METABOLOMICS ANALYSIS ON ANTIFUNGAL ACTIVITIES PRODUCED BY Penicillium oxalicum T3.3 GROWN ON DIFFERENT TYPES OF CARBON SOURCES

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By

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July 2015

Chairman : Associate Professor Umi Kalsom Md Shah, PhD
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Anthracnose is a disease caused by a fungal *Colletotrichum gleosporioides.* It is a common disease to dragon fruit plant and has caused a great loss to this industry. This pathogenic fungus can cause damage to most parts of plants including roots, stems, leaves, flowers and fruits. One of the potential microorganisms that able to produce antimicrobial activity against this plant pathogen is the endophytic fungus. However, research carried out on metabolomics of cellular metabolites produced by endophytic *Penicillium oxalicum* against *C. gleosporioides* is very limited. Thus, this study was conducted with the aims to evaluate the antifungal activities produced by *Penicillium oxalicum* T3.3 against *Colletotrichum gloeosporiodes* by using different types of carbon sources in fermentation medium and to identify the possible compounds produced by this strain through metabolomics approach.

Preliminary study on locally isolated; *P. oxalicum* T3.3 had shown a promising antagonism through antifungal secondary metabolites which suppressed the growth of *C. gloeosporioides*. Disc diffusion test was conducted in order to determine the inhibition zone on the growth of *C. gloeosproides*. Among the six carbon sources tested, glucose exhibited the highest percent inhibition of radial growth (PIRG) of 75% and producing inhibition zone ranges from 4 to 7 mm. The minimum inhibition concentration (MIC) and minimum fungicidal concentration (MFC) of the glucose crude extract was the highest with 78 µg/mL and 2500 µg/mL, respectively. Meanwhile, starch and xylitol crude extracts gave the lowest MIC value of 1250 µg/mL and no MFC can be recorded. The compounds were extracted with ethyl acetate and ^{1}H NMR analysis was carried out to identify candidate compounds that had been produced. Metabolomics studies were conducted by analyzing the spectrum using SIMCA P+, Principal Component Analysis (PCA) and Partial Least Square

(PLS) multivariate statistical method. The conducted metabolomics study showed that sugar crude extracts (glucose, sucrose and maltose) tend to produce more threonine, 2-heptanone, lactate, valine, butyrate, *O*-phosphoserine. Meanwhile complex sugar substrates (xylitol, starch and *Undaria pinnatifida*) produced more acetic acid, methionine and leucine. From this analysis, different metabolites produced by *P. oxalicum* T3.3 were clustered according to the carbon sources used. This research demonstrates the potential of using a combination of ^{1}H NMR spectroscopy and multivariate data analyses in differentiating the effect of carbon sources used based on the identification of possible metabolites contributing to their differences.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

ANALISIS METABOLOMIK KE ATAS AKTIVITI ANTIKULAT YANG DIHASILKAN OLEH *Penicillium oxalicum* T3.3 YANG TUMBUH DI ATAS PELBAGAI JENIS SUMBER KARBON

Oleh

NURLIYANA BINTI SALIKIN

Julai 2015

Pengerusi : Profesor Madya Umi Kalsom Md Shah, PhD
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Antraknos adalah penyakit yang disebabkan oleh kulat *Colletotrichum gleosporioides*. Ia adalah penyakit yang biasa untuk tanaman buah naga dan telah menyebabkan kehilangan besar kepada industri ini. Kulat pathogen ini boleh menyebabkan kerosakan pada kebanyakan bahagian tumbuhan termasuk akar, batang, daun, bunga dan buah. Salah satu mikroorganisma yang berpotensi dapat menghasilkan aktiviti anti-mikrob terhadap patogen tumbuhan ini adalah kulat endofitik. Walau bagaimanapun, penyelidikan yang dijalankan ke atas metabolomik metabolit selular yang dihasilkan oleh *Penicillium oxalicum* terhadap *C. gleosporioides* adalah sangat terhad. Oleh itu, kajian ini dijalankan dengan tujuan untuk menilai aktiviti anti-kulat yang dihasilkan oleh *P. oxalicum* T3.3 terhadap *Colletotrichum gloeosporiodes* dengan menggunakan pelbagai jenis sumber karbon dalam medium fermentasi dan untuk mengenal pasti sebatian yang mungkin dihasilkan oleh strain ini melalui pendekatan metabolomik.

Kajian awal mengenai isolat tempatan; *P. oxalicum* T3.3 telah menunjukkan penentangan yang menjanjikan melalui anti-kulat sebagai metabolit sekunder yang boleh menyekat pertumbuhan *C. gloeosporioides.* Ujian cakera penyebaran telah dijalankan untuk menentukan zon perencatan pada pertumbuhan *C. gloeosprioides*. Antara enam sumber karbon yang diuji, glukosa mempamerkan peratus perencatan pertumbuhan tertinggi (PIRG) sebanyak 75% dan menghasilkan zon perencatan antara 4-7 mm. Kepekatan minimum perencatan (MIC) dan kepekatan minimum berhubung dgn kulat (MFC) daripada ekstrak mentah glukosa adalah yang tertinggi dengan 78 µg/mL dan 2500 µg/mL, masing-masing. Sementara itu, kanji dan xylitol ekstrak mentah memberikan nilai MIC yang paling rendah dengan 1250 µg/mL dan tiada MFC boleh direkodkan. Sebatian ini diekstrak dengan etil asetat dan analisis ^{1}H NMR telah

dijalankan untuk mengenalpasti calon sebatian yang telah dihasilkan. Kajian metabolomik telah dijalankan dengan menganalisis spektrum menggunakan SIMCA P +, Analisis Komponen Utama (PCA) dan "Partial Least Square" (PLS) kaedah statistik multivariat. Kajian metabolomik yang telah dijalankan menunjukkan bahawa ekstrak gula mentah (glukosa, sukrosa dan maltosa) cenderung untuk menghasilkan lebih treonina, 2-heptanina, laktat, valina, butirat, dan *O*-fosfoserina. Sementara itu sampel gula kompleks (xylitol, kanji dan *Undaria pinnatifida*) menghasilkan lebih banyak asid asetik, metionina dan leusina. Daripada analisis ini, metabolit berbeza yang dihasilkan oleh *P.oxalicum* T3.3 dikelompokkan mengikut sumber karbon yang digunakan. Kajian ini menunjukkan potensi menggunakan gabungan ^{1}H NMR spektroskopi dan data multivariat analisis dalam membezakan kesan sumber karbon yang digunakan berdasarkan pengenalpastian metabolit yang mungkin menyumbang kepada perbezaan mereka.

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I certify that a Thesis Examination Committee has met on (10th July 2015) to conduct the final examination of Nurliyana Binti Salikin on her thesis entitled "Metabolomics Analysis on Antifungal Activities Produced by *Penicillium oxalicum* T3.3 Grown On Different types of Carbon Sources" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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This is to confirm that:

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LIST OF ABBREVIATIONS

NMR	Nuclear magnetic resonance
GC-MS	Gas chromatography-mass spectrometry
LC-MS	Liquid chromatography-mass spectrometry
FTIR	Fourier transform infrared spectroscopy
^{1}H-NMR	Proton nuclear magnetic resonance
MIC	Minimum inhibition concentration
MFC	Minimum fungicidal concentration
spp.	Species
pH	Potential of hydrogen
DNA	Deoxyribonucleic acid
α	Alpha
β	Beta
mRNA	Messenger RNA
TLC	Thin layer chromatography
GS	Gas chromatography
MS	Mass spectroscopy
^{1}H	Hydrogen-1
^{13}C	Carbon-13
^{19}F	Fluorine-19
^{31}P	Phosphorus-31
1D	One-dimensional
2D	Two-dimensional
COSY	Correlation spectroscopy
HMBC	Heteronuclear multiple bond correlation
NOESY	Nuclear overhauser effect spectroscopy
R&D	Research and development

PCA	Principal components analysis
PC	Principal components
PLS-DA	Partial least squares-discriminant analysis
OPLS-DA	Orthogonal projection to latent structures-discriminant analysis
DCW	Dry cell weight
FF microplates	Filamentous fungi microplates
nm	Nanometer
rpm	Rotation per minute
min	Minute
µg	Microgram
PIRG	Percent inhibition of radial growth
µl	Microliter
TMS	Tetramethylsilane
Hz	Hertz
ppm	Parts per million
δ	Chemical shift
PDB	Potato dextrose broth
MEB	Malt extract broth
par	Pareto
YMDB	Yeast metabolome database

CHAPTER 1

INTRODUCTION

1.1 General Background

In Malaysia, the first report on the occurrence of anthracnose disease in dragon fruit (*Hylocereus* spp.) caused by *Colletotrichum gloeosporioides* was reported by Masyahit *et al.* (2009). The infected stem and fruit had reddish-brown lesions or black spots symptoms where it can expand and merge to cover the whole affected area. At present, the great potential health benefit (Ching and Yusof, 2005), physico-chemical characteristics (Chuah *et al.,* 2008) and nutritional value (Rebecca *et al.*, 2008; Ariffin *et al.,* 2009) of dragon fruit had been a great interest among the researchers, however the exploitation of natural organism as biological control and the potentialities of these microorganisms in production of bioactive metabolites and bio-control agents in controlling the pathogenic fungi has not receive any further investigations yet.

Colletotrichum gloeosporioides, known as one of the world's most plant pathogenic fungi can cause a serious damage to most parts of plants including stems, fruits, roots, leaves, and flowers but are often highly specific to individual tissues (Bailey *et al.*, 1992). This pathogenic fungus attacked an extremely wide range of plants growing in both temperate and tropical environments. In Korea, *C. gloeosproriodes* had been identified as the cause of anthracnose disease that attack tulip trees as the necrotic lesions became black as the spots expanded on the leaves of that trees (Choi *et al.*, 2012). The first report of anthracnose of *Pisonia alba,* commonly called lettuce tree was reported in India described the *C. gloeosproriodes* as the fungus that produced white mycelia, which became dark grey with later formation of numerous salmon pink colored spore masses (Vidyalakshmi and Divya, 2013).

There is no agreement on which media are the optimal for metabolite production. However, according to Mathan *et al.* (2013), the growth media and incubation conditions have a very great influence on secondary metabolites production. The ability of microorganisms to produce their metabolites would depend on their ability to modulate their metabolic composition according to their environment. By understanding the metabolites produced, researchers are able to study the unique cellular process of certain microorganisms which may be influence by physiological and also environmental signals (Jensen *et al.*, 2006). Fingerprinting these chemical constituents that present in the microorganism may helps to further understand the microorganism antibiotic pathway. Some of the physical and chemical parameters like pH, temperature, carbon and nitrogen sources play a major role on fungal growth and production of bioactive compounds and antimicrobial agents (Gunasekaran and Poorniammal, 2008; Mathan *et al.,* 2013). The availability and type of carbon and nitrogen source give effect on polyketide production whereby carbon source such as

glucose and sucrose have been found to increase the fungal growth and sporulation along with the high aflatoxin production (Keller *et al.*, 2002).

Metabolomics can be described as a comprehensive quantitative and qualitative analysis of holistic metabolites present in a biological organism, which are the end-products of its gene expression (Van der kooy *et al*., 2009). Microbial metabolomic, focus on the low molecular mass metabolites which would indicate certain specific regulator or pathway mechanisms (Azizan *et al.*, 2012). Microbial profiling of extracellular metabolites had proved to give a better idea on the overall metabolites produced by the microorganisms compared to the used of intracellular metabolites (Kamenik *et al.,* 2010). Major benefit of profiling extracellular metabolites obtained from the fermentation broth, was the ability to determine the present of overall chemical properties that was produced during the fermentation process (Azizan *et al.*, 2012).

With the new development of tools for metabolomics study, it has allowed researchers to analyze broad range of metabolites (Fatma *et al.,* 2012). There are many tools that can be used to analyze large number of metabolites simultaneously such as nuclear magnetic resonance (NMR), gas chromatography-mass spectrometry (GC-MS), liquid chromatography-mass spectrometry (LC-MS) and Fourier transform infrared spectroscopy (FTIR). Some of them rely on chromatographic separation step and others do not require any in which represent a global view of the sample (Ulrich-Merzenich *et al.*, 2007). Among these tools, NMR method is able to provide a wide range of many molecular classes including sugars, amino acids, organic acids, alcohols or polyols, amine and ketones (Wishart, 2008) and allowed the detection of metabolites either from biofluid, tissue, whole organisms or even cell extract (Fernie *et al.*, 2004). For NMR analysis, ^{1}H-NMR has been the most frequently used tool for the metabolomics study due to the highly reproducible method, rapid and robust of the technique (Kim *et al.*, 2010; Ward *et. al.*, 2010).

In this study, the endophytic *P. oxalicum* T3.3 was subjected to fermentation and the impact of medium composition (specifically by using different carbon sources) was valued by using disc diffusion test, minimum inhibition concentration (MIC) and minimum fungicidal concentration (MFC) against the pathogenic fungi, *C. gloeosporioides*. Metabolomics study was performed to determine the metabolites responsible for the antifungal production. It is hypothesized that metabolites produced were an extracellular compounds and these compounds inhibited the growth of *C. gloeosporioides* through the mode of antibiosis.

1.2 Objectives

The specific objectives of this study were:

1) Screening of fermentation media for optimum growth and carbon sources for antifungal activity.
2) To evaluate the antifungal activities produced by *P. oxalicum* T3.3 against *C. gloeosporiodes* by using different types of carbon sources in selected fermentation medium.
3) To identify the possible metabolites produced by the strain T3.3 through metabolomics approach.

REFERENCES

Abdel-Motaal, F. F., Nassar, M. S., El-Zayat, S. A., El-Sayed, M. A., and Ito, S. I. (2010). Antifungal activity of endophytic fungi isolated from Egyptian henbane (Hyoscyamus muticus L.). *Pakistan Journal of Botany*. 42(4): 2883-2894.

Abdul Wahid, O. A. (2001). Occurrence of *Colletotrichum* anthracnose disease of guava fruit in Egypt. *International Journal of Pest Management*, 47(2): 147-152.

Aiyer, V. P. (2005). Amylases and their applications. *African Journal of Biotechnology*. 4:1525–1529.

Akihisa, T., and Yasukawa, K. (2006). Biomaterials from Aquatic and Terrestrial Organisms. M. Fingerman, R. Nagabhushanam (Eds.) (pp. 63). Enfield, Science Publisher.

Ariffin, A. A., Bakar, J., Tan, C. P., Rahman, R. A., Karim, R. and Loi, C. C. (2009). Essential fatty acids of pitaya (dragon fruit) seed oil. *Journal of Food Chemistry.* 114: 561-564.

Arnold, A. E., and Lutzoni, F. (2007). Diversity and host range of foliar fungal endophytes: are tropical leaves biodiversity hotspots. *Ecology*. 88(3): 541-549.

Azizan, K. A., Baharum, S. N., Ressom, H. W., and Noor, N. M. (2012). GC-MS analysis and PLS-DA validation of the trimethyl silyl-derivatization techniques. *America Journal of Applied Science.* 9(7): 1124-1136.

Bailey, J.A., O'Connell, R.J., Pring, R.J., and Nash, c. (1992). Infection strategies of colletotrichum species. In*:* J.A. Bailey (Ed.), *Colletotrichum: Biology, Pathology and Control.* (pp. 88). United Kingdom: C.A.B International.

Bajad, S. and Shulaev, V. (2011). LC-MS-Based Metabolomics. In T. O. Metz (Ed.), *Metabolomic Profiling, Methods and Protocols* (pp. 213-228). Springer Science and Business Media.

Bandara, W. M. M. S., Seneviratne, G., and Kulasooriya, S. A. (2006). Interactions among endophytic bacteria and fungi: effects and potentials. *Journal of Biosciences*. 31(5): 645-650.

Barker, M., and Rayens, W. (2003). Partial least squares for discrimination. *Journal of Chemometrics*. 17(3): 166-173.

Bauer A W, Kirby W M, Sherries J C and Turck M. (1966). Antibiotic susceptibility testing by a standardized single disk method. *American Journal of Clinical Pathology*. 45: 493–496.

Beyoğlu, D., and Idle, J. R. (2013). Metabolomics and its potential in drug development. *Biochemical Pharmacology*. 85(1): 12-20.

Blackwell, M. (2011). The Fungi: 1, 2, 3… 5.1 million species?. *American Journal of Botany*. *98*(3): 426-438.

Bloch, F. (1946). Nuclear induction. *Physical Review*. *70*(7-8): 460.

Brantner, A., Pfeiffer, K. P., and Brantner, H. (1994). Applicability of diffusion methods required by the pharmacopoeias for testing antibacterial activity of natural compounds. *Die Pharmazie*. 49(7): 512-516.

Brundrett, M. C. (2002). Coevolution of roots and mycorrhizas of land plants. *New Phytologist*. *154*(2): 275-304.

Buyer, J.S., Roberts, D.P., Millner, P., and Russek-Cohen, E. (2001). Analysis of fungal communities by sole carbon source profiles. *Journal of Microbiological Methods*. 45: 53–60.

Cai, L., Hyde, K. D., Taylor, P. W. J., Weir, B., Waller, J., Abang, M. M., and Johnston, P. R. (2009). A polyphasic approach for studying *Colletotrichum*. *Fungal Diversity*. 39(1): 183-204.

Campanile, G., Ruscelli, A., and Luisi, N. (2007). Antagonistic activity of endophytic fungi towards *Diplodia corticola* assessed by in vitro and in plant tests. *European Journal of Plant Pathology*. 117(3): 237-246.

Cevallos-Cevallos, J.M., Reyes-De-Corcuera, J.I., Etxeberria, E., Danyluk, M.D. and Rodrick, G.E. (2009). Metabolomic analysis in food science: a review. *Trends in Food Science & Technology*. 20: 557-566.

Chellapandi, P., Sivaramakrishnan, S., and Viswanathan, M. B. (2010). Systems Biotechnology: an Emerging Trend in Metabolic Engineering of Industrial Microorganisms. *Journal of Computer Science & Systems Biology*. 3(2).

Ching, K.M. and Yusof, R. M. *Effect of red pitaya fruit supplementation on lipids profiles of induced hypercholesterolemic rats*. Paper presented at the 20th Scientific Conference of the Nutrition Society of Malaysia, Kuala Lumpur. March 2005.

Choi, O., Choi, O., Kwak, Y. S., Kim, J., and Kwon, J. H. (2012). Spot anthracnose disease caused by *Colletotrichum gloeosporioides* on tulip tree in Korea. *Mycobiology*, 40(1), 82-84.

Chuah, T. G., Ling, H. L., Chin, N. L., Choong, T. S. Y. and Fakhru'l-Razi, A. (2008). Effects of temperature on rheological behavior of dragon fruit (*Hylocereus* sp.) juice. *International Journal of Food Engineering.* 4: 1-28.

Chun, S. C., Schneider, R. W., and Chung, I. M. (2003). Determination of carbon source utilization of Bacillus and Pythium species by Biolog® Microplate assay. *Journal of Microbiology Seoul*. 41(3): 252-258.

Copeland, L., Blazek, J., Salman, H., and Tang, M. C. M. (2009). Form and function of starch granules. *Food Hydrocolloids*. 23: 1527–1534.

Cui, H. B., Mei, W. L., Miao, C. D., Lin, H. P., Hong, K., and Dai, H. F. (2008). Antibacterial constituents from the endophytic fungus *Penicillium* sp. 0935030 of mangrove plant *Acrostichum aureurm*. *Chinese Journal of Antibiotics*. 33(7): 407-410.

da Silva, L. V., Tavares, C. B., Amaral, P. F., and Coelho, M. A. Z. (2012). Production of citric acid by *Yarrowia lipolytica* in different crude glycerol concentrations and in different nitrogen sources. *Chemical Engineering*. *27*.

Daisy, B. H., Strobel, G. A., Castillo, U., Ezra, D., Sears, J., Weaver, D. K., and Runyon, J. B. (2002). Naphthalene, an insect repellent, is produced by *Muscodor vitigenus*, a novel endophytic fungus. *Microbiology*. 148(11): 3737-3741.

de Hoog, G. S., Guarro, J., Gené, J., & Figueras, M. J. (2000). *Atlas of Clinical Fungi*. Centraalbureau voor Schimmelcultures (CBS).

de Laeter, J.R., Bohlke, J.K., De Bievre, P., Hidaka, H., Peiser, H.S., Rosman, K.J.R. and Taylor, P.D.P. (2003). Atomic weights of the elements. Review 2000 (IUPAC Technical Report). *Pure and Applied Chemistry*. 75(6): 683-800.

Demir, A., Topkaya, R. and Baykal, A. (2013). Green synthesis of supermagnetic Fe3O4 nanoparticles with maltose: Its magnetic investigation. *Polyhedron*. 65: 282-287.

Devi, K. P., Nisha, S. A., Sakthivel, R., and Pandian, S. K. (2010). Eugenol (an essential oil of clove) acts as an antibacterial agent against *Salmonella typhi* by disrupting the cellular membrane. *Journal of Ethnopharmacology*. *130*(1): 107-115.

Dodd, J. C., Estrada, A., and Jeger, M. J. (1992). Epidemiology of *Colletotrichum gloeosporioides* in the tropics. *Colletotrichum: Biology, Pathology and Control* (pp. 308-325). Wallingford: CAB International.

Drużyńska, B., Stępniewska, A., & Wołosiak, R. (2007). The influence of time and type of solvent on efficiency of the extraction of polyphenols from green tea and antioxidant properties obtained extracts. *Acta Scientiarum Polonorum Technologia Aliment*aria. 6(1), 27-36.

Dunn, W. B., and Ellis, D. I. (2005). Metabolomics: current analytical platforms and methodologies. *TrAC Trends in Analytical Chemistry*. *24*(4): 285-294.

Erikkson, L., Johansson, E., Kettaneh-Wold, N., Trygg, J., Wikstrom, C. and Wold, S. (2006). Multi- and Megavariate Data Analysis, Umetrics academy, Umea, Sweden.

Espinel-Ingroff, A., Fothergill, A., Peter, J., Rinaldi, M. G., and Walsh, T. J. (2002). Testing conditions for determination of minimum fungicidal concentrations of new and established antifungal agents for *Aspergillus* spp.: NCCLS collaborative study. *Journal of Clinical Microbiology*. *40*(9): 3204-3208.

Fatma, Y. B. A. B., Pianelli, K., Martine, D. N., Aline, L. M., Catherine, D., Mickael, M., Marie-Helene, A., Dominique, R., Christophe, R., Annick, M., Sodak, B. and Cecile, C. (2012). ^{1}H-NMR metabolomics: Profiling method for a rapid and efficient screening of transgenic plants. *African Journal of Biotechnology*. 11(52): 11386-11399.

Fernie, A. R., Trethewey, R. N., Krotzky, A. J., and Willmitzer, L. (2004). Innovation metabolite profiling: from diagnostics to systems biology. *Nature Reviews Molecular Cell Biology.* 5: 763-769.

Friedman, M., Henika, P. R., and Mandrell, R. E. (2002). Bactericidal activities of plant essential oils and some of their isolated constituents against *Campylobacter jejuni, Escherichia coli, Listeria monocytogenes, and Salmonella enterica*. *Journal of Food Protection®*. 65(10): 1545-1560.

Frisvad, J. C., and Filtenborg, O. (1989). *Terverticillate penicillia*: chemotaxonomy and mycotoxin production. *Mycologia*. 837-861.

Ge, H. M., Shen, Y., Zhu, C. H., Tan, S. H., Ding, H., Song, Y. C., and Tan, R. X. (2008). Penicidones A–C, three cytotoxic alkaloidal metabolites of an endophytic *Penicillium* sp. *Phytochemistry*. 69(2): 571-576.

Gebreel, H. M., El-Mehalawy, A. A., El-Kholy, I. M., Rifaat, H. M., and Humid, A. A. (2008). Antimicrobial activities of certain bacteria isolated from egyptian soil against pathogenic fungi. *Research Journal of Agriculture and Biological Sciences*. 4(4): 331-339.

Georgiev, M. I., Ali, K., Alipieva, K., Verpoorte, R., and Choi, Y. H. (2011). Metabolic differentiations and classification of *Verbascum* species by NMR-based metabolomics. *Phytochemistry*. *72*(16): 2045-2051.

Giblin, F. R., Coates, L. M., and Irwin, J. A. G. (2010). Pathogenic diversity of avocado and mango isolates of *Colletotrichum gloeosporioides* causing anthracnose and pepper spot in Australia. *Australasian Plant Pathology*. 39(1): 50-62.

Girivasan, K. P., and Suryanarayanan, T. S. (2004). Intact leaves as substrate for fungi: distribution of endophytes and phylloplane fungi in rattan palms. *Czech Mycology*. 56(1/2): 33-44.

Gond, S. K., Verma, V. C., Kumar, A., Kumar, V., and Kharwar, R. N. (2007). Study of endophytic fungal community from different parts of *Aegle marmelos Correae* (Rutaceae) from Varanasi (India). *World journal of Microbiology and Biotechnology*. *23*(10): 1371-1375.

Griffin, D.H (1996). *Fungal physiology*. New York: John Wiley & Sons.

Grivet, J. P., and Delort, A. M. (2009). NMR for microbiology: *In vivo* and *in situ* applications. *Progress in Nuclear Magnetic Resonance Spectroscopy*. *54*(1): 1-53.

Gummer, J. P., Krill, C., Du Fall, L., Waters, O. D., Trengove, R. D., Oliver, R. P., and Solomon, P. S. (2012). Metabolomics protocols for filamentous fungi. In *Plant Fungal Pathogens* (pp. 237-254). Humana Press.

Gunasekaran S, and Poorniammal R. (2008). Optimization of fermentation conditions for red pigment production from *Penicillium* sp. Under submerged cultivation. *African Journal of Biotechnology*. 7: 1894-1898.

Gunasena, H. P. M. and Pushpakumara, D. K. N. G. (2006). Dragon fruit – *Hylocereus undatus* (Haw.) Britton and Rose: a fruit for the future. Sri Lanka Council for Agricultural Policy, Wijerama Mawatha, Colombo 7, Sri Lanka.

Gunatilaka, A. L. (2006). Natural Products from Plant-Associated Microorganisms: Distribution, Structural Diversity, Bioactivity, and Implications of Their Occurrence. *Journal of Natural Products*. 69(3): 509-526.

Gupta, V., Misra, A., and Gaur, R. (2010). Growth characteristics of *Fusarium* spp. causing wilt disease in *Psidium guajava* L. in India. *Journal of Plant Protection Research*. 50(4): 452-462.

Han, Z., Mei, W. L., Cui, H. B., Zeng, Y. B., Lin, H. P., Hong, K., and DAI, H. F. (2008). Antibacterial constituents from the endophytic fungus *Penicillium* sp. of mangrove plant *Cerbera manghas*. *Chemical Journal of Chinese Universities*. *29*(4).

Harper, J. K., Arif, A. M., Ford, E. J., Strobel, G. A., Porco Jr, J. A., Tomer, D. P., and Grant, D. M. (2003). Pestacin: a 1, 3-dihydro isobenzofuran from *Pestalotiopsis microspora* possessing antioxidant and antimycotic activities. *Tetrahedron*. 59(14): 2471-2476.

Hawksworth, D. L. (1991). The fungal dimension of biodiversity: magnitude, significance, and conservation. *Mycological Research*. 95(6): 641-655.

He, L., Zhou, G., Lu, L., and Liu, J. (2009). Isolation and identification of endophytic bacteria antagonistic to *Camellia oleifera* anthracnose. *African Journal of Microbiology Research*. 3(6): 315-318.

Heyman, H. M., and Meyer, J. J. M. (2012). NMR-based metabolomics as a quality control tool for herbal products. *South African Journal of Botany*. 82: 21-32.

Hindorf, H., Blanke, M., and Pohlan, J. (2000). *Colletotrichum* species causing anthracnose of tropical crops. *Plant Patholo*gy. 39: 343-366.

Holmes, E., Nicholls, A. W., Lindon, J. C., Connor, S. C., Connelly, J. C., Haselden, J. N., and Nicholson, J. K. (2000). Chemometric models for toxicity classification based on NMR spectra of biofluids. *Chemical Research in Toxicology*. 13(6): 471-478.

Hosakawa, M., Bhaskar, N., Sashima, T., and Miyashita, K. (2006). Fucoxanthin as a bioactive and nutritionally beneficial marine carotenoid: A review. *Carotenoid Science*. 10(1): 15–28.

Ikeda, T., Kanaya, S., Yonetani, T., Kobayashi, A., and Fukusaki, E. (2007). Prediction of Japanese green tea ranking by Fourier transform near-infrared reflectance spectroscopy. *Journal of Agricultural and Food Chemistry*. 55(24): 9908-9912.

Ikotun, T. (1984). Production of oxalic acid by Penicillium oxalicum in culture and in infected yam tissue and interaction with macerating enzyme. *Mycopathologia*. 88(1): 9-14.

Islam, M.S. and Indrajit, M. (2012). Effects of xylitol on blood glucose, glucose tolerance, serum insulin and lipid profile in a type 2 diabetes model of rats. *Annals of Nutrition and Metabolism*. 61(1): 57-64.

Ivanović, M. S., Duduk, B. B., Ivanović, M. M., and Ivanović, M. S. (2007). Anthracnose: A new strawberry disease in Serbia and its control by fungicides. *Zbornik Matice srpske za prirodne nauke*. (113): 71-81.

Jensen, P. R., Philip, G. W., Oh, D. C., Zeigler, L. and Fenical, W. (2006). Species-specific secondary metabolite production in marine actinomycetes of the genus *Salinispora. Applied and Environmental Microbiology*. 73(4): 1146-1152.

Johnston P, Dodd S, Park D, Massey B, Charuchinda B, Waipara N, and Buckley T (2008). Are stable, consistent, reliable, and useful species names possible within *Colletotrichum*? In *Colletotrichum Diseases of Fruit Crops, Pre-Congress workshop* (pp. 1-9). ICPP 2008, Torino, Italy.

Jorgensen, J. H., and Ferraro, M. J. (2009). Antimicrobial Susceptibility Testing: A Review of General Principles and Contemporary Practices. *Clinical Infectious Diseases*. 49(11).

Kamenik, Z., Hadacek, Z., Mareckova, M., Ulanova, D. and Kopecky, J. (2010). Ultra high-performance liquid chromatography fingerprinting method for chemical screening of metabolites in cultivation broth. *Journal of Chromatography A.* 1217: 8016-8025.

Kefialew, Y. and Ayalew, A. (2008). Postharvest biological control of anthracnose (*Colletotrichum gleosporioides*) on mango (*Mangifera indica*). *Postharvest Biology and Technology.* 50:8-11.

Keller, N. P., Calvo, A., Wilson, R. and Bok, J. (2002) Relationship between secondary metabolism and fungal development. *Microbiology and Molecular Biology Reviews.* 66: 447-459.

Khaddor, M., Saidi, R., Aidoun, A., Lamarti, A., Tantaoui-Elaraki, A., Ezziyyani, M., and Badoc, A. (2007). Antibacterial effects and toxigenesis of *Penicillium aurantiogriseum* and *P. viridicatum*. *African Journal of Biotechnology*. 6(20).

Kharwar, R. N., Verma, V. C., Kumar, A., Gond, S. K., Harper, J. K., Hess, W. M., and Strobel, G. A. (2009). Javanicin, an antibacterial naphthaquinone from an endophytic fungus of neem, *Chloridium* sp. *Current Microbiology*. 58(3): 233-238.

Khatib, A., Shaari, K., Abas, F., Shitan, M., Kneer, R., Neto, V., and Lajis, N. H. (2011). Discrimination of three pegaga (*Centella*) varieties and determination of growth-lighting effects on metabolites content based on the chemometry of ^{1}H Nuclear Magnetic Resonance spectroscopy. *Journal of Agricultural and Food Chemistry*. 60(1): 410-417.

Khokhar, I., Mukhtar, I., and Mushtaq, S. (2011). Antifungal effect of *Penicillium* metabolites against some fungi. *Archives of Phytopathology and Plant Protection*. 44(14): 1347-1351.

Kim, H. K., Choi, Y. H. and Verpoorte, R. (2010). NMR based metabolomic analysis of plants. *Nature protocol.* 3: 1001-1012.

Kim, H. K., Choi, Y. H., and Verpoorte, R. (2011). NMR-based plant metabolomics: where do we stand, where do we go? *Trends in Biotechnology*. 29(6): 267-275.

Kim, H. R., Lim, T. H., Kim, J., Kim, Y. H., and Kim, H. T. (2009). Potential of cross-infection of *Colletotrichum* species causing anthracnose in persimmon and pepper. *The Plant Pathology Journal*. 25(1): 13-20.

Kim, H. S., Park, S. J., Hyun, S. H., Yang, S. O., Lee, J., Auh, J. H., and Choi, H. K. (2011). Biochemical monitoring of black raspberry (*Rubus coreanus* Miquel) fruits according to maturation stage by ^{1}H NMR using multiple solvent systems. *Food Research International*. 44(7): 1977-1987.

Kim, J., Choi, J. N., Ku, K. M., Kang, D., Kim, J. S., Park, J. H. Y., and Lee, C. H. (2011). A correlation between antioxidant activity and metabolite release during the blanching of Chrysanthemum coronarium L. *Bioscience, Biotechnology, and Biochemistry*. 75(4): 674-680.

Krishnan, P., Kruger, N. J., and Ratcliffe, R. G. (2005). Metabolite fingerprinting and profiling in plants using NMR. *Journal of Experimental Botany*. 56(410): 255-265.

Kusari, P., Kusari, S., Spiteller, M., and Kayser, O. (2012). Endophytic fungi harbored in Cannabis sativa L.: diversity and potential as biocontrol agents against host plant-specific phytopathogens. *Fungal Diversity*. 1-15.

Kusari, S., Zühlke, S., and Spiteller, M. (2009). An endophytic fungus from *Camptotheca acuminata* that produces camptothecin and analogues. *Journal of Natural Products*. 72(1): 2-7.

Kwon, O. E., Rho, M. C., Song, H. Y., Lee, S. W., Chung, M. Y., Lee, J. H., and Kim, Y. K. (2002). Phenylpyropene A and B, new inhibitors of acyl-CoA: cholesterol acyltransferase produced by *Penicillium griseofulvum* F1959. *Journal of Antibiotics*. 55: 1004-1008.

Lai, D., Brötz-Oesterhelt, H., Müller, W. E., Wray, V., and Proksch, P. (2013). Bioactive polyketides and alkaloids from *Penicillium citrinum*, a fungal endophyte isolated from *Ocimum tenuiflorum*. *Fitoterapia*. 91: 100-106.

Larsen, T. O., Lange, L., Schnorr, K., Stender, S., & Frisvad, J. C. (2007). Solistatinol, a novel phenolic compactin analogue from *Penicillium solitum. Tetrahedron Letters*. 48(7): 1261-1264.

Larsen, T. O., Smedsgaard, J., Nielsen, K. F., Hansen, M. E., and Frisvad, J. C. (2005). Phenotypic taxonomy and metabolite profiling in microbial drug discovery. *Natural Product Reports*, *22*(6), 672-695.

Lazzarini, A., Cavaletti, L., Toppo, G., and Marinelli, F. (2000). Rare genera of actinomycetes as potential producers of new antibiotics. *Antonie van Leeuwenhoek.* 78(3-4): 399-405.

Lee, Y., K., Lim, D., Lee, Y., and Park, Y. (2006). Variation in fucoidan contents and monosaccharide compositions of Korean Undaria pinnatifida (Harvey) Suringar (Phaeophyta). *Algae-Inchon.* 21(1): 157.

Li, H. Q., Li, X. J., Wang, Y. L., Zhang, Q., Zhang, A. L., Gao, J. M., and Zhang, X. C. (2011). Antifungal metabolites from *Chaetomium globosum*, an endophytic fungus in *Ginkgo biloba*. *Biochemical Systematics and Ecology*. 39(4): 876-879.

Li, J. Y., Strobel, G., Harper, J., Lobkovsky, E., and Clardy, J. (2000). Cryptocin, a Potent Tetramic Acid Antimycotic from the Endophytic Fungus *Cryptosporiopsis cf*. quercina. *Organic Letters*. 2(6): 767-770.

Liang, Y. S., Lefeber, A. W. M., Erkelens, C., Kim, H. K., Choi, Y. H. and Verpoorte, R. (2006). Identification of phenylpropanoids in *Brassica rapa* leaves treated with methyl jasmonate using two-dimensional nuclear magnetic resonance spectroscopy. *Journal of Chromatography.*1112: 148-155.

Lin, Y., Wu, X., Feng, S., Jiang, G., Luo, J., Zhou, S., and 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.

Lindon, J. C., Holmes, E. and Nicholson, J. K. (2001). Pattern recognition methods and applications in biomedical magnetic resonance. *Progress in Nuclear Magnetic Resonance Spectroscopy.* 39:1-40.

Lindon, J.C., Holmes, E., and Nicholson, J.K. (2007). Metabonomics in pharmaceutical R&D. *Federation of European Biochemical Societies Journal.* 274:1140–1151.

Lindon, J.C., Holmes, E., Bollard, M.E., Stanley, E.G. and Nicholson, J.K. (2004). Metabonomics technologies and their application in physiological monitoring, drug safety assessment and disease diagnosis. *Biomarkers*. 9(1): 1-31.

Liu, B., Louws, F. J., Sutton, T. B., and Correll, J. C. (2012). A rapid qualitative molecular method for the identification of *Colletotrichum acutatum* and *C. gloeosporioides*. *European Journal of Plant Pathology*. 132(4): 593-607.

Lodge, D. J., Fisher, P. J., and Sutton, B. C. (1996). Endophytic fungi of Manilkara bidentata leaves in Puerto Rico. *Mycologia*. 733-738.

Lucas, E. M., Castro, M. C., and Takahashi, J. A. (2007). Antimicrobial properties of sclerotiorin, isochromophilone VI and pencolide, metabolites from a Brazilian cerrado isolate of *Penicillium sclerotiorum* Van Beyma. *Brazilian Journal of Microbiology*. 38(4): 785-789.

Macías-Rubalcava, M. L., Hernández-Bautista, B. E., Jiménez-Estrada, M., González, M. C., Glenn, A. E., Hanlin, R. T. and Anaya, A. L. (2008). Naphthoquinone spiroketal with allelochemical activity from the newly discovered endophytic fungus *Edenia gomezpompae*. *Phytochemistry*. 69(5): 1185-1196.

Maisuthisakul, P., Pasuk, S., and Ritthiruangdej, P. (2008). Relationship between antioxidant properties and chemical composition of some Thai plants. *Journal of Food Composition and Analysis*. 21(3): 229-240.

Maria, G. L., and Sridhar, K. R. (2003). Endophytic fungal assemblage of two halophytes from west coast mangrove habitats, India. *Czech Mycology*. *55*(2-4): 241-251.

Marinho, A. M., Rodrigues-Filho, E., Moitinho, M. D. L. R., and Santos, L. S. (2005). Biologically active polyketides produced by *Penicillium janthinellum* isolated as an endophytic fungus from fruits of Melia azedarach. *Journal of the Brazilian Chemical Society*. 16(2): 280-283.

Masyahit, M., Sijam, K., Awang, Y. and Satar, M. G. M. (2008). *Fungi Associated with Diseases on Dragon Fruit (Hylocereus spp.) in Peninsular Malaysia.* (234-237). Pekan Pahang Publishers, Malaysia.

Masyahit, M., Sijam, K., Awang, Y., and Satar, M. G. (2009). The First Report of the Occurrence of Anthracnose Disease Caused by *Colletotrichum gloeosporioides* (Penz.) Penz. & Sacc. on Dragon Fruit (*Hylocereus* spp.) in Peninsular Malaysia. *American Journal of Applied Sciences*. 6(5): 902-912.

Mat Amin, N., Bunawan, H., Redzuan, R. A., and Jaganath, I. B. S. (2010). *Erwinia mallotivora* sp., a new pathogen of Papaya (*Carica papaya*) in Peninsular Malaysia. *International Journal of Molecular Sciences*. 12(1): 39-45.

Mathan, S., Subramanian, V and Nagamony, S. (2013). Optimization and antimicrobial metabolite production from endophytic fungi *Aspergillus terreus* KC 582297. *Eurioean Journal of Experimental Biology*. 3(4): 138-144.

Mediani, A., Abas, F., Khatib, A., Maulidiani, H., Shaari, K., Choi, Y. H., and Lajis, N. H. (2012). ^{1}H-NMR-based metabolomics approach to understanding the drying effects on the phytochemicals in *Cosmos caudatus*. *Food Research International*. 49(2): 763-770.

Meletiadis, J., Meis, J. F., Mouton, J. W. and Verweij, P. E. (2001). Analysis of growth characteristics of filamentous fungi in different nutrient media. *Journal of Clinical Microbiology*. *39*(2), 478-484.

Miyashita, K., and Hosokawa, M. (2008). Beneficial health effects of seaweed carotenoid, fucoxanthin. In C. Barrow & F. Shahidi (Eds.), *Marine Nutraceuticals and Functional Foods* (pp. 297–320). Boca Raton, USA: CRC Press.

Moore-Landecker, E. Fundamentals of Fungi, Prentice Hall, Upper Saddle River, NJ, USA, 4th edition, 1996.

Mostert, L., Crous, P. W., and Petrini, O. (2000). Endophytic fungi associated with shoots and leaves of Vitis vinifera, with specific reference to the Phomopsis viticola complex. *Sydowia*. 52(1): 46-58.

Muzzamal, H., Sarwar, R., Sajid, I., and Hasnain, S. (2012). Isolation, identification and screening of endophytic bacteria antagonistic to biofilm formers. *Pakistan Journal of Zoology*. 44: 249-257.

National Committee for Clinical Laboratory Standards. (2002). *References Method for Broth Dilution Antifungal Susceptibility Testing of Filamentous Fungi: Approved standard M38-A.* NCCLS: Wayne, PA, USA.

Nicoletti, R., De Stefano, M., De Stefano, S., Trincone, A., and Marziano, F. (2004). Antagonism against Rhizoctonia solani and fungitoxic metabolite production by some *Penicillium* isolates. *Mycopathologia*. 158(4): 465-474.

Nicoletti, R., Lopez-Gresa, M. P., Manzo, E., Carella, A., and Ciavatta, M. L. (2007). Production and fungitoxic activity of Sch 642305, a secondary metabolite of *Penicillium canescens*. *Mycopathologia*. 163(5): 295-301.

Nielsen, J. (1992). Modelling the growth of filamentous fungi. In *Modern Biochemical Engineering* (pp. 187-223). Springer Berlin Heidelberg.

O'Gorman, A. (2010). Metabolic Profiling and Fingerprinting for the Detection and Discrimination of Mechanical Damage in Mushrooms (Agaricus bisporus) during Storage.

Owen, N. L., and Hundley, N. (2004). Endophytes the chemical synthesizers inside plants. *Science Progress*. 87(2): 79-99.

Palmateer, A. J., Ploetz, R. C., Van Santen, E., and Correll, J. C. (2007). First occurrence of anthracnose caused by *Colletotrichum gloeosporioides* on pitahaya. *Plant Disease*. 91(5): 631-631.

Papaspyridi, L. M., Katapodis, P., Gonou-Zagou, Z., Kapsanaki-Gotsi, E., and Christakopoulos, P. (2011). Growth and biomass production with enhanced β-glucan and dietary fibre contents of Ganoderma australe ATHUM 4345 in a batch-stirred tank bioreactor. *Engineering in Life Sciences*. 11(1): 65-74.

Paranthaman, R., Vidyalakshmi, R., Murugesh, S., and Singaravadivel, K. (2009). Optimization of various culture media for tannase production in submerged fermentation by Aspergillus flavus. *Advances in Biological Research*. 3(1-2): 34-39.

Pascual, S., Rico, J. R., De Cal, A., and Melgarejo, P. (1997). Ecophysiological factors affecting growth, sporulation and survival of the biocontrol agent Penicillium oxalicum. *Mycopathologia*. 139(1): 43-50.

Patil, K. R., Rocha, I., Förster, J., and Nielsen, J. (2005). Evolutionary programming as a platform for in silico metabolic engineering. *BMC Bioinformatics*. 6(1): 308.

Pazouki, M., and Panda, T. (2000). Understanding the morphology of fungi.*Bioprocess Engineering*. 22(2): 127-143.

Petit, P., Lucas, E. M., Abreu, L. M., Pfenning, L. H., and Takahashi, J. A. (2009). Novel antimicrobial secondary metabolites from a *Penicillium* sp. isolated from Brazilian cerrado soil. *Electronic Journal of Biotechnology*. 12(4): 8-9.

Petrini, O. (1996). Ecological and physiological aspects of host-specificity in endophytic fungi. *Endophytic Fungi in Grasses and Woody Plants*. 87-100.

Pierens, G. K., Palframan, M. E., Tranter, C. J., Carroll, A. R., and Quinn, R. J. (2005). A robust clustering approach for NMR spectra of natural product extracts. *Magnetic Resonance in Chemistry*. 43(5): 359-365.

Pieri, V., Sturm, S., Seger, C., Franz, C., and Stuppner, H. (2012). ^{1}H NMR-based metabolic profiling and target analysis: a combined approach for the quality control of Thymus vulgaris. *Metabolomics*. 8(2): 335-346.

Pischetsrieder, M. (2000). Chemistry of glucose and biochemical pathways of biological interest. *Peritoneal Dialysis International*. 20 (2): 26-30.

Pitt, J. I. (1979). The genus Penicillium and its teleomorphic states Eupenicillium and Talaromyces. *The genus Penicillium and its teleomorphic states Eupenicillium and Talaromyces.*

Powers, R. (2009). NMR metabolomics and drug discovery. *Magnetic Resonance in Chemistry*. 47(S1): S2-S11.

Prihastuti, H., Cai, L., Chen, H., McKenzie, E. H. C., and Hyde, K. D. (2009). Characterization of Colletotrichum species associated with coffee berries in northern Thailand. *Fungal Diversity*. 39: 89.

Promputtha, I., Lumyong, S., Dhanasekaran, V., McKenzie, E. H. C., Hyde, K. D., and Jeewon, R. (2007). A phylogenetic evaluation of whether endophytes become saprotrophs at host senescence. *Microbial Ecology*. 53(4): 579-590.

Purcell, E. M. (1946). Spontaneous emission probabilities at radio frequencies. *Physical Review*. 69: 681.

Qian-Cutrone, J., Huang, S., Shu, Y. Z., Vyas, D., Fairchild, C., Menendez, A. and Gao, Q. (2002). Stephacidin A and B: two structurally novel, selective inhibitors of the testosterone-dependent prostate LNCaP cells. *Journal of the American Chemical Society*. 124(49): 14556-14557.

Raamsdonk, L. M., Teusink, B., Broadhurst, D., Zhang, N., Hayes, A., Walsh, M. C. and Oliver, S. G. (2001). A functional genomics strategy that uses metabolome data to reveal the phenotype of silent mutations. *Nature Biotechnology*. 19(1): 45-50.

Rahmansyah, M. (2013). Endophytic fungi isolated from mangrove plant and have antagonism role against fusarium wilt. *Journal of Agricultural & Biological Science*. 8(3): 251-257.

Raper, K. B., and Thom, C. (1949). A manual of the Penicillia. *A manual of the Penicillia.*

Ratcliffe, R.G. and Shachar-Hill, Y. (2005). Revealing metabolic phenotypes in plants:Inputs from NMR analysis. *Biological Reviews of the Cambridge Philosophical Society.* 80(1): 27-43.

Rebecca, O. P. S., Zuliana, R., Boyce, A. N. and Chandran, S. (2008). Determining pigment extraction efficiency and pigment stability of dragon fruit (*Hylocereus polyrhizus*). *Journal of Bioogical Sciences.* 8: 1174-1180.

Redko, F., Clavin, M. L., Weber, D., Ranea, F., Anke, T., and Martino, V. (2007). Antimicrobial isoflavonoids from Erythrina crista galli infected with *Phomopsis* sp. *Zeitschrift fur Naturforschung C*. 62(3/4): 164.

Reino, J. L., Guerrero, R. F., Hernández-Galán, R., and Collado, I. G. (2008). Secondary metabolites from species of the biocontrol agent Trichoderma. *Phytochemistry Reviews*. 7(1): 89-123.

Rice, A. V., and Currah, R. S. (2005). Profiles from Biolog FF plates and morphological characteristics support the recognition of *Oidiodendron fimicola* sp. nov. *Studies in Mycology*. *53*: 75-82.

Rocha, A. C., Garcia, D., Uetanabaro, A. P., Carneiro, R. T., Araújo, I. S., Mattos, C. R., and Góes-Neto, A. (2011). Foliar endophytic fungi from Hevea brasiliensis and their antagonism on Microcyclus ulei. *Fungal Diversity*. 47(1): 75-84.

Rochfort, S. (2005). Metabolomics reviewed: a new "omics" platform technology for systems biology and implications for natural products research. *Journal of Natural Products*. 68(12): 1813-1820.

Rodriguez, R. J., White Jr, J. F., Arnold, A. E., and Redman, R. S. (2009). Fungal endophytes: diversity and functional roles. *New Phytologist*. 182(2): 314-330.

Roessner, U. and Bowne, J. (2009). What is metabolomics all about?.*Biotechniques*. 46(5): 363.

Roessner, U., Willmitzer, L., and Fernie, A. (2002). Metabolic profiling and biochemical phenotyping of plant systems. *Plant Cell Reports*. 21(3): 189-196.

Rothman, D. L., Behar, K. L., Hyder, F., and Shulman, R. G. (2003). In vivo NMR studies of the glutamate neurotransmitter flux and neuroenergetics: implications for brain function. *Annual Review of Physiology*. 65(1): 401-427.

Rukayadi, Y., and Hwang, J. K. (2007). In vitro antimycotic activity of xanthorrhizol isolated from Curcuma xanthorrhiza Roxb. against opportunistic filamentous fungi. *Phytotherapy Research*. 21(5): 434-438.

Saithong, P., Panthavee, W., Stonsaovapak, S., and Congfa, L. (2010). Isolation and primary identification of endophytic fungi from Cephalotaxus mannii trees. *Maejo International Journal of Science and Technology*. 4(3): 446-453.

Sanchez Marquez S., Bills G.F., and Zabalgogeazcoa, I. (2007). The endophytic mycobiota of the grass Dactylis glomerata. *Fungal Diversity*. 27: 171-195.

Santamarina, M. P., Roselló, J., Llacer, R., and Sanchis, V. (2002). Antagonistic activity of *Penicillium oxalicum* Corrie and Thom, *Penicillium decumbens* Thom and *Trichoderma harzianum* Rifai isolates against fungi, bacteria and insects in vitro. *Revista Iberoamericana de Micología*. 19(2): 99-103.

Santos, D. A., Barros, M. E. S., and Hamdan, J. S. (2006). Establishing a method of inoculum preparation for susceptibility testing of *Trichophyton rubrum* and *Trichophyton mentagrophytes*. *Journal of Clinical Microbiology*. 44(1): 98-101.

Sati, S. C. and Bisht, S. (2006). Utilization of various carbon sources for the growth of waterborne conidial fungi. *Mycologia*. 98(5): 678-681.

Schiller, M., Lübeck, M., Sundelin, T., Meléndez, L. F. C., Danielsen, S., Jensen, D. F., and Ordeñana, K. M. (2006). Two subpopulations of Colletotrichum acutatum are responsible for anthracnose in strawberry and leatherleaf fern in Costa Rica. *European Journal of Plant Pathology*. 116(2), 107-118.

Schneider P, Misiek M, and Hoffmeister D. (2008). *In vivo* and *in vitro* production options for fungal secondary metabolites. *Molecular Pharmaceutics*. 5: 234-242.

Schulz, B., and Boyle, C. (2005). The endophytic continuum. *Mycological Research*. 109(6): 661-686

Schulz, B., Boyle, C., Draeger, S., Römmert, A. K., and Krohn, K. (2002). Endophytic fungi: a source of novel biologically active secondary metabolites.*Mycological Research*. 106(9): 996-1004.

Seidel, V. (2012). Initial and bulk extraction of natural products isolation. In *Natural Products Isolation* (pp. 27-41). Humana Press.

Sempere F. and Santamarina M.P. (2008). Suppression of Nigospora oryzae (Berk. & Broome) Petch by an aggressive mycoparasite and competitor, *Penicillium oxalicum* Currie & Thom. *International Journal of Food Microbiology*.122:35-43.

Silveira, C. P., Torres-Rodríguez, J. M., Alvarado-Ramírez, E., Murciano-Gonzalo, F., Dolande, M., Panizo, M., and Reviakina, V. (2009). MICs and minimum fungicidal concentrations of amphotericin B, itraconazole, posaconazole and terbinafine in Sporothrix schenckii. *Journal of Medical Microbiology*. 58(12): 1607-1610.

Singh, H. P., Batish, D. R., and Kohli, R. K. (2003). Allelopathic interactions and allelochemicals: new possibilities for sustainable weed management. *Critical Reviews in Plant Sciences*. 22(3-4): 239-311.

Singh, M. P. (2009). Application of Biolog FF MicroPlate for substrate utilization and metabolite profiling of closely related fungi. *Journal of Microbiological Methods*. 77(1): 102-108.

Son, H. S., Hwang, G. S., Ahn, H. J., Park, W. M., Lee, C. H., and Hong, Y. S. (2009). Characterization of wines from grape varieties through multivariate statistical analysis of ^{1}H NMR spectroscopic data. *Food Research International*, 42(10): 1483-1491.

Song, Y. C., Huang, W. Y., Sun, C., Wang, F. W., and Tan, R. X. (2005). Characterization of graphislactone A as the antioxidant and free radical-scavenging substance from the culture of Cephalosporium sp. IFB-E001, an endophytic fungus in Trachelospermum jasminoides. *Biological and Pharmaceutical Bulletin*. 28(3): 506-509.

Stone, J. K., Polishook, J. D., and White, J. F. (2004). Endophytic fungi. *Biodiversity of Fungi.* (pp. 241-270). Burlington: Elsevier Academic Press.

Strobel, G. A. (2003). Endophytes as sources of bioactive products. *Microbes and Infection*. 5(6): 535-544.

Strobel, G. A., Miller, R. V., Martinez-Miller, C., Condron, M. M., Teplow, D. B., and Hess, W. M. (1999). Cryptocandin, a potent antimycotic from the endophytic fungus Cryptosporiopsis cf. quercina. *Microbiology*. 145(8): 1919-1926.

Strobel, G., and Daisy, B. (2003). Bioprospecting for microbial endophytes and their natural products. *Microbiology and Molecular Biology Reviews*. 67(4): 491-502.

Strobel, G., Ford, E., Worapong, J., Harper, J. K., Arif, A. M., Grant, D. M., and Ming Wah Chau, R. (2002). Isopestacin, an isobenzofuranone from *Pestalotiopsis microspora*, possessing antifungal and antioxidant activities. *Phytochemistry*. 60(2): 179-183.

Suhaila, M. (2014). Isolation and characterization of antifungal activity of endophytic *Penicillium oxalicum* T3.3 for anthracnose biocontrol in dragon fruit (*Hylocereus* sp.). Master thesis, UPM.

Sun, Z. L., Zhang, M., Zhang, J. F., & Feng, J. (2011). Antifungal and cytotoxic activities of the secondary metabolites from endophytic fungus Massrison sp.*Phytomedicine*, *18*(10), 859-862.

Sunesson, A. L. (1995). Volatile metabolites from microorganisms in indoor environments: sampling, analysis and identification.

Szymańska, E., Saccenti, E., Smilde, A. K., and Westerhuis, J. A. (2012). Double-check: validation of diagnostic statistics for PLS-DA models in metabolomics studies. *Metabolomics*. 8(1): 3-16.

Taba, S., Mikami, D., Takaesu, K., Ooshiro, A., Moromizato, Z., Nakasone, S., and Kawano, S. (2006). Anthracnose of pitaya (*Hylocereus undatus*) by *Colletotrichum gleosporioides. Japanese Journal of Phytopathology*. 72(1): 25-27.

Taboada, C., Millan, R., and Miguez, I. (2013). Evaluation of marine algae *U. pinnatifida* and Porphyra purpurea as a food supplement: composition, nutritional value and effect of intake on intestinal, hepatic and renal enzyme activities in rats. *Journal of the Science of Food and Agriculture*. 93(8): 1863-1868.

Taechowisan, T., Peberdy, J. F., and Lumyong, S. (2003). Isolation of endophytic actinomycetes from selected plants and their antifungal activity. *World Journal of Microbiology and Biotechnology*. 19(4): 381-385.

Takahashi, L. M., Rosa, D. D., Basseto, M. A., de Souza, H. G., and Furtado, E. L. (2008). First report of Colletotrichum gloeosporioides on Hylocereus megalanthus in Brazil. *Australasian Plant Disease Notes*. 3(1): 96-97.

Tan, K. C., Ipcho, S. V., Trengove, R. D., Oliver, R. P., and Solomon, P. S. (2009). Assessing the impact of transcriptomics, proteomics and metabolomics on fungal phytopathology. *Molecular Plant Pathology*. 10(5): 703-715.

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

Tang J. C., Taniguchi H, Chu H, Zhou Q. and Nagata S. (2009). Isolation and characterization of alginate-degrading bacteria fordisposal of seaweed wastes. *Letter Applied Microbiology.* 48(1): 38-43.

Than, P. P., Prihastuti, H., Phoulivong, S., Taylor, P. W., and Hyde, K. D. (2008). Chilli anthracnose disease caused by Colletotrichum species. *Journal of Zhejiang University Science B*. 9(10): 764-778.

Tosiah, S. (2013). Carbon utilization pattern of *Exserohilum monoceras* isolates from Malaysian rice fields. *Journal of Tropical Agriculture and Food Science.* 41(1): 109-118.

Ulrich-Merzenich, G., Zeitler, H., Jobst, D., Panek, D., Vetter, H., and Wagner, H. (2007). Application of the "-Omic-" technologies in phytomedicine. *Phytomedicine*. 14(1): 70-82.

Van der Kooy, F., Maltese, F., Choi, Y. H., Kim, H. K., and Verpoorte, R. (2009). Quality control of herbal material and phytopharmaceuticals with MS and NMR based metabolic fingerprinting. *Planta Medica*. 75(07): 763-775.

Van Loon, L. C., Bakker, P. A. H. M., and Pieterse, C. M. J. (1998). Systemic resistance induced by rhizosphere bacteria. *Annual Review of Phytopathology*. 36(1): 453-483.

Verpoorte, R., Choi, Y. H., and Kim, H. K. (2007). NMR-based metabolomics at work in phytochemistry. *Phytochemistry Reviews*. 6(1): 3-14.

Vidyalakshmi, A., and Divya, C.V. (2013). New report of *Colletotrichum gloeosporioides* causing anthracnose of *Pisonia alba* in India. *Archives of Phytopathology and Plant Protection.* 46(2): 201-204.

Villas-Boas, S. G. (2013). Analytical Techniques & Applications of Metabolomics in Systems Medicine and Systems Biotechnology. *Computational and Structural Biotechnology Journal*. *4*.

Vipra, A., Desai, S.N., Junjappa, R. P., Roy, P., Poonacha, N., Ravinder, P. and Padmanabhan, S. (2013). Determining the minimum inhibitory concentration of bacteriphages: Potential advantages. *Advances in Microbiology*. 3: 181-190.

Wang, L., Chen, J., Chen, L., Deng, P., Bu, Q., Xiang, P., Li, M., Lu, W., Xu, Y., Lin, H., Wu, T., Wang, H., Hu, J., Shao, X., Cen, X., and Zhao, Y-L. (2013). ^{1}H-NMR based metabonomic profiling of human esophageal cancer tissue. *Molecular Cancer.* 12:25.

Wang, S., Sharp, P., and Copeland, L. (2011). Structural and functional properties of starches from field peas. *Food Chemistry.* 126(4): 1546-1552.

Ward, J. L., Baker, J. M., and Beale, M. H. (2007). Recent applications of NMR spectroscopy in plant metabolomics. *Federation of European Biochemical Societies Journal*. 274(5): 1126-1131.

Ward, J. L., Baker, J. M., Miler, S. J., Deborde, C., Maucourt, M., Biais, B., Rolin, D., Moing, A., Moco, S., Vevoort, J., Lommen, A., Schafer, H., Humpfer, E. and Beale, M. H. (2010). An inter laboratory comparison demonstrates that ^{1}H-NMR metabolite fingerprinting is a robust technique for collaborative plant metabolomic data collection. *Metabolomics.* 6:263-273.

Weber, D. (2009). Endophytic fungi, occurrence and metabolites. In *Physiology and Genetics* (pp. 153-195). Springer Berlin Heidelberg.

Wishart, D. S. (2007). Discovering drug targets through the web. *Comparative Biochemistry and Physiology Part D: Genomics and Proteomics.* 2(1): 9-17.

Wishart, D. S. (2008). Quantitative metabolomics using NMR. *TrAC Trends in Analytical Chemistry*. 27(3): 228-237.

Xue-Yun, L. I. U. X. J. I. E. L., and Qing-Tao, L. X. F. C. (1988). Taxonomic determination of toxigenic arthrinium strains isolated from poisoning sugarcane. *Mycosystema*. *4*: 005.

Yang, S. O., Shin, Y. S., Hyun, S. H., Cho, S., Bang, K. H., Lee, D., and Choi, H. K. (2012). NMR-based metabolic profiling and differentiation of ginseng roots according to cultivation ages. *Journal of Pharmaceutical and Biomedical Analysis*. 58: 19-26.

Zhang, A., Sun, H., Wang, P., Han, Y., and Wang, X. (2012). Modern analytical techniques in metabolomics analysis. *Analyst*. 137(2): 293-300.