INHIBITORY EFFECTS OF THE CRUDE EXTRACT FROM Xylaria sp. ON SEVERAL PATHOGENIC FUNGI

NURUL ASYIQIN BINTI AZIZI

FH 2019 46

INHIBITORY EFFECTS OF THE CRUDE EXTRACT FROM *Xylaria* sp. ON SEVERAL PATHOGENIC FUNGI

By

NURUL ASYIQIN BINTI AZIZI

A Project Report Submitted in Partial Fulfilment of the Requirements

For the Degree of Bachelor of Forestry Science in the

Faculty of Forestry

Universiti Putra Malaysia

2019

DEDICATION

"Do not say it is wheat until you harvest it." – Arabic proverb

I am dedicating all of my hard works for my beloved family, Forestry Faculty and my friends, especially to the person who always be by my side and keep on motivating me to strive for excellence. Upon this completed thesis, I am cherishing over myself for my hard work and commitment.

Dear my beloved:

Dad, Azizi Bin Rosli and mum, Kornia Binti Ahmat

Thank you for all the motivations, hard works, efforts and loves. I am lucky enough to be growing up in this family. My home is such a fortress, my safety hide-out, that I will always look for it whenever I feel unmotivated.

Project supervisor, Prof. Dr. Rozi Mohamed

Thank you for showing me what is a great and respected teacher looks like. I will never forget the first impression you left us in our first class.

Baba (my late Grandpa)

I am dedicating my Bachelor's degree for you. This is your dream to see one of your grandchildren to have an achievement in the tertiary education. I thought that we still have much time to make you attend my graduation day. However, Allah loves you more than I can ever love you.

ABSTRACT

The genus *Xylaria* belongs to the phylum Ascomycota from the kingdom Fungi. A majority of the *Xylaria* species are known plant endophytes. Some have properties against phytopathogenic fungi, however, scientific evidence on the presence of the active compounds in *Xylaria* spp. is limited. Here, the inhibitory effects of an isolate of *Xylaria* sp. were demonstrated against three species of phytopathogenic fungi. *Xylaria* sp. crude extract (XCE) was obtained from a 14-day Potato Dextrose Broth (PDB) culture using ethyl acetate (EtOAc) as solvent. Non-volatile assays revealed that the XCE had the strongest inhibitory effect on the growth of *Ceratocystis fimbriata* from 79% to 100% rate of antifungal activity (AFA), followed by *Fusarium oxysporum,* 26% to 53%. There was little to no inhibition against *Phellinus noxius*. The XCE was further purified using a silica gel column yielding six different eluents (XH, XHD, XD, XDM, XMH, XM) and tested against *Ceratocystis fimbriata* in disc-diffusion assay. XH gave the highest average AFA (26%), followed by XDM (21%), while the other eluents exerted between 9% to 17% inhibition. Further studies should identify the potential compounds in XH against *C. fimbriata.*

ABSTRAK

Genus *Xylaria* berada di dalam filum Ascomycota yang terdiri daripada kumpulan Kulat. Majoriti spesis daripada genus *Xylaria* dikenali sebagai endofit tumbuhan. Sebahagian kulat dari genus ini mempunyai sifat melawan kulat patogenik yang menyerang tumbuhan, namun begitu, pembuktian saintifik mengenai kewujudan kompone aktif di dalam *Xylaria* spp. adalah terbatas. Maka, kajian ini mendemonstrasikan kesan penghalangan tumbesaran daripada ekstrak mentah isolasi *Xylaria* sp. terhadap tiga spesis kulat patogenik tumbuhan. Ekstrak mentah *Xylaria* sp. (XCE) ini diperolehi daripada kultur 'Potato Dextrose Broth' (PDB) selama 14 hari dan diekstrak menggunakan etil asetat (EtOAc) sebagai pelarut. Ujian 'non-volatile' mendapati bahawa kesan penghalangan terbaik berlaku *Ceratocystis fimbriata* dengan kadar aktiviti antikulat (AFA) sebanyak 79% hingga 100%, diikuti dengan kesan sederhana AFA ke atas *Fusarium oxysporum,* 26% hingga 53%. Walaupun begitu, *Phellinus noxius* menunjukkan kesan AFA paling rendah hingga tiada kesan. Ekstrak EtOAc dilakukan pengasingan lanjut dengan menggunakan kolum gel silika Sep-pak kepada enam eluen (XH, XHD, XD, XDM, XMH, XM). Keenam-enam eluen tersebut diuji menggunakan 'disk-diffusion assays' ke atas *Ceratocystis fimbriata*, memberi keputusan bahawa kesan AFA terbaik adalah daripada XH dengan catatan 26% kesan terhadap tumbesaran kulat, diikuti oleh XDM sebanyak 21% serta meninggalkan baki empat eluens lain dengan kadar AFA di antara 9% hingga 17%. Kajian lanjut perlu diadakan bagi mengenalpasti kompaun yang terdapat di dalam eluen XH terhadap *C. fimbriata*.

ACKNOWLEDGEMENTS

I would like to express my endless gratitude to my supervisor, Prof. Dr. Rozi Mohamed for her guidance throughout this project. I was able to conduct and complete this study due to her support. I hope this study could be useful for the forest industry sector. Thank you for all the knowledge and time spent, guidance with patience and for the constructive advices to make us into a good student and researcher in the future. You are a great teacher that had all my respects since the first class I have learnt with you.

I would like to thank my laboratory mate, Rasyiffa' Hayati Binti Rasidan. We have spend our time and thought together, to figure out how to solve a problem, improving our skills and sharing the ideas throughout this project. I appreciate your hard work and commitments, we had go through thick and thin until we finish the project successfully.

I am very grateful to have met Dr. Lee Syiou Yih, Muhammad Syahmi Hishamuddin, Ahmad Syazwan Samsuddin, Tuan Noraida Tuan Hamzah and Mdm. Noorfaizan Anuar (Science Officer). Thank you for all the tips, guidance, knowledge and advices since the first day I put my step into our beloved Forest Biotechnology Laboratory. These people have makes my day better, increase my knowledge greater and thought me to be nicer. Thank you for helping and guiding me with the laboratories works and help me improving the quality of my writing. I cherish all the knowledge that I had acquired from them to be use in the future. May Allah grant them with good deeds.

Finally and foremost, I would like to thanks my family and friends for their extra ordinary support, including moral and physical supports throughout this research and the whole four years of study. May Allah grant us with His Grace and Mercy.

APPROVAL SHEET

I certify that this research project report entitled “Inhibitory Effects Of The Crude Extract From *Xylaria* sp. On Several Pathogenic Fungi” by Nurul Asyiqin Binti Azizi has been examined and approved as a partial fulfilment of the requirements for the Degree of Bachelor of Forestry Science in the Faculty of Forestry, Universiti Putra Malaysia.

:

_____

Prof. Dr. Rozi Mohamed
Faculty of Forestry
Universiti Putra Malaysia
(Supervisor)

_____

Prof. Dr. Mohamed Zakaria Bin Hussin
Dean
Faculty of Forestry
Universiti Putra Malaysia

Date: May 2019

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

^{o} C	degree centigrade
%	percentage
x	times
f. sp.	forma specialis
ff. spp.	formae speciales
FOSC	*Fusarium oxysporum* species complex
DNA	Deoxyribonucleic Acid
K	coefficient
gcm^{-3}	gram per centimetre cubic
µl	microliter
cm	centimeter
mm	milimeter
ml	mililiter
gm	gram
AFA	Antifungal activity
rpm	revolution per minute
PDA	Potato Dextrose Agar
PDB	Potato Dextrose Broth
PDA/XF	PDA with filtered *Xylaria* sp. liquid culture
XF/PDA	PDA with filtered *Xylaria* sp. liquid culture of different concentration
MIC	Minimum Inhibitory Concentration
NMR	Nuclear Magnetic Resonance
bp	boiling point
EtOAc	ethyl acetate
MeOH	methanol
C_6H_{14}	hexane
CH_2Cl_2	dichloromethane
XFC	Xylaria filtered culture with different volume
XF	*Xylaria* filtered culture

XCE	*Xylaria* crude extract
XH	*Xylaria* in Hexane
XHD	*Xylaria* in Hexane + Dichloromethane
XD	*Xylaria* in Dichloromethane
XDM	*Xylaria* in Dichloromethane + Methanol
XM	*Xylaria* in Methanol
XMH	*Xylaria* in Methanol and Hexane
CC	Column chromatograph
HPLC	High Performance Liquid Chromatography

CHAPTER ONE

INTRODUCTION

1.1 General Background

1.1.1 Endophyte Fungi and Secondary Metabolites

Endophyte is a biological organism inhabiting intercellularly or intracellularly of the host body. Not giving any symptoms of the occupation nor visible to the naked eyes are the main characteristics of the endophytes. However, to gain something means to give something. In order to enable the inhabiting in the host body, the endophytes produce functional secondary metabolites as the exchange materials. The functional metabolites are produce even before they starting to colonize the host living and healthy tissue to induce a balance chemical reaction between the host and the endophytes (Kusari et al., 2012). The symbiosis must be unique and beneficial to the both party. The secondary metabolites produced always favourable and beneficial to the host. Generally, the secondary metabolites produce by the endophytes either for promoting growth of the host by producing phytohormone such as cytokines or/and for improvement ecological adaptability of the host such as protecting from pest, phytopathogen, microbial activity, competition with other tree and even help in tolerate such extreme condition (Tan and Zou, 2001).

1.1.2 Secondary Metabolites Produced by *Xylaria* sp.

Endophytes of *Xylaria* sp. attract the interest of researchers and become the focus in the functional secondary metabolites study. Exploration and compilation of databases of the endophytes species is actively carry out by researchers from China, India and many other countries from different region and niche area. Endophyte *Xylaria* sp. is an attractive subject of study that always surprise the researcher with novel compounds from its secondary metabolites. For example, a study of endophytes *Xylaria* sp. on mangrove from South China Sea Coast have found five novel unique compounds of xyloketals named as xyloketals A, B, C, D and E and one known compound (Lin et al., 2001). Another study of secondary metabolites produced by *Xylaria* sp. isolated from the stem of *Isodon sculponeatus* afforded ten compounds (Chen et al., 2018). Six of the compounds are new compounds, xylariahgins A–F, two new natural products, along with two known compounds. They showed positive inhibitory effects against human tumor cell lines. Recent research on *Xylaria* sp. has made a discovery of a new compound known as Compound 1 with antimicrobial activities against two species, *Escherichia coli* and *Staphylococcus aureus* with MIC values 50 g/mL (Zheng et al., 2018).

Griseofulvin is a popular compounds used as an antifungal antibiotic for the treatment of mycotic diseases of humans and veterinary animals. There was a research conducted where the purpose of the study was to identify a griseofulvin-producing endophytic fungus from *Abies holophylla* through the

secondary metabolites analysis. Based on nuclear ribosomal ITS1-5.8S-ITS2 sequence analysis, the fungus identified as *Xylaria* sp. The griseofulvin showed high *in vivo* and *in vitro* antifungal activity, and effectively controlled the development of rice blast (*Magnaporthe grisea*), rice sheath blight (*Corticium sasaki*), wheat leaf rust (*Puccinia recondita*), and barley powdery mildew (*Blumeria graminis* f. sp. *hordei*) (Park et al., 2005).

1.2 Problem Statement

Disease outbreak in commercial tree species caused by pathogenic fungi is a major economic downturn, especially in the large-scale plantation. Short-term solution for the disease outbreaks could easily handle by the application of chemical derived fungicide. However, the resistance of the pathogen may build up to the chemical overtime due to the rapid evolution of fungi genetics. Furthermore, the action modes of fungicide have never been well-classified, and the side effects of the chemicals are not fully understood. Artificial chemical derived fungicides usage may have negative impacts that are difficult to predict towards the plants and environments (Yang et al., 2011).

Xylaria sp. an endophyte of the mangrove tree, has been shown to contain bioactive compounds (Hamzah et al., 2018). Mangrove area is the shallow tidal area with high intensity of salinity in the water. Trees inhabiting this area possess strong viability to survive in such extreme condition (Yu et al.,

2009). There is a possibility of the tree's survival due to the contribution of the functional secondary metabolites produced by the endophytic fungi. This study was to identify whether the secondary metabolites produced by *Xylaria* sp. have the ability to inhibit the growth of several pathogenic fungi, of economic importance. Positive results from the test may further the screening process to acquire the most effective fraction that can inhibit the growth of the pathogenic fungi. Novel compounds from endophytic fungi may serve as an alternative fungicide to control the outbreak of diseases in agriculture and forest plantations.

1.3 Research Objectives

- To determine inhibitory effect of the crude extract from *Xylaria* sp. on three species of phytopathogenic fungi, *Ceratocystis fimbriata, Fusarium oxysporum* and *Phellinus noxius*
- To identify purified eluents from the crude extract, which are active against the selected pathogens

REFERENCES

Abdulkhair, W. M., & Alghuthaymi, M. A. (2016). Plant Pathogens. In *Plant Growth*. IntechOpen.

Alurappa, R., Chowdappa, S., Narayanaswamy, R., Sinniah, U. R., Mohanty, S. K., & Swamy, M. K. (2018). Endophytic fungi and bioactive metabolites production: an update. In Patra J., Das G., Shin HS. (eds), *Microbial Biotechnology* (pp. 455-482). Singapore, Springer.

Ashiglar, S. M., Cannon, P. G., & Klopfenstein, N. B. (2015). Aggressive root pathogen Phellinus noxius and implications for western Pacific Islands. In: Murray, Michael; Palacios, Patsy, comps. Proceedings of the 62nd annual Western International Forest Disease Work Conference; September 8-12, 2014; (pp. 79-81) .Cedar City, Utah.

Atanasov, A. G., Waltenberger, B., Pferschy-Wenzig, E. M., Linder, T., Wawrosch, C., Uhrin, P., Temmi, V., Wang, L., Schwaiger, S., Heiss, E. H., Schuster, D., Breuss, J.M., Bochkov, V., Mihovilovic, M. D., Kopp, B., Bauer, R., Dirsch, V.M., Stuppner, H., & Rollinger, J. M. (2015). Discovery and resupply of pharmacologically active plant-derived natural products: A review. *Biotechnology Advances*, 33(8), 1582-1614.

Barnes, I., Fourie, A., Wingfield, M.J., Harrington, T.C., McNew, D.L., Sugiyama, L.S., Luiz, B.C., Heller, W.P., & Keith, L.M. (2018). New Ceratocystis species associated with rapid death of Metrosideros polymorpha in Hawai`i. *Persoonia, 40*, 154-181.

Bartz, F. (2007). Pathogen Profile: *Phellinus noxius* (Corner) G. H. Cunningam. Retrieved from https://projects.ncsu.edu/cals/course/pp728/Phellinus/Phellinus_noxius.html. Accessed on 24 January 2019.

Bayman, P., Angulo-Sandoval, P., Báez-ortiz, Z., & Lodge, D. J. (1998). Distribution and dispersal of Xylaria endophytes in two tree species in Puerto Rico. *Mycological Research*, *102*(8), 944-948.

De Beer, Z. W., Duong, T. A., Barnes, I., Wingfield, B. D., & Wingfield, M. J. (2014). Redefining Ceratocystis and allied genera. *Studies in Mycology*, *79*, 187-219.

Brunner, F., & Petrini, O. (1992). Taxonomy of some Xylaria species and xylariaceous endophytes by isozyme electrophoresis. *Mycological Research*, *96*(9), 723-733.

Cantwell, F. F., & Losier, M. (2002). Liquid—liquid extraction. In *Comprehensive Analytical Chemistry* (Vol. 37, pp. 297-340). Elsevier.

Chacko, R. J., & Rogers, J. D. (1981). Cultural characteristics of some species of Xylaria. *Mycologia*, *73*(3), 415-428.

Chen, R., Tang, J. W., Li, X. R., Liu, M., Ding, W. P., Zhou, Y. F., Wang, W. G., Sun, H. D., Du, X., & Puno, P. T. (2018). Secondary Metabolites from the Endophytic Fungus Xylaria sp. hg1009. *Natural Products and Bioprospecting*, *8*(2), 121-129.

Cos, P., Vlietinck, A. J., Berghe, D. V., & Maes, L. (2006). Anti-infective potential of natural products: how to develop a stronger in vitro 'proof-of-concept'. *Journal of Ethnopharmacology*, *106*(3), 290-302.

Das, K., Tiwari, R. K. S., & Shrivastava, D. K. (2010). Techniques for evaluation of medicinal plant products as antimicrobial agent: Current methods and future trends. *Journal of Medicinal Plants Research*, *4*(2), 104-111.

Delgoda, R., & Murray, J. E. (2017). Evolutionary perspectives on the role of plant secondary metabolites. In *Pharmacognosy* (pp.93-100). Academic Press.

Elias, L.M., Fortkamp, D., Sartori, S.B., Ferreira, M.C., Gomes, L.H., Azevedo, J.L., Montoya, Q.V., Rodrigues, A., Ferreira, A. G. & Lira, S.B. (2018). The potential of compounds isolated from Xylaria spp. as antifungal agents against anthracnose. *Brazilian Journal of Microbiology*, *49*(4), 840-847.

Gest, H. (2009). *Historical adventures in scientific discovery: Microbiology /biochemistry*. Bloomington, Indiana University Press.

Gimenez, C., Cabrera, R., Reina, M., & Gonzalez-Coloma, A. (2007). Fungal endophytes and their role in plant protection. *Current Organic Chemistry*, *11*(8), 707-720.

Hadacek, F., & Greger, H. (2000). Testing of antifungal natural products: methodologies, comparability of results and assay choice. *Phytochemical analysis*, *11*(3), 137-147.

Hamzah, T. N. T., Lee, S. Y., Hidayat, A., Terhem, R., Faridah-Hanum, I., & Mohamed, R. (2018). Diversity and characterization of endophytic fungi isolated from the tropical mangrove species, Rhizophora mucronata, and identification of potential antagonists against the soil-borne fungus, Fusarium solani. *Frontiers in Microbiology*, *9*, 1707.

Heath, M. C. (1981). A generalized concept of host-parasite specificity. *Phytopathology*, *71*(11), 1121-1123.

Jones, T. M., Anderson, A. J., & Albersheim, P. (1972). Host-pathogen interactions IV. Studies on the polysaccharide-degrading enzymes secreted by Fusarium oxysporum f. sp. lycopersici. *Physiological Plant Pathology*, *2*(2), 153-166.

Jones, W. P., & Kinghorn, A. D. (2006). Extraction of plant secondary metabolites. In SD Sarker, Z Latif, AI Gray (Eds), 2nd edn. Natural products isolation (pp. 323–351). *Methods in Biotechnology*, vol 20. Totowa, Humana Press.

Kang, S., Demers, J., del Mar Jimenez-Gasco, M., & Rep, M. (2014). Fusarium oxysporum. In *Genomics of Plant-Associated Fungi and Oomycetes: Dicot Pathogens* (pp. 99-119). Heidelberg, Springer

Karthikeyan, B., Abitha, B., Henry, A. J., Sa, T., & Joe, M. M. (2016). Interaction of rhizobacteria with arbuscular mycorrhizal fungi (AMF) and their role in stress abetment in agriculture. In *Recent Advances on Mycorrhizal Fungi* (pp. 117-142). Cham, Springer.

Kusari, S., Hertweck, C., & Spiteller, M. (2012). Chemical ecology of endophytic fungi: origins of secondary metabolites. *Chemistry & Biology*, *19*(7), 792-798.

Lalitha, M. K. (2004). Manual on antimicrobial susceptibility testing. *Performance standards for antimicrobial testing: Twelfth Informational Supplement*, *56238*, 454-456.

Liang, Y., Xu, W., Liu, C., Zhou, D., Liu, X., Qin, Y., Cao, F., Li, J., Yang, R., & Qin, J. (2018). Eremophilane sesquiterpenes from the endophytic fungus Xylaria sp. GDG-102. *Natural Product Research*, *33*(9), 1304-1309.

Lin, Y., Wu, X., Feng, S., Jiang, G., Luo, J., Zhou, S., Vrijmoed, L. L. P., Jones, E. B. G., Krohn, K., Steingrover, K., & Zsila, F. (2001). Five unique compounds: xyloketals from mangrove fungus Xylaria sp. from the South China Sea coast. *The Journal of Organic Chemistry*, *66*(19), 6252-6256.

Liu, X., Dong, M., Chen, X., Jiang, M., Lv, X., & Zhou, J. (2008). Antimicrobial activity of an endophytic Xylaria sp. YX-28 and identification of its antimicrobial compound 7-amino-4-methylcoumarin. *Applied Microbiology and Biotechnology*, *78*(2), 241-247.

Lomelí-Ramírez, M. G., Dávila-Soto, H., Silva-Guzmán, J. A., Ochoa-Ruíz, H. G., & García-Enriquez, S. (2016). Fungitoxic Potential of Extracts of Four Pinus spp. Bark to Inhibit Fungus Trametes versicolor (L. ex. Fr.) Pilát. *BioResources*, *11*(4), 10575-10584.

Magaldi, S., Mata-Essayag, S., De Capriles, C. H., Perez, C., Colella, M. T., Olaizola, C., & Ontiveros, Y. (2004). Well diffusion for antifungal susceptibility testing. *International Journal of Infectious Diseases*, *8*(1), 39-45.

Mohd Farid, A., Lee, S.S., Maziah, Z., Rosli, H. & Norwati, M. (2005). Basal Root Rot, a new Disease of Teak (*Tectona grandis*) in Malaysia caused by Phellinus noxius. *Malaysian Journal of Microbiology, 1*(2), 40-45.

Mori, M., Aoyama, M., Doi, S., Kanetoshi, A., & Hayashi, T. (1995). Antifungal activity of bark extracts of conifers. *European Journal of Wood and Wood Products*, *53*(2), 81-82.

Nett, J. E. & Andes, D. R. (2016). Antifungal agents: spectrum of activity, pharmacology, and clinical indications. *Infectious Disease Clinics*, *30*(1), 51-83.

Nevalainen, H., Kautto, L., & Te'o, J. (2014). Methods for isolation and cultivation of filamentous fungi. In *Environmental Microbiology* (pp. 3-16). Totowa, Humana Press.

Oliveira, C. M., Regasini, L. O., Silva, G. H., Pfenning, L. H., Young, M. C., Berlinck, R. G., & Araujo, A. R. (2011). Dihydroisocoumarins produced by Xylaria sp. and Penicillium sp., endophytic fungi associated with Piper aduncum and Alibertia macrophylla. *Phytochemistry letters*, *4*(2), 93-96.

Park, J-H., Gyung, J. C., Hyang, B. L., Kyoung, M. K., Hack, S.J., Lee, S-W., Kyoung, S.J., Kwang, Y.C., & Kim, J-C., (2005). Griseofulvin from *Xylaria* sp. Strain F0010, an endophytic fungus of Abies holophylla and its antifungal activity against plant pathogenic fungi. *Journal of Microbiology and Biotechnology*, *15*(1), 112-117.

Petrini, L. (1985). Xylariaceous fungi as endophytes. *Sydowia*, *38*, 216-234.

Pongcharoen, W., Rukachaisirikul, V., Phongpaichit, S., Kühn, T., Pelzing, M., Sakayaroj, J., & Taylor, W. C. (2008). Metabolites from the endophytic fungus Xylaria sp. PSU-D14. *Phytochemistry*, *69*(9), 1900-1902.

Quiroga, E. N., Sampietro, A. R., & Vattuone, M. A. (2001). Screening antifungal activities of selected medicinal plants. *Journal of Ethnopharmacology*, *74*(1), 89-96.

Rodrigues, K. F. (1993). Endophytic species of Xylaria: cultural and isozymic studies. *Sydowia*, *45*, 116-138.

Shen, B. (2015). A new golden age of natural products drug discovery. *Cell, 163*(6), 1297-1300.

Silva, G. H., de Oliveira, C. M., Teles, H. L., Pauletti, P. M., Castro-Gamboa, I., Silva, D. H., Bolzani, V. S., Young, M. C. M., Costa-Neto, C. M., Pfenning, L. H., Araujo, A. R., & Berlinck, R. G. (2010). Sesquiterpenes from Xylaria sp., an endophytic fungus associated with Piper aduncum (Piperaceae). *Phytochemistry Letters*, *3*(3), 164-167.

Starmans, D. A., & Nijhuis, H. H. (1996). Extraction of secondary metabolites from plant material: a review. *Trends in Food Science & Technology*, *7*(6), 191-197.

Tan, R. X., & Zou, W. X. (2001). Endophytes: a rich source of functional metabolites. *Natural product reports*, *18*(4), 448-459.

Tan, S. Y., & Tatsumura, Y. (2015). Alexander Fleming (1881–1955): discoverer of penicillin. *Singapore Medical Journal, 56*(7), 366.

Wu, W., Dai, H., Bao, L., Ren, B., Lu, J., Luo, Y., Guo, L., Zhang, L., & Liu, H. (2011). Isolation and structural elucidation of proline-containing cyclopentapeptides from an endolichenic Xylaria sp. *Journal of Natural Products*, *74*(5), 1303-1308.

Xu, F., Zhang, Y., Wang, J., Pang, J., Huang, C., Wu, X., She, Z., Vrijmoed, L. L. P., Jones, E. B. G., & Lin, Y. (2008). Benzofuran derivatives from the mangrove endophytic fungus Xylaria sp. (#2508). *Journal of natural products*, *71*(7), 1251-1253.

Xing, K., Li, T. J., Liu, Y. F., Zhang, J., Zhang, Y., Shen, X. Q., Li, X. Y., Miao, X. M., Feng, Z. Z., Peng, X., Qin, S., & Li, Z. Y. (2018). Antifungal and eliciting properties of chitosan against Ceratocystis fimbriata in sweet potato. *Food chemistry*, *268*, 188-195.

Zheng, N., Liu, Q., He, D. L., Liang, Y., Li, J., & Yang, R. Y. (2018). A New Compound from the Endophytic Fungus Xylaria sp. from Sophora tonkinensis. *Chemistry of natural compounds*, *54*(3), 447-449.