacterial protease secretion or proteolytic activity as well as reduction in biofilm formation.

6. CONCLUSIONS

This study provided a comprehensive overview of the potential effect of prodigiosin against plant pathogenic organisms. PG was evidenced as a potent nematicidal, insecticidal, fungicidal, and bactericidal compound, which has promising applications in agriculture. Though the bioactivities via in-vitro tests were widely investigated, the mechanism action as well as the evaluation in greenhouses and the fields are quite limited. Thus, for applications of this compound in agriculture, more studies on the conditions of greenhouses and the fields should be further conducted.

AUTHOR CONTRIBUTION

Conceptualization, resources, writing original draft preparation, NVB; project administration, NVB; writing review, and editing, NVB and TBP.

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TỔNG QUAN VỀ TIỀM NĂNG ỨNG DỤNG CỦA PRODIGIOSIN TRONG KIỂM SOÁT SINH VẬT GÂY BỆNH THỰC VẬT

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TÓM TẮT

Prodigiosin (PG) là một sắc tố đỏ chủ yếu được sinh tổng hợp bởi vi khuẩn *Serratia marcescens*. Hợp chất màu này có tiềm năng ứng dụng trong nhiều lĩnh vực nên được quan tâm nghiên cứu. Đã có nhiều bài báo tổng quan về sinh tổng hợp và tiềm năng ứng dụng của PG. Tuy nhiên, hầu hết các bài báo tập trung trình bày và thảo luận về tiềm năng ứng dụng của PG trong y học. Cho đến nay, PG đã được nghiên cứu rộng rãi về ứng dụng trong nông nghiệp với hoạt tính kháng tiềm năng trên các tác nhân gây bệnh thực vật như tuyến trùng, nấm và vi khuẩn. Để nhấn mạnh tiềm năng ứng dụng PG trong nông nghiệp, bài báo tổng quan này trình bày và thảo luận về các ứng dụng của PG trong nông nghiệp thông qua các nghiên cứu đánh giá hoạt tính trong ống nghiệm, thử nghiệm nhà kính và nghiên cứu thực địa. Cơ chế hoạt động của PG cũng được trình bày trong báo cáo này.

Từ khóa: *Tác dụng kháng khuẩn, tác dụng kháng nấm, tác dụng diệt tuyến trùng, Prodigiosin, S. Marcescens.*

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