UNIVERSITI PUTRA MALAYSIA

ISOLATION, MOLECULAR AND BIOMEDICAL CHARACTERISATION OF ENDOPHYTES FROM SELECTED MEDICINAL PLANTS

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FPSK(P) 2017 19

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By

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Thesis submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Doctor of Philosophy

June 2017

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Doctor of Philosophy

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June 2017

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Plants are primary sources of natural product drugs. However, with every new bioactive molecule reported from a plant source, there follows reports of endangered status or even extinction of a medicinally important plant due to over-harvesting. Hence, the attention turned towards fungi and bacteria namely the endophytes, which reside within plants. They have been found to produce secondary metabolites which are significant sources of novel compounds that have the potential for pharmaceutical, agricultural and biotechnological applications. The objectives in this study were to investigate the diversity and biomedical properties of endophytes in selected local medicinal plants. In efforts to bioprospect for possible antibacterial and anticancer metabolites, a total of 203 endophytic fungi were isolated from 10 medicinal plants. These selected plants were local medicinal plants indigenously used and known traditionally to have antibacterial and anticancer properties. They are *Clinacanthus nutans* (SK 2280/13), *Strobilanthes crispus* (SK 2281/13), *Lonicera japonica* (SK 2282/13), *Senna obtusifolia* (SK 2283/13), *Elephantopus scaber* (SK 2284/13), *Leea indica* (SK 2285/13), *Pereskia sacharosa* (SK 2286/13), *Pereskia bleo* (SK 2287/13), *Hippobroma longiflora* (SK 2288/13), and *Persicaria chinensis* (SK 2289/13). These endophytes were isolated and grown on 3 medium plates which are actinomycetes isolation agar (ATC), potato dextrose agar (PDA) and starch casein agar (SCA). Genetic diversity studies on the endophyte isolates done on random polymorphic DNA (RAPD) showed that the monomers (OPO 6, OPO 10 and OPO16) used for the amplification were able to cluster majority of the isolates into different parts of the plant. Antibacterial screening results showed that plant *Clinacanthus nutans* and *Strobilanthes crispus* have more potential of bioactive properties in comparison to the other 8 plants. A total of

30 fungal endophytes from these 2 plants were then further subjected to anticancer screening and molecular identification. Results from the alignment of the ITS rDNA regions of phylogenetic trees show that plant *Clinacanthus nutans* with 11 fungal endophytes were attributed to 8 genera whereas, plant *Strobilanthes crispus* with 19 fungal endophytes were attributed to 8 genera and 1 class. After much screening from the myriad of 203 fungal endophytes for antibacterial and anticancer properties, (SCA)AL3 closely identified as *Neosartorya hiratsukae* showed the highest significant antibacterial activity against 5 gram-positive bacteria at concentration 200 µg/disc and anticancer activity against all the 5 cancer cell lines tested with half maximal inhibitory concentration (IC_{50}) ranging from 17.67 µg/ml to 88.33 µg/ml. As for the gas chromatography coupled with mass spectrometry (GC-MS) results, a total of 4 volatile metabolites were identified from the dichloromethane crude extract of *Neosartorya hiratsukae* having more than 10% abundance. It is postulated that the synergistic effects of the 4 volatile metabolites were the contribution to the antibacterial and anticancer properties of (SCA)AL3, *Neosartorya hiratsukae.* From a total of 203 fungal endophytes which underwent molecular studies and screened against 24 bacterial pathogens and 5 cancer cell lines, the most significant findings was (SCA)AL3, *Neosartorya hiratsukae*, which was the first reported fungus having medicinal properties isolated from a medicinal plant, *Clinacanthus nutans,* found in Malaysia.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

ISOLASI, MOLEKULAR DAN KARAKTERISTIK BIOPERUBATAN ENDOPHIT DARIPADA TUMBUHAN UBATAN YANG TERPILIH

Oleh

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Tumbuh-tumbuhan adalah sumber utama ubat-ubatan produk semula jadi. Walau bagaimanapun, dengan setiap molekul bioaktif baru dilaporkan dari sumber tumbuhan, terdapat berikut laporan status terancam atau kepupusan tumbuhan penting secara perubatan kerana terlalu menuai. Oleh itu, perhatian diutamakan ke arah kulat dan bakteria iaitu endofitik, yang tinggal di dalam tumbuh-tumbuhan. Mereka didapati dapat menghasilkan metabolit sekunder yang merupakan sumber penting sebatian novel yang mempunyai potensi untuk aplikasi farmaseutikal, pertanian dan bioteknologi. Objektif kajian ini adalah untuk menyiasat kepelbagaian dan sifat bioperubatan endophytes dalam tumbuhan ubatan tempatan. Dalam usaha untuk memperolehi metabolit yang mempunyai anti-kanser dan anti-bakteria, sebanyak 203 kulat endofitik telah diasingkan daripada 10 tumbuhan perubatan iaitu *Clinacanthus nutans* (SK 2280/13), *Strobilanthes crispus* (SK 2281/13*), Lonicera japonica* (SK 2282/13), *Senna obtusifolia* (SK 2283/13), *Elephantopus scaber* (SK 2284/13), *Leea indica* (SK 2285/13), *Pereskia sacharosa* (SK 2286/13), *Pereskia bleo* (SK 2287/13), *Hippobroma longiflora* (SK 2288/13), *dan Persicaria chinensis* (SK 2289/13). Semua endofit ini telah diasingkan dan ditanam atas 3 plat agar iaitu actinomycetes isolation agar (ATC), potato dextrose agar (PDA) and starch casein agar (SCA). Kajian kepelbagaian genetik antara endofit dengan menggunakan kaedah random polymorphic DNA (RAPD) menunjukkan bahawa monomer (OPO 6, OPO 10 dan OPO16) yang digunakan dapat menghasilkan pengelompokan majoriti diasingkan kepada bahagian-bahagian tumbuhan. Daripada pemeriksaan anti-bakteria, keputusan menunjukkan bahawa tumbuhan *Clinacanthus nutans* dan *Strobilanthes crispus* mempunyai akitiviti yang paling banyak berbanding dengan 8 tumbuhan perubatan yang lain. Sebanyak, 30 endofitik

kulat dari 2 pokok ini kemudian tertakluk kepada pemeriksaan anti-kanser dan pengenalan molekul. Hasil daripada analysis ITS rDNA, pokok filogenetik menunjukkan bahawa tumbuhan *Clinacanthus nutans* yang terdiri daripada 11 endofitik kulat adalah daripada 8 genera manakala, tumbuhan *Strobilanthes crispus* yang terdiri daripada 19 endofitik kulat adalah disebabkan oleh 8 genera dan 1 kelas. Selepas pemeriksaan anti-bakteria dan anti-kanser 203 endofitik kulat, (SCA)AL3 yang juga dikenal pasti sebagai *Neosartoya hiratsukae* menunjukkan aktiviti anti-bakteria yang paling tinggi iaitu terhadap 5 bakteria gram-positif pada kepekatan 200 µg/cakera dan aktiviti anti-kanser terhadap semua 5 sel kanser diuji dengan separuh kepekatan perencatan maksimal (IC_{50}) antara 17.67 µg/ml hingga 88.33 µg/ml. Bagi keputusan kromatografi gas spektrometri jisim (GC-MS), sebanyak 17 metabolit telah dikenal pasti daripada ekstrak mentah diklorometana daripada *Neosartorya hiratsukae* yang mempunyai lebih daripada 1% dan daripada 17 metabolit ini hanya 4 metabolit dikenal pasti mempunyai lebih banyak daripada 10%. Ia dijangka adalah kerana akitiviti sinergi 4 metabolit ini yang menyumbang kepada sifat-sifat anti-bakteria dan anti-kanser daripada (SCA)AL3. Daripada 203 endophytes yang menjalani kajian molekul dan pemeriksaan terhadap 24 patogen bakteria dan 5 sel kanser, penemuan yang paling penting ialah (SCA)AL3, *Neosartorya hiratsukae*, merupakan laporan pertama *Neosartorya hiratsukae* mempunyai sifat perubatan yang diasingkan dari tumbuhan perubatan *Clinacanthus nutans* yang terdapat di Malaysia.

ACKNOWLEDGEMENTS

Rome was not built in a day" – so goes the famous saying, and the completion of a project of any scale would most definitely not be accomplished with the efforts of one individual alone. Therefore, I would like to take this opportunity to express my deepest gratitude to several individuals, who lent their support in various ways throughout the duration of my study.

First and foremost, I would like to express my deepest gratitude to my supervisor, Associate Professor Dr. Cheah Yoke Kqueen for his valuable guidance, suggestions, encouragement and believing in my research capabilities throughout my project and preparation of the thesis. I would like to extend my sincere gratitude to my co-supervisor, Dr. Ho Kok Lian and Professor Dr. Tan Soon Guan as well as my church advisor Dr. Kenny Teoh Guan Cheng for their support, valuable comments and inspirations all these years.

I am also very grateful to all the science officers, assistants and technicians of Molecular Biology Laboratory, Cell Biology and Immunology Laboratory and Multi-purpose Laboratory of Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Thank you very much for the guidance, kind assistance, informative description about the equipment, chemicals in the laboratory as well as the methods of handling and operating them. Special thanks go to my laboratory group members, CSSUPM members and friends who have helped me directly and indirectly for the past years. Thank you for the sharing of knowledge and continuous moral support.

I would also like to acknowledge the financial support from Ministry of Education Malaysia for the MyBrain15 (MyPhD) Scholarship. Millions of thanks go out to Malaysian Toray Science Foundation and University Putra Malaysia Research University Grant for funding the research studies.

Last but not least, my deepest appreciation goes out to my parents who have constantly supported me all throughout my life and made me who I am today, my siblings and Thet Naing who have always been there for me and the one above all of us, the omnipresent God, for answering my prayers for giving me the strength to plod on as the saying goes "I can do all things through Christ who strengthens me", thank you so much Dear Lord God

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

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LIST OF ABBREVIATIONS

TCM	Traditional Chinese medicine
TIM	Traditional Indian medicine
CN	*Clinacanthus nutans*
SC	*Strobilanthes crispus*
LJ	*Lonicera japonica*
SO	*Senna obtusifolia*
ES	*Elephantopus scaber*
LI	*Leea indica*
PS	*Pereskia sacharosa*
PB	*Pereskia bleo*
HL	*Hippobroma longiflora*
PC	*Persicaria chinensis*
ATC	Actinomycetes isolation agar
PDA	Potato dextrose agar
SCA	Starch casein agar
RAPD	Random polymorphic DNA
ATCC	American Type Culture Collection
OD	Optical density
SPSS	Statistical Package for Social Science
ITS	Internal Transcribed Spacer
PC-3	Human prostatic adenocarcinoma cells
HEPG2	Human hepatocellular carcinoma cells
A549	Human alveolar adenocarcinoma cells
HT-29	Human colorectal adenocarcinoma cells
MCF-7	Human breast adenocarcinoma cells
HEK-293	Human embryonic kidney 293 cells
IC_{50}	Half maximal inhibitory concentration
RTCA	Real Time Cell Analyser
NCBI	National Center for Biotechnology Information
GC-MS	Gas chromatography-mass spectrometry
GC	Gas chromatography
MS	Mass spectrometry
VOC	Volatile organic compound
LPCB	Lactophenol cotton blue stain
cfu	Colony forming unit

CHAPTER 1

INTRODUCTION

1.1 General introduction

In the past few decades, many researchers have begun to realise that plants may serve as a reservoir of untold numbers of organisms known as endophytes. The existence of endophytes has been known for hundreds of years (Petrini and Carroll, 1981). Endophytes are often fungi and bacteria, which live in living plant cells. These microorganisms reside inter- or intra-cellularly in plant tissues and are able to produce secondary metabolites to enhance the ecological fitness of their host plants. As a direct result of the role that these secondary metabolites play in plant physiology and nature, they have the potential for pharmaceutical, agricultural and biotechnological applications (Strobel *et al.,* 2004). Endophytes are also known as the chemical synthesisers that are capable of synthesising bioactive compounds used by plants for defense against pathogens and some of these compounds have been proven useful for novel drug discovery (Owen *et al.,* 2004).

Endophytes are ubiquitous with rich biodiversity, which have been found in every plant species examined to date. It is noteworthy that, of the nearly 300,000 plant species that exist on the earth, each individual plant is the host to one or more endophytes (Strobel, 2003). In view of special colonisation in certain hosts, it is estimated that there may be as many as 1 million different endophyte species, however only a handful of them have been described (Petrini *et al.,* 1991) indicating that the opportunity to find new and targeting natural products from interesting endophytic microorganisms among myriads of plants in different niches and ecosystems is great.

Of the myriad of ecosystems on earth, tropical and temperate rainforests are the most biologically diverse terrestrial ecosystems on earth and it seems to be the ones having the greatest number and most diverse endophytes. Plants that grow in unique environments usually struggle to compete or that need as much assistance as possible to survive, are likely to host a variety of endophytes which may assist the survival plant (Strobel *et al.,* 2004). Many scientists have predicted that plants growing in lush tropical rainforests, where competition for light and nutrients are great, resources are limited, and selection pressure is at its peak are most likely to host the greatest number of bioactive endophytes. Previous studies noted that endophytes from tropical regions produce significantly higher bioactive secondary metabolites than those from temperate parts of the world (Bills *et al.,* 2002).

As an area in the tropical rainforest region, Malaysia could serve as an important and great source to further research on the endophytes found in the medicinal plants grown here. In Malaysia, extract from many types of local plants are used in traditional manner for treatments of various ailments. For instance, previous studies have shown that the aborigines or indigenous people have utilised many wild medicinal plants for many centuries. They healed themselves with traditional herbal medicines and ancient remedies from immemorial time passed down through generations (Samuel *et al.,* 2010). The most common parts of the plant used in the preparation of herbal medicine are leaves, stems, roots and whole plant. However, other plant parts were also used which are fruits, flowers, seeds, rhizomes, tubers, bulbs and saps (Ahmad and Holdsworth, 2003; Ong *et al.,* 2011). The 10 medicinal plants selected for this study were plants indigenously used for traditional treatment against antibacterial and anticancer diseases. These plants are still naturally taken for treatment up to date. They are *Clinacanthus nutans*, *Strobilanthes crispus*, *Lonicera japonica*, *Senna obtusifolia*, *Elephantopus scaber*, *Leea indica*, *Pereskia sacharosa*, *Pereskia bleo*, *Hippobroma longiflora*, *and Persicaria chinensis*.

The question is whether these medicinal effects are produced by the plant itself or as a consequence of mutualistic relationships with beneficial organisms in their tissue. Studies have shown that it seems likely that some of the healing properties in plants, as discovered by indigenous peoples, might be facilitated by compounds produced by one or more specific plant-associated endophytes as well as the plant products themselves. For instance, one notable endophyte with medicinal benefits to humans was discovered from *Taxomyces andreanae*, an endophytic fungus of *Taxus brevifolia* (Pacific yew tree). It was found to produce taxol also known as paclitaxel, the world's billion dollar anticancer drug and also known to treat a number of other human tissue-proliferating diseases (Strobel *et al.,* 2003).

Only limited studies have been carried to evaluate the potential of fungal endophytes inhabiting Malaysian medicinal plants (Radu and Cheah, 2002; Hazalin *et al.,* 2009; Harun *et al.,* 2015). The rich biodiversity and in distinct ecological settings in Malaysia suggests the possibility that the endophytes contained in them may have unique biosynthetic capabilities, leading to the production of unique metabolites with varied biological activities.

Recent studies have shown an increase development of multi-drug resistant in human pathogens and cancer incidence rate in the world. The need for new drugs is much required for survival. Thus, with the vast source of medicinal plants found in Malaysia which have yet to be extensively studied, there is a need to research further on the endophytes of medicinal plants in Malaysia. It was hypothesised that there are promising endophytes of interest having antibacterial and anticancer properties. It would be of a great achievement once a new discovery is obtained.

1.2 Objectives

The general objective of this study was to investigate the diversity and biomedical properties of endophytes in selected Malaysian medicinal plants.

The specific objectives of this study were:

a) To isolate endophytes from different parts of the selected medicinal plants.
b) To determine the diversity of the isolated endophytes in the medicinal plants via random amplified polymorphic DNA (RAPD) and internal transcribed spacer (ITS) region.
c) To determine the antibacterial and anticancer properties of the isolated endophytes.
d) To determine the potential bioactive components of the crude extract of the selected endophyte of interest.

Figure 1.1 summarises the work conducted in this study from collection of plant samples to ultrastructure viewing of endophytes. The objectives are indicated at their respective steps.

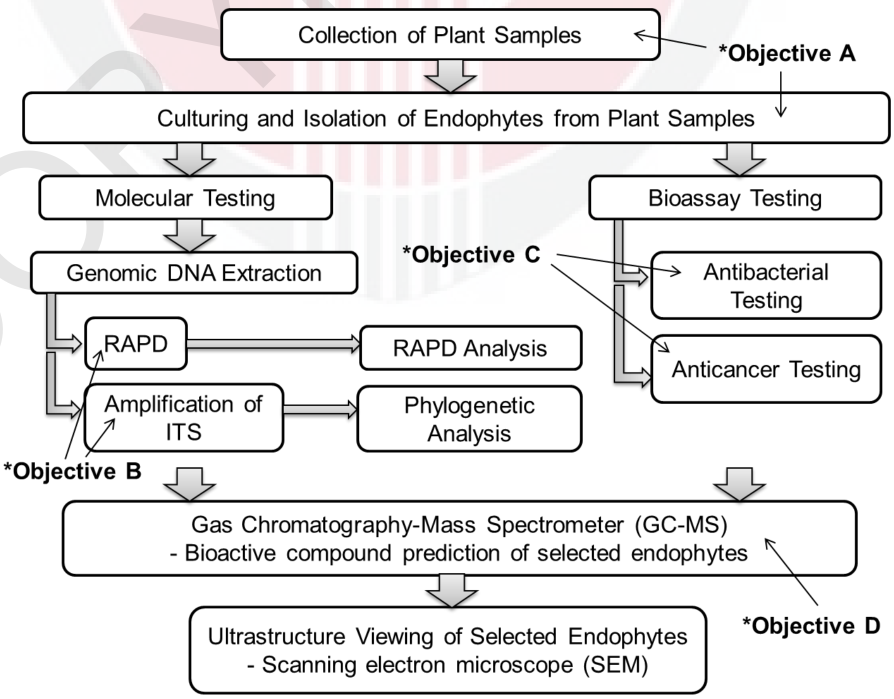

Figure 1.1: Flow chart of the experimental design. Flow chart indicates designated objectives to be achieved throughout this study.

REFERENCES

Agrawal, V., Sharma, K., Gupta, S., Kumar, R., & Prasad, M. (2007). Identification of sex in *Simmondsia chinensis* (Jojoba) using RAPD markers. *Plant Biotechnology Reports, 1*(4), 207-210.

Ahmad, F. B., & Holdsworth, D. K. (2003). Medicinal plants of Sabah, East Malaysia–Part I. *Pharmaceutical Biology*, *41*(5), 340-346.

Akinsanya, M. A., Ting, A., Goh, J. K., & Lim, S. P. (2016). Biodiversity, enzymatic and antimicrobial activities of bacterial endophytes in selected local medicinal plants. *Journal of Biomedical and Pharmaceutical Research, 5*(1), 76-88.

Albrectsen, B. R., Bjorken, L., Varad, A., Hagner, A., Wedin, M., Karlsson, J., & Jansson, S. (2010). Endophytic fungi in European aspen (*Populus tremula*) leaves diversity, detection, and a suggested correlation with herbivory resistance. *Fungal Diversity, 41*(1), 17-28.

Al-Samarrai, T., & Schmid, J. (2000). A simple method for extraction of fungal genomic DNA. *Letters in Applied Microbiology, 30*(1), 53-56.

Alsarhan, A., Sultana, N., Al-Khatib, A., & Kadir, M. R. A. (2014). Review on some Malaysian traditional medicinal plants with therapeutic properties. *Journal of Basic and Applied Sciences, 10*(1), 149-159.

Alvarez, I., & Wendel, J. F. (2003). Ribosomal ITS sequences and plant phylogenetic inference. *Molecular Phylogenetics and Evolution, 29*(3), 417-434.

Alvin, A., Miller, K. I., & Neilan, B. A. (2014). Exploring the potential of endophytes from medicinal plants as sources of antimycobacterial compounds. *Microbiological Research, 169*(7), 483-495.

Aly, A. H., Edrada-Ebel, R., Indriani, I. D., Wray, V., Muller, W. E., Totzke, F., Zirrgiebel, U., Schachtele, C., Kubbutat, M. H., Lin, W. H., Proksch, P., & Ebel R. (2008). Cytotoxic metabolites from the fungal endophyte *Alternaria* sp. and their subsequent detection in its host plant *Polygonum senegalense*. *Journal of Natural Products, 71*(6), 972-980.

Aly, A. H., Edrada-Ebel, R., Wray, V., Muller, W. E., Kozytska, S., Hentschel, U., Proksch, P., & Ebel, R. (2008). Bioactive metabolites from the endophytic fungus *Ampelomyces* sp. isolated from the medicinal plant *Urospermum picroides*. *Phytochemistry, 69*(8), 1716-1725.

Aly, A. H., Debbab, A., Kjer, J., & Proksch, P. (2010). Fungal endophytes from higher plants: a prolific source of phytochemicals and other bioactive natural products. *Fungal Diversity, 41*(1), 1-16.

Anderson, I. C., Campbell, C. D., & Prosser, J. I. (2003). Potential bias of fungal 18S rDNA and internal transcribed spacer polymerase chain reaction primers for estimating fungal biodiversity in soil. *Environmental Microbiology, 5*(1), 36-47.

Ang, J. Y., Ezike, E., & Asmar, B. I. (2004). Antibacterial resistance. *The Indian Journal of Pediatrics, 71*(3), 229-239.

Arnold, A. E., Maynard, Z., Gilbert, G. S., Coley, P. D., & Kursar, T. A. (2000). Are tropical fungal endophytes hyperdiverse? *Ecology Letters, 3*(4), 267-274.

Arnold, A. E., Mejía, L. C., Kyllo, D., Rojas, E. I., Maynard, Z., Robbins, N., & Herre, E. A. (2003). Fungal endophytes limit pathogen damage in a tropical tree. *Proceedings of the National Academy of Sciences, 100*(26), 15649-15654.

Arnold, A. E., & Herre, E. A. (2003). Canopy cover and leaf age affect colonization by tropical fungal endophytes: ecological pattern and process in *Theobroma cacao* (Malvaceae). *Mycologia, 95*(3), 388-398.

Arullappan, S., Rajamanickam, P., Thevar, N., & Kodimani, C. C. (2014*). In vitro* screening of cytotoxic, antimicrobial and antioxidant activities of *Clinacanthus nutans* (Acanthaceae) leaf extracts. *Tropical Journal of Pharmaceutical Research, 13*(9), 1455-1461.

Aschehoug, E. T., Metlen, K. L., Callaway, R. M., & Newcombe, G. (2012). Fungal endophytes directly increase the competitive effects of an invasive forb. *Ecology, 93*(1), 3-8.

Atalla, M. M., Zeinab, H. K., Eman, R. H., Amani, A. Y., & Abeer, A. (2008). Production of some biologically active secondary metabolites from marine-derived fungus *Varicosporina ramulosa*. *Malaysian Journal of Microbiology, 4*(1), 14-24.

Atta-ur-Rahman, Choudhary M. I. & William, J. T. (2001) *Bioassay Technique for Drug Development*, (pp. 30-38). Harwood Academic Press, Reading.

Avani, K., & Neeta, S. (2005). A study of the antimicrobial activity of *Elephantopus scaber*. *Indian Journal Pharmacology, 37*(2), 126-128.

Avinash, K., Ashwini, H., Babu, H., & Krishnamurthy, Y. (2015). Antimicrobial potential of crude extract of *Curvularia lunata*, an endophytic fungi isolated from *Cymbopogon caesius*. *Journal of Mycology, 2015*(1), 1-4.

Avise, J. C. (1995). Mitochondrial DNA polymorphism and a connection between genetics and demography of relevance to conservation. *Conservation Biology, 9*(3), 686-690.

Awasthi, A. K., Nagaraja, G., Naik, G., Kanginakudru, S., Thangavelu, K., & Nagaraju, J. (2004). Genetic diversity and relationships in mulberry (genus *Morus*) as revealed by RAPD and ISSR marker assays. *BioMed Central Genetics, 5*(1), 1-9.

Ayerst, G. (1969). The effects of moisture and temperature on growth and spore germination in some fungi. *Journal of Stored Products Research, 5*(2), 127-141.

Balachandran, C., Duraipandiyan, V., & Ignacimuthu, S. (2012). Cytotoxic (A549) and antimicrobial effects of *Methylobacterium* sp. isolate (ERI-135) from Nilgiris forest soil, India. *Asian Pacific Journal of Tropical Biomedicine, 2*(9), 712-716.

Baldwin, B. G., Sanderson, M. J., Porter, J. M., Wojciechowski, M. F., Campbell, C. S., & Donoghue, M. J. (1995). The ITS region of nuclear ribosomal DNA: A valuable source of evidence on angiosperm phylogeny. *Annals of the Missouri Botanical Garden*, *88*(2), 247-277.

Balouiri, M., Sadiki, M., & Ibnsouda, S. K. (2016). Methods for *in vitro* evaluating antimicrobial activity: A review. *Journal of Pharmaceutical Analysis, 6*(2), 71-79.

Bandyopadhyay, S., & Mukherjee, S. K. (2005). Ethnoveterinary medicine from Koch Bihar district, West Bengal. *Indian Journal of Traditional Knowledge, 4*(4), 456-461.

Bartnicki-Garcia, S. (1968). Cell wall chemistry, morphogenesis, and taxonomy of fungi. *Annual Reviews in Microbiology, 22*(1), 87-108.

Bascom-Slack, C. A., Ma, C., Moore, E., Babbs, B., Fenn, K., Greene, J. S., Hann, B. D., Keehner, J., Kelley-Swift, E. G., Kembaiyan, V., & Lee, S. J. (2009). Multiple, novel biologically active endophytic actinomycetes isolated from upper Amazonian rainforests. *Microbial Ecology, 58*(2), 374-383.

Bej, A. K., Mahbubani, M. H., Atlas, R. M., & Salkl, R. K. (1991). Amplification of nucleic acids by polymerase chain reaction (PCR) and other methods and their applications. *Critical Reviews in Biochemistry and Molecular Biology, 26*(3-4), 301-334.

Berbee, M. L., & Taylor, J. W. (1992). Detecting morphological convergence in true fungi, using 18S rRNA gene sequence data. *Biosystems, 28*(1-3), 117-125.

Bhagobaty, R. K., & Joshi, S. (2011). Multi-loci molecular characterisation of endophytic fungi isolated from five medicinal plants of Meghalaya, India. *Mycobiology, 39*(2), 71-78.

Bills, G. F., & Polishook, J. D. (1991). Microfungi from *Carpinus caroliniana*. *Canadian Journal of Botany, 69*(7), 1477-1482.

Bills, G. F., Redlin, S., & Carris, L. (1996). Isolation and analysis of endophytic fungal communities from woody plants. *Endophytic fungi in grasses and woody plants: Systematics, Ecology, and Evolution,* (pp. 31-65). American Phytopathological Society (APS Press), Minnesota.

Bills, G., Dombrowski, A., Pelaez, F., Polishook, J., An, Z. Q., Watling, R., & Robinson, C. H. (2002). Recent and future discoveries of pharmacologically active metabolites from tropical fungi. *Tropical Mycology: Volume 2, Micromycetes*, (pp. 165-194). CABI Publishing New York.

Bioassay. The American Heritage® *Science Dictionary.* Retrieved August 10, 2016 from Dictionary.com website. http://www.dictionary.com/browse/bioassay

Bisht, D., Owais, M., & Venkatesan, K. (2006). Potential of plant-derived products in the treatment of Mycobacterial infections. *Modern Phytomedicine: Turning Medicinal Plants into Drugs*, (pp. 293-311). Wiley Publisher, New Jersey.

Botstein, D., White, R. L., Skolnick, M., & Davis, R. W. (1980). Construction of a genetic linkage map in man using restriction fragment length polymorphisms. *American Journal of Human Genetics, 32*(3), 314-331.

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

Brundrett, M. C. (2006). Understanding the roles of multifunctional mycorrhizal and endophytic fungi *Microbial Root Endophytes* (pp. 281-298): Springer Publisher, New York.

Bugrysheva, J. V., Lascols, C., Sue, D., & Weigel, L. M. (2016). Rapid antimicrobial susceptibility testing of *Bacillus anthracis*, *Yersinia pestis*, and *Burkholderia pseudomallei* by use of laser light scattering technology. *Journal of Clinical Microbiology, 54*(6), 1462-1471.

Cabral, D., Stone, J. K., & Carroll, G. C. (1993). The internal mycobiota of *Juncus* spp.: Microscopic and cultural observations of infection patterns. *Mycological Research, 97*(3), 367-376.

Cai, J., Collins, M., McDonald, V., & Thompson, D. (1992). PCR cloning and nucleotide sequence determination of the 18S rRNA genes and internal transcribed spacer 1 of the protozoan parasites *Cryptosporidium parvum* and *Cryptosporidium muris*. *Biochimica et Biophysica Acta (BBA)-Gene Structure and Expression, 1131*(3), 317-320.

Carroll, G. (1986). Biology of endophytism in plants with particular reference to woody perennials. *Microbiology of the Phyllosphere,* ed. NJ

Fokkema and J. van den Heuvel, (pp. 205-222). Cambridge University Press, Cambridge.

Carroll, G. (1988). Fungal endophytes in stems and leaves: From latent pathogen to mutualistic symbiont. *Ecology, 69*(1), 2-9.

Cheah, Y. K., Salleh, N. A., Lee, L. H., Radu, S., Sukardi, S., & Sim, J. H. (2008). Comparison of PCR fingerprinting techniques for the discrimination of *Salmonella enterica* subsp. *enterica* serovar Weltevreden isolated from indigenous vegetables in Malaysia. *World Journal of Microbiology and Biotechnology, 24*(3), 327-335.

Chen, W. C., Liou, S. S., Tzeng, T. F., Lee, S. L., & Liu, I. M. (2012). Wound repair and anti-inflammatory potential of *Lonicera japonica* in excision wound-induced rats. *BioMed Central Complementary and Alternative Medicine, 12*(1), 1-9.

Chomcheon, P., Wiyakrutta, S., Sriubolmas, N., Ngamrojanavanich, N., Kengtong, S., Mahidol, C., Kittakoop, P. (2009). Aromatase inhibitory, radical scavenging and antioxidant activities of depsidones and diaryl ethers from the endophytic fungus *Corynespora cassiicola* L36. *Phytochemistry*, *70*(3), 407-413.

Chomnawang, M. T., Surassmo, S., Wongsariya, K., & Bunyapraphatsara, N. (2009). Antibacterial activity of Thai medicinal plants against methicillin-resistant *Staphylococcus aureus*. *Fitoterapia, 80*(2), 102-104.

Christian, N., Sullivan, C., Visser, N. D., & Clay, K. (2016). Plant host and geographic location drive endophyte community composition in the face of perturbation. *Microbial Ecology*, *72*(3), 621-632.

Clay, K., & Holah, J. (1999). Fungal endophyte symbiosis and plant diversity in successional fields. *Science, 285*(5434), 1742-1744.

Clay, K., & Schardl, C. (2002). Evolutionary origins and ecological consequences of endophyte symbiosis with grasses. *The American Naturalist, 160*(4), 99-127.

Compant, S., Duffy, B., Nowak, J., Clement, C., & Barka, E. A. (2005). Use of plant growth-promoting bacteria for biocontrol of plant diseases: Principles, mechanisms of action, and future prospects. *Applied and Environmental Microbiology, 71*(9), 4951-4959.

Cragg, G. M., Newman, D. J., & Snader, K. M. (1997). Natural products in drug discovery and development. *Journal of Natural Products*, *60*(1), 52-60.

Cui, J. I., Guo, S. X., & Xiao, P. G. (2011). Antitumor and antimicrobial activities of endophytic fungi from medicinal parts of *Aquilaria sinensis*. *Journal of Zhejiang University Science B, 12*(5), 385-392.

Cundliffe, E. (1984). Self-defence in antibiotic-producing organisms. *British Medical Bulletin, 40*(1), 61-67.

Cundliffe, E. (1989). How antibiotic-producing organisms avoid suicide. *Annual Reviews in Microbiology, 43*(1), 207-233.

Daisy, P., Jasmine, R., Ignacimuthu, S., & Murugan, E. (2009). A novel steroid from *Elephantopus scaber* L. an ethnomedicinal plant with antidiabetic activity. *Phytomedicine, 16*(2), 252-257.

Dalirsefat, S. B., da Silva Meyer, A., & Mirhoseini, S. Z. (2009). Comparison of similarity coefficients used for cluster analysis with amplified fragment length polymorphism markers in the silkworm, *Bombyx mori*. *Journal of Insect Science, 9*(71), 1-8.

Dalu, D., Duggirala, S., & Akarapu, S. (2014). Anti hyperglycemic and hypolipidemic activity of *Leea indica*. *International Journal of Bioassays, 3*(07), 3155-3159.

Darzynkiewicz, Z., Bruno, S., Del Bino, G., Gorczyca, W., Hotz, M., Lassota, P., & Traganos, F. (1992). Features of apoptotic cells measured by flow cytometry. *Cytometry, 13*(8), 795-808.

De Jonckheere, J. F. (1998). Sequence variation in the ribosomal internal transcribed spacers, including the 5.8 S rDNA, of *Naegleria* spp. *Protist, 149*(3), 221-228.

De Silva, L., Herath, W., Jennings, R., Mahendrant, M., & Wannigama, G. (1982). A new sesquiterpene lactone from *Elephantopus scaber. Phytochemistry, 21*(5), 1173-1175.

De Siqueira, V. M., Conti, R., de Araujo, J. M., & Souza-Motta, C. M. (2011). Endophytic fungi from the medicinal plant *Lippia sidoides* Cham. and their antimicrobial activity. *Symbiosis, 53*(2), 89-95.

De Smet, P. A. (1997). The role of plant-derived drugs and herbal medicines in healthcare. *Drugs, 54*(6), 801-840.

Debbab, A., Aly, H. A., Edrada-Ebel, R. A., Muller, W. E., Mosaddak, M., Hakiki, A., Ebel, R., & Proksch, P. (2009). Bioactive secondary metabolites from the endophytic fungus *Chaetomium* sp. isolated from *Salvia officinalis* growing in Morocco. *Biotechnologie, Agronomie, Societe et Environnement, 13*(2), 229-234.

Demain, A. L., & Vaishnav, P. (2011). Natural products for cancer chemotherapy. *Microbial Biotechnology, 4*(6), 687-699.

Dice, L. R. (1945). Measures of the amount of ecologic association between species. *Ecology, 26*(3), 297-302.

Ding, T., & Melcher, U. (2016). Influences of plant species, season and location on leaf endophytic bacterial communities of non-cultivated plants. *PloS One, 11*(3), 1-13.

Dingrong, W., Yujie, C., Ling, W., Cheng, Y., & Zhongmei, Z. (2009). A study on comparative identification of *Polygonum chinense* L. and *Polygonum chinense* L. var. hispidum Hook. f. *Journal of South-Central University for Nationalities (Natural Science Edition), 28*(4), 54-57.

Dirar, H. A. (1984). Kawal, meat substitute from fermented *Cassia obtusifolia* leaves. *Economic Botany, 38*(3), 342-349.

Dixon, L. J., Schlub, R. L., Pernezny, K., & Datnoff, L. (2009). Host specialization and phylogenetic diversity of *Corynespora cassiicola*. *Phytopathology, 99*(9), 1015-1027.

Donald, T., Shoshannah, R., Deyrup, S. T., & Gloer, J. B. (2005). A protective endophyte of maize: *Acremonium zeae* antibiotics inhibitory to *Aspergillus flavus* and *Fusarium verticillioides*. *Mycological Research, 109*(05), 610-618.

Dorworth, C. E., & Callan, B. E. (1996). Manipulation of endophytic fungi to promote their utility as vegetation biocontrol agents. *Endophytic fungi in grasses and woody plants: Systematics, Ecology, and Evolution,* (pp. 209-219). American Phytopathological Society (APS Press), Minnesota.

Doughari, J., El-Mahmood, A., & Tyoyina, I. (2008). Antimicrobial activity of leaf extracts of *Senna obtusifolia* (L). *African Journal of Pharmacy and Pharmacology, 2*(1), 7-13.

Droeser, R. A., Hirt, C., Viehl, C. T., Frey, D. M., Nebiker, C., Huber, X., Zlobec, I., Eppenberger-Castori, S., Tzankov, A., Rosso, R, & Zuber, M. (2013). Clinical impact of programmed cell death ligand 1 expression in colorectal cancer. *European Journal of Cancer, 49*(9), 2233-2242.

Dweikat, I., Mackenzie, S., Levy, M., & Ohm, H. (1993). Pedigree assessment using RAPD-DGGE in cereal crop species. *Theoretical and Applied Genetics, 85*(5), 497-505.

Edwards, B. K., Noone, A. M., Mariotto, A. B., Simard, E. P., Boscoe, F. P., Henley, S. J., & Kohler, B. A. (2014). Annual report to the nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. *Cancer, 120*(9), 1290-1314.

Ekor, M. (2014). The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology*, *4*(1), 177-187.

Elaine, J. C., Rafi, M. I. M., Hoon, K. C., Lian, H. K., & Kqueen, C. Y. (2017). Analysis of chemical constituents, antimicrobial and anticancer activities of dichloromethane extracts of *Sordariomycetes* sp.

endophytic fungi isolated from *Strobilanthes crispus*. *World Journal of Microbiology and Biotechnology, 33*(5), 1-19

Eldeen, I. M. (2014). Isolation of 12 Bacterial endophytes from some mangrove plants and determination of, antimicrobial properties of the isolates and the plant extracts. *International Journal of Phytomedicine, 6*(3), 425-432.

Ellsworth, K. T., Clark, T. N., Gray, C. A., & Johnson, J. A. (2013). Isolation and bioassay screening of medicinal plant endophytes from eastern Canada. *Canadian Journal of Microbiology, 59*(11), 761-765.

Er, H. M., Cheng, E.-H., & Radhakrishnan, A. K. (2007). Anti-proliferative and mutagenic activities of aqueous and methanol extracts of leaves from *Pereskia bleo* (Kunth) DC (Cactaceae). *Journal of Ethnopharmacology, 113*(3), 448-456.

Eyberger, A. L., Dondapati, R., & Porter, J. R. (2006). Endophyte fungal isolates from *Podophyllum peltatum* produce podophyllotoxin. *Journal of Natural products, 69*(8), 1121-1124.

Faeth, S. H., & Hammon, K. E. (1997). Fungal endophytes in oak trees: Experimental analyses of interactions with leaf miners. *Ecology, 78*(3), 820-827.

Fernandes, P. (2006). Antibacterial discovery and development the failure of success. *Nature Biotechnology, 24*(12), 1497-1503.

Fiehn, O., Kopka, J., Dormann, P., Altmann, T., Trethewey, R. N., & Willmitzer, L. (2000). Metabolite profiling for plant functional genomics. *Nature Biotechnology, 18*(11), 1157-1161.

Fischbach, M. A., & Walsh, C. T. (2009). Antibiotics for emerging pathogens. *Science, 325*(5944), 1089-1093.

Freeman, S., & Rodriguez, R. J. (1993). Genetic conversion of a fungal plant pathogen to a nonpathogenic, endophytic mutualist. *Science, 260*(5104), 75-78.

Fujii, Y., Fujii, H., & Yamazaki, M. (1983). Separation and determination of cardiac glycosides in *Digitalis purpurea* leaves by micro high-performance liquid chromatography. *Journal of Chromatography A, 258*(1), 147-153.

Gahan, J., & Schmalenberger, A. (2015). Arbuscular mycorrhizal hyphae in grassland select for a diverse and abundant hyphospheric bacterial community involved in sulfonate desulfurization. *Applied Soil Ecology, 89*, 113-121.

Gangadevi, V., Sethumeenal, S., Yogeswari, S., & Rani, G. (2008). Screening endophytic fungi isolated from a medicinal plant, *Acalypha indica* L. for antibacterial activity. *Indian Journal of Science and Technology, 1*(5), 1-6.

Garibyan, L., & Avashia, N. (2013). Polymerase chain reaction. *Journal of Investigative Dermatology, 133*(3), 1-8.

Gas chromatography–mass spectrometry, "GCMS." The Oxford Dictionary of Abbreviations. 1998. Retrieved August 11, 2016 from Encyclopedia.com: http://www.encyclopedia.com/doc/1O25-GCMS.html

Gasong, B. T., & Tjandrawinata, R. R. (2016). Production of secondary metabolite E2. 2 from *Phaleria macrocarpa* endophytic fungus. *Asian Pacific Journal of Tropical Biomedicine, 6*(10), 881-885.

Gaspar, D., Veiga, A. S., & Castanho, M. A. (2013). From antimicrobial to anticancer peptides. A review. *Frontiers in Microbiology*, *4*(1), 1-16..

Gautschi, M., Schmid, J. P., Peppard, T. L., Ryan, T. P., Tuorto, R. M., & Yang, X. (1997). Chemical characterization of diketopiperazines in beer. *Journal of Agricultural and Food Chemistry, 45*(8), 3183-3189.

Genotype. *The American Heritage® Science Dictionary*. Retrieved August 9, 2016 from Dictionary.com website http://www.dictionary.com/browse/genotype

Giauque, H., & Hawkes, C. V. (2013). Climate affects symbiotic fungal endophyte diversity and performance. *American Journal of Botany, 100*(7), 1435-1444.

Gil-Lamaignere, C., Roilides, E., Hacker, J., & Muller, F. (2003). Molecular typing for fungi: A critical review of the possibilities and limitations of currently and future methods. *Clinical Microbiology and Infection, 9*(3), 172-185.

Giridharan, P., Verekar, S. A., Khanna, A., Mishra, P., & Deshmukh, S. K. (2012). Anticancer activity of sclerotiorin, isolated from an endophytic fungus *Cephalotheca faveolata* Yaguchi, Nishim. & Udagawa. *Indian Journal of Experimental Biology, 50*(1), 464-468.

Glassbrook, N., Beecher, C., & Ryals, J. (2000). Metabolic profiling on the right path. *Nature Biotechnology, 18*(11), 1142-1143.

Glassbrook, N., & Ryals, J. (2001). A systematic approach to biochemical profiling. *Current Opinion in Plant Biology, 4*(3), 186-190.

Glazko, A. J., McGinty, D., Dill, W. A., Wilson, M., & Ward, C. (1949). Biochemical studies on diphenhydramine (Benadryl) III. Application of radioactive carbon to metabolic studies of benadryl. *Journal of Biological Chemistry, 179*(1), 409-416.

Goh, K. (2000). Malaysian herbaceous plants. *Millennium Edition,* Advanco Press, Malaysia.

Goldstein, J., Newbury, D. E., Echlin, P., Joy, D. C., Romig Jr, A. D., Lyman, C. E., Fiori, C., & Lifshin, E. (2012). Scanning electron microscopy and X-ray microanalysis*: A Text for Biologists, Materials Scientists, and Geologists*. Springer Science & Business Media. Springer Publisher, New York.

Gond, S. K., Mishra, A., Sharma, V. K., Verma, S. K., Kumar, J., Kharwar, R. N., & Kumar, A. (2012). Diversity and antimicrobial activity of endophytic fungi isolated from *Nyctanthes arbor-tristis*, a well-known medicinal plant of India. *Mycoscience, 53*(2), 113-121.

Gu, W., Ge, H., Song, Y., Ding, H., Zhu, H., Zhao, X., & Tan, R. (2007). Cytotoxic benzo [j] fluoranthene metabolites from *Hypoxylon truncatum* IFB-18, an endophyte of *Artemisia annua*. *Journal of Natural Products, 70*(1), 114-117.

Guarro, J., Kallas, E. G., Godoy, P., Karenina, A., Gene, J., Stchigel, A., & Colombo, A. L. (2002). Cerebral aspergillosis caused by *Neosartorya hiratsukae*, Brazil.(Dispatches). *Emerging Infectious Diseases, 8*(9), 989-992.

Gul, F., Hussain, A., Jan, G., & Hamayun, M. (2017). Genomic DNA extraction for molecular identification of endophytic fungi: An easy and efficient protocol. *Biosciences Biotechnology Research Asia, 14*(2), 667-671.

Gundel, P. E., Perez, L. I., Helander, M., & Saikkonen, K. (2013). Symbiotically modified organisms: Nontoxic fungal endophytes in grasses. *Trends in Plant Science, 18*(8), 420-427.

Gunther, E. (1945). *Ethnobotany of Western Washington* Vol. 10, (pp. 1-62). University of Washington Press, Seattle.

Guo, L., Hyde, K., & Liew, E. (2000). Identification of endophytic fungi from *Livistona chinensis* based on morphology and rDNA sequences. *New Phytologist, 147*(3), 617-630.

Guo, B., Wang, Y., Zhou, X., Hu, K., Tan, F., Miao, Z., & Tang, K. (2006). An endophytic taxol-producing fungus BT2 isolated from *Taxus chinensis* var. mairei. *African Journal of Biotechnology, 5*(10), 875-877.

Guo, B., Wang, Y., Sun, X., & Tang, K. (2008). Bioactive natural products from endophytes: A review. *Applied Biochemistry and Microbiology, 44*(2), 136-142.

Gupta, M., Monge, A., Karikas, G., Lopez de Cerain, A., Solis, P., De Leon, E., & Montenegro, G. (1996). Screening of Panamanian medicinal plants for brine shrimp toxicity, crown gall tumor inhibition, cytotoxicity and DNA intercalation. *International Journal of Pharmacognosy, 34*(1), 19-27.

Gurib-Fakim, A. (2006). Medicinal plants: Traditions of yesterday and drugs of tomorrow. *Molecular Aspects of Medicine, 27*(1), 1-93.

Gwynn, M. N., Portnoy, A., Rittenhouse, S. F., & Payne, D. J. (2010). Challenges of antibacterial discovery revisited. *Annals of the New York Academy of Sciences, 1213*(1), 5-19.

Hammer, M. L., & Johns, E. A. (1993). Tapping an Amazonian plethora: Four medicinal plants of Marajo Island, Para (Brazil). *Journal of Ethnopharmacology, 40*(1), 53-75.

Han, J. I., & Na, K. J. (2008). Dermatitis caused by *Neosartorya hiratsukae* infection in a hedgehog. *Journal of Clinical Microbiology, 46*(9), 3119-3123.

Hanon, E., Vanderplasschen, A., & Pastoret, P. P. (1996). The use of flow cytometry for concomitant detection of apoptosis and cell cycle analysis. *Biochemica, 2*(1), 25-27.

Hardoim, P. R., Van Overbeek, L. S., Berg, G., Pirttilä, A. M., Compant, S., Campisano, A., Döring, M., & Sessitsch, A. (2015). The hidden world within plants: Ecological and evolutionary considerations for defining functioning of microbial endophytes. *Microbiology and Molecular Biology Reviews, 79*(3), 293-320.

Harris, J. L. (2000). Safe, low-distortion tape touch method for fungal slide mounts. *Journal of Clinical Microbiology, 38*(12), 4683-4684.

Harun, A., Vidyadaran, S., Lim, S. M., Cole, A. L., & Ramasamy, K. (2015). Malaysian endophytic fungal extracts-induced anti-inflammation in Lipopolysaccharide-activated BV-2 microglia is associated with attenuation of NO production and, IL-6 and TNF-α expression. *BioMed Central Complementary and Alternative Medicine, 15*(1), 1-9.

Harvey, M., & Botha, F. (1996). Use of PCR-based methodologies for the determination of DNA diversity between *Saccharum* varieties. *Euphytica, 89*(2), 257-265.

Hawksworth, D. L., & Rossman, A. Y. (1997). Where are all the undescribed fungi? *Phytopathology, 87*(9), 888-891.

Hayden, R. T., Clinton, L. K., Hewitt, C., Koyamatsu, T., Sun, Y., Jamison, G., Perkins, R., Tang, L., Pounds, S., & Bankowski, M. J. (2016). Rapid antimicrobial susceptibility testing using forward laser light scatter technology. *Journal of Clinical Microbiology, 54*(11), 2701-2706.

Hazalin, N. A., Ramasamy, K., Lim, S. S. M., Wahab, I. A., Cole, A. L., & Majeed, A. B. A. (2009). Cytotoxic and antibacterial activities of endophytic fungi isolated from plants at the National Park, Pahang, Malaysia. *BioMed Central Complementary and Alternative Medicine, 9*(1), 1-5.

Heinig, U., Scholz, S., & Jennewein, S. (2013). Getting to the bottom of Taxol biosynthesis by fungi. *Fungal diversity, 60*(1), 161-170.

Higginbotham, S. J., Arnold, A. E., Ibanez, A., Spadafora, C., Coley, P. D., & Kursar, T. A. (2013). Bioactivity of fungal endophytes as a function of endophyte taxonomy and the taxonomy and distribution of their host plants. *PloS One, 8*(9), 1-10.

Hiradeve, S. M., & Rangari, V. D. (2014). *Elephantopus scaber* Linn.: A review on its ethnomedical, phytochemical and pharmacological profile. *Journal of Applied Biomedicine, 12*(2), 49-61.

Hoffman, A. M., Mayer, S. G., Strobel, G. A., Hess, W. M., Sovocool, G. W., Grange, A. H., Harper, J. K., Arif, A. M., Grant, D. M., & Kelley-Swift, E. G. (2008). Purification, identification and activity of phomodione, a furandione from an endophytic *Phoma* species. *Phytochemistry, 69*(4), 1049-1056.

Horton, T. R., & Bruns, T. D. (2001). The molecular revolution in ectomycorrhizal ecology: Peeking into the black-box. *Molecular Ecology, 10*(8), 1855-1871.

Hossen, M. J., Baek, K.-S., Kim, E., Yang, W. S., Jeong, D., Kim, J. H., Kim, J.-H. (2015). *In vivo* and *in vitro* anti-inflammatory activities of *Persicaria chinensis* methanolic extract targeting Src/Syk/NF-κB. *Journal of Ethnopharmacology, 159*(1), 9-16.

Hsieh, M. J., Chien, S. Y., Chou, Y. E., Chen, C. J., Chen, J., & Chen, M. K. (2014). Hispolon from *Phellinus linteus* possesses mediate caspases activation and induces human nasopharyngeal carcinomas cells apoptosis through ERK1/2, JNK1/2 and p38 MAPK pathway. *Phytomedicine, 21*(12), 1746-1752.

Huang, W., Cai, Y., Hyde, K., Corke, H., & Sun, M. (2008). Biodiversity of endophytic fungi associated with 29 traditional Chinese medicinal plants. *Fungal Diversity*, *33*(1), 61-75.

Huang, X. Z., Zhu, Y., Guan, X. L., Tian, K., Guo, J. M., Wang, H. B., & Fu, G. M. (2012). A novel antioxidant isobenzofuranone derivative from fungus *Cephalosporium* sp. AL031. *Molecules, 17*(4), 4219-4224.

Hubbard, M., Germida, J., & Vujanovic, V. (2012). Fungal endophytes improve wheat seed germination under heat and drought stress. *Botany, 90*(2), 137-149.

Hussin, K., & Rahman, M. R. A. (2006). *Anatomical Atlas of Malaysian Medicinal Plants*, (pp. 122-125). Universiti Kebangsaan Malaysia Publisher, Malaysia.

Inta, A., Shengji, P., Balslev, H., Wangpakapattanawong, P., & Trisonthi, C. (2008). A comparative study on medicinal plants used in Akha's traditional medicine in China and Thailand, cultural coherence or ecological divergence. *Journal of Ethnopharmacology, 116*(3), 508-517.

Isaka, M., Jaturapat, A., Rukseree, K., Danwisetkanjana, K., Tanticharoen, M., & Thebtaranonth, Y. (2001). Phomoxanthones A and B, novel xanthone dimers from the endophytic fungus *Phomopsis* species. *Journal of Natural Products, 64*(8), 1015-1018.

Isaka, M., Palasarn, S., Lapanun, S., Chanthaket, R., Boonyuen, N., & Lumyong, S. (2009). γ-Lactones and ent-eudesmane sesquiterpenes from the endophytic fungus *Eutypella* sp. BCC 13199. *Journal of Natural Products, 72*(9), 1720-1722.

Isaka, M., Chinthanom, P., Boonruangprapa, T., Rungjindamai, N., & Pinruan, U. (2010). Eremophilane-type sesquiterpenes from the fungus *Xylaria* sp. BCC 21097. *Journal of Natural Products, 73*(4), 683-687.

Itharat, A., Houghton, P. J., Eno-Amooquaye, E., Burke, P., Sampson, J. H., & Raman, A. (2004). *In vitro* cytotoxic activity of Thai medicinal plants used traditionally to treat cancer. *Journal of Ethnopharmacology, 90*(1), 33-38.

Jacobs, M., Mithal, Y., Robins-Browne, R., Gaspar, M., & Koornhof, H. (1979). Antimicrobial susceptibility testing of pneumococci: Determination of Kirby-Bauer breakpoints for penicillin G, erythromycin, clindamycin, tetracycline, chloramphenicol, and rifampin. *Antimicrobial Agents and Chemotherapy, 16*(2), 190-197

Jana, T., Sharma, T. R., Prasad, R. D., & Arora, D. K. (2003). Molecular characterization of *Macrophomina phaseolina* and *Fusarium* species by a single primer RAPD technique. *Microbiological Research, 158*(3), 249-257.

Jazayeri, A., Falck, J., Lukas, C., Bartek, J., Smith, G. C., Lukas, J., & Jackson, S. P. (2006). ATM-and cell cycle-dependent regulation of ATR in response to DNA double-strand breaks. *Nature Cell Biology, 8*(1), 37-45.

Jones, N., Ougham, H., & Thomas, H. (1997). Markers and mapping: We are all geneticists now. *New Phytologist, 137*(1), 165-177.

Kathiravan, M. K., Khilare, M. M., Nikoomanesh, K., Chothe, A. S., & Jain, K. S. (2013). Topoisomerase as target for antibacterial and anticancer drug discovery. *Journal of Enzyme Inhibition and Medicinal Chemistry, 28*(3), 419-435.

Kaul, S., Gupta, S., Ahmed, M., & Dhar, M. K. (2012). Endophytic fungi from medicinal plants: A treasure hunt for bioactive metabolites. *Phytochemistry Reviews, 11*(4), 487-505.

Kazama, C. C., Uchida, D. T., Canzi, K. N., de Souza, P., Crestani, S., Junior, A. G., & Junior, A. L. (2012). Involvement of arginine-vasopressin in the diuretic and hypotensive effects of *Pereskia grandifolia* Haw.(Cactaceae). *Journal of Ethnopharmacology, 144*(1), 86-93.

Kesting, J. R., Tolderlund, I. L., Pedersen, A. F., Witt, M., Jaroszewski, J. W., & Staerk, D. (2009). Piperidine and tetrahydropyridine alkaloids from *Lobelia siphilitica* and *Hippobroma longiflora*. *Journal of Natural products, 72*(2), 312-315.

Kidwell, M. G., & Lisch, D. (1997). Transposable elements as sources of variation in animals and plants. *Proceedings of the National Academy of Sciences, 94*(15), 7704-7711.

Kinzler, K. W., & Vogelstein, B. (1989). Whole genome PCR: Application to the identification of sequences bound by gene regulatory protein. *Nucleic Acids Research, 17*(10), 3645-3653.

Kjer, J., Wray, V., Edrada-Ebel, R., Ebel, R., Pretsch, A., Lin, W., & Proksch, P. (2009). Xanalteric acids I and II and related phenolic compounds from an endophytic *Alternaria* sp. isolated from the mangrove plant *Sonneratia alba*. *Journal of Natural Products, 72*(11), 2053-2057.

Kharwar, R. N., Mishra, A., Gond, S. K., Stierle, A., & Stierle, D. (2011). Anticancer compounds derived from fungal endophytes: Their importance and future challenges. *Natural Product Reports, 28*(7), 1208-1228.

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

Klayman, D. L. (1985). Qinghaosu (Artemisinin): An antimalarial drug from China. *Science, 228*(4703), 1049-1055.

Klemke, C., Kehraus, S., Wright, A. D., & Konig, G. M. (2004). New secondary metabolites from the marine endophytic fungus *Apiospora montagnei*. *Journal of Natural Products, 67*(6), 1058-1063.

Koay, Y. C., Wong, K. C., Osman, H., Eldeen, I., & Asmawi, M. Z. (2013). Chemical constituents and biological activities of *Strobilanthes crispus* L. *Records of Natural Products*, *7*(1), 59-64.

Kobayashi, H., Sunaga, R., Furihata, K., Morisaki, N., & Iwasaki, S. (1995). Isolation and structures of an antifungal antibiotic, fusarielin A, and related compounds produced by a *Fusarium* sp. *The Journal of Antibiotics, 48*(1), 42-52.

Koech, K., Wachira, F., Ngure, R., Wanyoko, J., Bii, C., & Karori, S. (2013). Antibacterial and synergistic activity of different tea crude extracts against antibiotic resistant *S. aureus, E. coli* and a clinical isolate of *S. typhi. Science Journal of Microbiology*, 2013(1), 1-9.

Koller, B., Lehmann, A., McDermott, J., & Gessler, C. (1993). Identification of apple cultivars using RAPD markers. *Theoretical and Applied Genetics, 85*(6-7), 901-904.

Korpi, A., Jarnberg, J., & Pasanen, A. L. (2009). Microbial volatile organic compounds. *Critical Reviews in Toxicology, 39*(2), 139-193.

Koutroutsos, K., Arabatzis, M., Bougatsos, G., Xanthaki, A., Toutouza, M., & Velegraki, A. (2010). *Neosartorya hiratsukae* peritonitis through continuous ambulatory peritoneal dialysis. *Journal of Medical Microbiology, 59*(7), 862-865.

Koval, O. A., Sakaeva, G. R., Fomin, A. S., Nushtaeva, A. A., Semenov, D. V., Kuligina, E. V., Gulyaeva, L. F., Gerasimov, A. V., & Richter, V. A. (2015). Sensitivity of endometrial cancer cells from primary human tumor samples to new potential anticancer peptide lactaptin. *Journal of Cancer Research and Therapeutics, 11*(2), 345-351.

Kralj, A., Kehraus, S., Krick, A., Eguereva, E., Kelter, G., Maurer, M., Wortmann, A., Fiebig, H-H., & Konig, G. M. (2006). Arugosins G and H: Prenylated polyketides from the marine-derived fungus *Emericella nidulans* var. acristata. *Journal of Natural Products*, *69*(7), 995-1000.

Kronvall, G., Giske, C. G., & Kahlmeter, G. (2011). Setting interpretive breakpoints for antimicrobial susceptibility testing using disk diffusion. *International Journal of Antimicrobial Agents, 38*(4), 281-290.

Kuete, V., Ngameni, B., Simo, C. F., Tankeu, R. K., Ngadjui, B. T., Meyer, J., Lall, N., & Kuiate, J. (2008). Antimicrobial activity of the crude extracts and compounds from *Ficus chlamydocarpa* and *Ficus cordata* (Moraceae). *Journal of Ethnopharmacology, 120*(1), 17-24.

Kumar, S., Nei, M., Dudley, J., & Tamura, K. (2008). MEGA: A biologist-centric software for evolutionary analysis of DNA and protein sequences. *Briefings in Bioinformatics, 9*(4), 299-306.

Kumar, A., Kumari, P., & Somasundaram, S. T. (2014). Gas chromatography-mass spectrum (GC-MS) analysis of bioactive components of the methanol extract of halophyte, *Sesuvium portulacastrum* L. *International Journal of Advances In Pharmacy, Biology and Chemistry, 3*(3), 766-772.

Kuswanto, L., & Krisantini, P. S. (2015). Status of traditional herb *Tetrastigma glabratum* (Blume). Planch in Mt Prau, Central Java, Indonesia. *Journal of Pharmacognosy and Phytochemistry, 4*(4), 179-184.

Lai, S. M., Sudhahar, D., & Anandarajagopal, K. (2012). Evaluation of antibacterial and antifungal activities of *Persicaria chinensis* leaves. *International Journal of Pharmaceutical Sciences and Research, 3*(8), 2825-2830.

Lange, R. P., Locher, H. H., Wyss, P. C., & Then, R. L. (2007). The targets of currently used antibacterial agents: Lessons for drug discovery. *Current Pharmaceutical Design, 13*(30), 3140-3154.

Latch, G., Hunt, W., & Musgrave, D. (1985). Endophytic fungi affect growth of perennial ryegrass. *New Zealand Journal of Agricultural Research, 28*(1), 165-168.

Lattif, A., Omar, I., Said, I., & Kadri, A. (1984). A multi-variate approach to the study of medicinal plants in Malaysia. *Journal of the Singapore National Academy of Science, 13*(1), 101-105.

Lee, J. C., Strobel, G. A., Lobkovsky, E., & Clardy, J. (1996). Torreyanic acid: A selectively cytotoxic quinone dimer from the endophytic fungus *Pestalotiopsis microspora*. *The Journal of Organic Chemistry, 61*(10), 3232-3233.

Leslie, J. F., Zeller, K. A., Lamprecht, S. C., Rheeder, J. P., & Marasas, W. F. (2005). Toxicity, pathogenicity, and genetic differentiation of five species of *Fusarium* from sorghum and millet. *Phytopathology, 95*(3), 275-283.

Levin, L., Papinutti, L., & Forchiassin, F. (2004). Evaluation of Argentinean white rot fungi for their ability to produce lignin-modifying enzymes and decolorize industrial dyes. *Bioresource Technology, 94*(2), 169-176.

Levy, S. B., & Marshall, B. (2004). Antibacterial resistance worldwide: Causes, challenges and responses. *Nature Medicine, 10*, S122-S129.

Lewis, D. (1985). Symbiosis and mutualism: Crisp concepts and soggy semantics. Oxford University Press, Oxford.

Li, J. Y., & Strobel, G. A. (2001). Jesterone and hydroxy-jesterone antioomycete cyclohexenone epoxides from the endophytic fungus *Pestalotiopsis jesteri*. *Phytochemistry, 57*(2), 261-265.

Li, H., Qing, C., Zhang, Y., & Zhao, Z. (2005). Screening for endophytic fungi with antitumour and antifungal activities from Chinese medicinal plants. *World Journal of Microbiology and Biotechnology, 21*(8), 1515-1519.

Li, C., Li, M., Chang, W., & Guo, B. (2008). Purification and characterization of a novel cholesterol-lowering protein from the seeds of *Senna obtusifolia*. *Science in China Series C: Life Sciences, 51*(11), 1020-1024.

Ling, Y. H., Liebes, L., Jiang, J. D., Holland, J. F., Elliott, P. J., Adams, J., Muggia, F. M., & Perez-Soler, R. (2003). Mechanisms of proteasome inhibitor PS-341-induced G2-M-phase arrest and apoptosis in human non-small cell lung cancer cell lines. *Clinical Cancer Research, 9*(3), 1145-1154.

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.

Lord, N., Kaplan, C. W., Shank, P., Kitts, C. L., & Elrod, S. L. (2002). Assessment of fungal diversity using terminal restriction fragment (TRF) pattern analysis: Comparison of 18S and ITS ribosomal regions. *FEMS Microbiology Ecology, 42*(3), 327-337.

Luitel, D. R., Rokaya, M. B., Timsina, B., & Munzbergova, Z. (2014). Medicinal plants used by the Tamang community in the Makawanpur district of central Nepal. *Journal of Ethnobiology and Ethnomedicine, 10*(1), 1-11.

Mack, K. M., & Rudgers, J. A. (2008). Balancing multiple mutualists: Asymmetric interactions among plants, arbuscular mycorrhizal fungi, and fungal endophytes. *Oikos, 117*(2), 310-320.

Malek, S. N. A., Shin, S. K., Wahab, N. A., & Yaacob, H. (2009). Cytotoxic components of *Pereskia bleo* (Kunth) DC.(Cactaceae) leaves. *Molecules, 14*(5), 1713-1724.

Manamgoda, D. S., Rossman, A. Y., Castlebury, L. A., Chukeatirote, E., & Hyde, K. D. (2015). A taxonomic and phylogenetic re-appraisal of the genus *Curvularia* (Pleosporaceae): Human and plant pathogens. *Phytotaxa, 212*(3), 175-198.

Mbaveng, A. T., Kuete, V., Mapunya, B. M., Beng, V. P., Nkengfack, A. E., Meyer, J. J. M., & Lall, N. (2011). Evaluation of four Cameroonian medicinal plants for anticancer, antigonorrheal and antireverse transcriptase activities. *Environmental Toxicology and Pharmacology, 32*(2), 162-167.

McAlpine, J. B., Pazoles, C., & Stafford, A. (1999). Phytera's strategy for the discovery of novel anti-Infective agents from plant cell cultures. *Bioassay Methods in Natural Product Research and Drug Development,* (pp. 159-166). Springer Publisher, New York.

Medicinal plants. *The Columbia Electronic Encyclopedia*®. (2013). Retrieved July 31 2016 http://encyclopedia2.thefreedictionary.com/medicinal+plants

Mejia, L. C., Rojas, E. I., Maynard, Z., Van Bael, S., Arnold, A. E., Hebbar, P., Herre, E. A. (2008). Endophytic fungi as biocontrol agents of *Theobroma cacao* pathogens. *Biological Control, 46*(1), 4-14.

Mekalanos, J. J. (1992). Environmental signals controlling expression of virulence determinants in bacteria. *Journal of Bacteriology, 174*(1), 1-7.

Melendez, P., & Capriles, V. (2006). Antibacterial properties of tropical plants from Puerto Rico. *Phytomedicine, 13*(4), 272-276.

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

Metwaly, A. M., Kadry, H. A., Atef, A., Mohammad, A.-E. I., Ma, G., Cutler, S. J., & Ross, S. A. (2014). Nigrosphaerin A a new isochromene derivative from the endophytic fungus *Nigrospora sphaerica*. *Phytochemistry Letters, 7*(1), 1-5.

Micales, J., Bonde, M., & Peterson, G. (1992). Isozyme analysis in fungal taxonomy and molecular genetics. *Handbook of Applied Mycology, 4*(1), 57-79.

Miller, R., Jolles, C., & Rapoport, H. (1973). Morphine metabolism and normorphine in *Papaver somniferum*. *Phytochemistry, 12*(3), 597-603.

Mishra, A., Gond, S. K., Kumar, A., Sharma, V. K., Verma, S. K., Kharwar, R. N., & Sieber, T. N. (2012). Season and tissue type affect fungal endophyte communities of the Indian medicinal plant *Tinospora cordifolia* more strongly than geographic location. *Microbial Ecology, 64*(2), 388-398.

Mishra, G., Khosa, R., Singh, P., & Jha, K. (2014). Hepatoprotective activity of ethanolic extract of *Leea indica* (Burm. f.) Merr.(Leeaceae) stem bark against paracetamol induced liver toxicity in rats. *Nigerian Journal of Experimental and Clinical Biosciences, 2*(1), 59-63.

Mishra, V. K., Singh, G., Passari, A. K., Yadav, M. K., Gupta, V. K., & Singh, B. P. (2016). Distribution and antimicrobial potential of endophytic fungi associated with ethnomedicinal plant *Melastoma malabathricum* L. *Journal of Environmental Biology, 37*(2), 229-237.

Moricca, S., & Ragazzi, A. (2008). Fungal endophytes in Mediterranean oak forests: A lesson from *Discula quercina*. *Phytopathology, 98*(4), 380-386.

Muller, C. B., & Krauss, J. (2005). Symbiosis between grasses and asexual fungal endophytes. *Current Opinion in Plant Biology, 8*(4), 450-456.

Mullis, K. B. (1990). The unusual origin of the polymerase chain reaction. *Scientific American, 262*(4), 56-61.

Mustafa, M., Mokhtar, D., Aziz, A., Azwady, N., Nordin, C. K., & Nurshaira, C. K. (2009). Antibacterial activity of methanolic crude extracts from selected plant against *Bacillus cereus*. *Pertanika Journal of Tropical Agricultural Science, 32*(2), 175-183.

Mustapa, A. N., Martin, A., Mato, R. B., & Cocero, M. J. (2015). Extraction of phytocompounds from the medicinal plant *Clinacanthus nutans* Lindau by microwave-assisted extraction and supercritical carbon dioxide extraction. *Industrial Crops and Products, 74*, 83-94.

Nakanishi, K., Sasaki, I., Kiang, A., Go, J., Kakisawa, H., Ohashi, M., Goto, M., Watanabe, J., Yokotani, H., Matsumura, C., & Togashi, M. (1965). Phytochemical survey of Malaysian plants preliminary chemical and pharmacological screening. *Chemical and Pharmaceutical Bulletin, 13*(7), 882-890.

Newman, D. J., & Cragg, G. M. (2012). Natural products as sources of new drugs over the 30 years from 1981 to 2010. *Journal of Natural products, 75*(3), 311-335.

Nicolini, F., Burmistrova, O., Marrero, M. T., Torres, F., Hernandez, C., Quintana, J., & Estevez, F. (2014). Induction of G_2/M phase arrest and apoptosis by the flavonoid tamarixetin on human leukemia cells. *Molecular Carcinogenesis, 53*(12), 939-950.

Nikaido, H., & Vaara, M. (1985). Molecular basis of bacterial outer membrane permeability. *Microbiological Reviews, 49*(1), 1-32.

Nikaido, H. (1994). Prevention of drug access to bacterial targets: Permeability barriers and active efflux. *Science-AAAS-Weekly Paper Edition-including Guide to Scientific Information, 264*(5157), 382-387.

Nikaido, H. (1996). Multidrug efflux pumps of gram-negative bacteria. *Journal of Bacteriology, 178*(20), 5853-5859.

Nilsson, R. H., Kristiansson, E., Ryberg, M., Hallenberg, N., & Larsson, K. H. (2008). Intraspecific ITS variability in the kingdom fungi as expressed in the international sequence databases and its implications for molecular species identification. *Evolutionary Bioinformatics, 4*(1), 193-201.

Nurestri, A. S., Sim, K., & Norhanom, A. (2009). Phytochemical and cytotoxic investigations of *Pereskia grandifolia* Haw.(Cactaceae) leaves. *Journal of Biological Sciences, 9*(5), 488-493.

Nurraihana, H., & Norfarizan-Hanoon, N. (2013). Phytochemistry, pharmacology and toxicology properties of *Strobilanthes crispus*. *International Food Research Journal, 20*(5), 2045-2056.

Ong, H. C., Zuki, R. M., & Milow, P. (2011). Traditional knowledge of medicinal plants among the Malay villagers in Kampung Mak Kemas, Terengganu, Malaysia. *Ethno Medicine*, *5*(3), 175-185.

Onn, M., Lim, P., Aazani, M., Proksch, P., & Muller, M. (2016). Initial screening of mangrove endophytic fungi for antimicrobial compounds and heavy metal biosorption potential. *Sains Malaysiana, 45*(7), 1063-1071.

Ooi, K. K., Yeo, C. I., Ang, K. P., Akim, A. M., Cheah, Y. K., Halim, S. N. A., Seng, H. L., & Tiekink, E. R. (2015). Phosphanegold (I) thiolates, Ph_3PAu [SC (OR)= NC_6H_4Me-4] for R= Me, Et and iPr, induce apoptosis, cell cycle arrest and inhibit cell invasion of HT-29 colon cancer cells through modulation of the nuclear factor-κB activation pathway and ubiquitination. *Journal of Biological Inorganic Chemistry, 20*(5), 855-873.

Oono, R., Lefevre, E., Simha, A., & Lutzoni, F. (2015). A comparison of the community diversity of foliar fungal endophytes between seedling and adult loblolly pines (*Pinus taeda*). *Fungal Biology, 119*(10), 917-928.

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

Park, H. S., Park, K. I., Lee, D. H., Kang, S. R., Nagappan, A., Kim, J. A., & Kim, G. S. (2012). Polyphenolic extract isolated from Korean *Lonicera japonica* Thunb. induce G_2/M cell cycle arrest and apoptosis in HepG2 cells: Involvements of PI3K/Akt and MAPKs. *Food and Chemical Toxicology, 50*(7), 2407-2416.

Passari, A. K., Mishra, V. K., Saikia, R., Gupta, V. K., & Singh, B. P. (2015). Isolation, abundance and phylogenetic affiliation of endophytic actinomycetes associated with medicinal plants and screening for their *in vitro* antimicrobial biosynthetic potential. *Frontiers in Microbiology, 6*(1), 273-286.

Paterson, D. L. (2006). Resistance in Gram-negative bacteria: Enterobacteriaceae. *The American Journal of Medicine, 119*(6), 20-28.

Patwardhan, B., Warude, D., Pushpangadan, P., & Bhatt, N. (2005). Ayurveda and traditional Chinese medicine: A comparative overview. *Evidence-Based Complementary and Alternative Medicine, 2*(4), 465-473.

Payne, D. J., Gwynn, M. N., Holmes, D. J., & Pompliano, D. L. (2007). Drugs for bad bugs: Confronting the challenges of antibacterial discovery. *Nature Reviews Drug Discovery, 6*(1), 29-40.

Pelaez, F., Collado, J., Arenal, F., Basilio, A., Cabello, A., Matas, M. D., Garcia J. B., Del Val A. G. , Gonzalez V., Gorrochategui J., & Hernández P. (1998). Endophytic fungi from plants living on gypsum soils as a source of secondary metabolites with antimicrobial activity. *Mycological Research, 102*(06), 755-761.

Petrini, O., & Carroll, G. (1981). Endophytic fungi in foliage of some Cupressaceae in Oregon. *Canadian Journal of Botany, 59*(5), 629-636.

Petrini, O. (1991). Fungal endophytes of tree leaves. *In Microbial Ecology of Leaves*, (pp. 179-197). Springer Publisher, New York.

Phenotype. *American Heritage® Dictionary of the English Language, Fifth Edition*. (2011). Retrieved August 9 2016 from http://www.thefreedictionary.com/phenotypic.

Philip, K., Malek, S. N., Sani, W., Shin, S. K., Kumar, S., Lai, H. S., Rahman, S. N. (2009). Antimicrobial activity of some medicinal plants from Malaysia. *American Journal of Applied Sciences, 6*(8), 1613-1617.

Phongpaichit, S., Rungjindamai, N., Rukachaisirikul, V., & Sakayaroj, J. (2006). Antimicrobial activity in cultures of endophytic fungi isolated from *Garcinia* species. *FEMS Immunology & Medical Microbiology, 48*(3), 367-372.

Pinto, C., Rodrigues, L. S., Azevedo, J. L., Pereira, J. O., Carneiro Vieira, M. L., & Labate, C. A. (2000). Symptomless infection of banana and maize by endophytic fungi impairs photosynthetic efficiency. *New Phytologist, 147*(3), 609-615.

Pistelli, L., Bertoli, A., Zucconelli, S., Morelli, I., Panizzi, L., & Menichini, F. (2000). Antimicrobial activity of crude extracts and pure compounds of *Hypericum hircinum*. *Fitoterapia, 71*(1), 138-140.

Poeaim, S., Tongkantom, K., Jabamrung, P., Bo-kaew, O., & Soytong, M. (2016). Isolation, characterization and screening for anticancer and antimicrobial properties of the crude extract from genus *Neosartorya*. *Bioengineering and Bioscience, 4*(5), 71-75.

Poli, A., Nicolau, M., Simoes, C. M. O., Nicolau, R. M. R.-d.-V., & Zanin, M. (1992). Preliminary pharmacologic evaluation of crude whole plant extracts of *Elephantopus scaber.* Part I: *In vivo* studies. *Journal of Ethnopharmacology, 37*(1), 71-76.

Pommier, Y., Leo, E., Zhang, H., & Marchand, C. (2010). DNA topoisomerases and their poisoning by anticancer and antibacterial drugs. *Chemistry and Biology, 17*(5), 421-433.

Porras-Alfaro, A., & Bayman, P. (2011). Hidden fungi, emergent properties: endophytes and microbiomes. *Phytopathology, 49*(1), 291-315

Porter, C. H., & Collins, F. H. (1991). Species-diagnostic differences in a ribosomal DNA internal transcribed spacer from the sibling species *Anopheles freeborni* and *Anopheles hermsi* (Diptera: Culicidae). *The American Journal of Tropical Medicine and Hygiene, 45*(2), 271-279.

Power, E. (1996). RAPD typing in microbiology: A technical review. *Journal of Hospital Infection, 34*(4), 247-265.

Pujiyanto, S., Lestari, Y., Suwanto, A., Budiarti, S., & Darusman, L. K. (2012). Alpha-glucosidase inhibitor activity and characterization of endophytic actinomycetes isolated from some Indonesian diabetic medicinal plants. *International Journal of Pharmacy and Pharmaceutical Sciences, 4*(1), 327-333.

Puri, S. C., Verma, V., Amna, T., Qazi, G. N., & Spiteller, M. (2005). An endophytic fungus from *Nothapodytes foetida* that produces camptothecin. *Journal of Natural Products, 68*(12), 1717-1719.

Puri, S. C., Nazir, A., Chawla, R., Arora, R., Riyaz-ul-Hasan, S., Amna, T., Ahmed, B., Verma, V., Singh, S., Sagar, R., & Sagar, R. (2006). The endophytic fungus *Trametes hirsuta* as a novel alternative source of podophyllotoxin and related aryl tetralin lignans. *Journal of Biotechnology, 122*(4), 494-510.

Raaijmakers, J. M., & Mazzola, M. (2012). Diversity and natural functions of antibiotics produced by beneficial and plant pathogenic bacteria. *Annual Review of Phytopathology, 50*(1), 403-424.

Radu, S., & Kqueen, C. Y. (2002). Preliminary screening of endophytic fungi from medicinal plants in Malaysia for antimicrobial and antitumor activity. *Malaysian Journal of Medical Sciences*, *9*(2), 23-33.

Rahman, M. A., Uddin, S., & Wilcock, C. (2007). Medicinal plants used by Chakma tribe in Hill Tracts districts of Bangladesh. *Indian Journal of Traditional Knowledge, 6*(3), 508-517.

Rahman, S., Salehin, F., & Iqbal, A. (2011). *In vitro* antioxidant and anticancer activity of young *Zingiber officinale* against human breast carcinoma cell lines. *BioMed Central Complementary and Alternative Medicine, 11*(1), 1-7.

Rahman, M. A., bin Imran, T., & Islam, S. (2013). Antioxidative, antimicrobial and cytotoxic effects of the phenolics of *Leea indica* leaf extract. *Saudi Journal of Biological Sciences, 20*(3), 213-225.

Rahman, H., Hasan, C. K., Ahmed, M., Islam, K. D., & Hossain, M. A. (2015). Promising natural products against nosocomial infections. *European Journal of Biotechnology and Bioscience, 3*(1), 63-85.

Ramasamy, K., Lim, S. M., Bakar, H. A., Ismail, N., Ismail, M. S., Ali, M. F., Faizal Weber, J. F., & Cole, A. L. (2010). Antimicrobial and cytotoxic activities of Malaysian endophytes. *Phytotherapy Research, 24*(5), 640-643.

Rapley, R. (1994). Enhancing PCR amplification and sequencing using DNA-binding proteins. *Molecular Biotechnology, 2*(3), 295-298.

Rapley, R. (1998). Polymerase chain reaction. *Molecular Biomethods Handbook*, (pp. 305-325). Humana Press, New York.

Raue, H., Klootwijk, J., & Musters, W. (1988). Evolutionary conservation of structure and function of high molecular weight ribosomal RNA. *Progress in Biophysics and Molecular Biology, 51*(2), 77-129.

Redecker, D., Hijri, M., Dulieu, H., & Sanders, I. R. (1999). Phylogenetic analysis of a dataset of fungal 5.8S rDNA sequences shows that highly divergent copies of internal transcribed spacers reported from *Scutellospora castanea* are of Ascomycete origin. *Fungal Genetics and Biology, 28*(3), 238-244

Redman, R. S., Dunigan, D. D., & Rodriguez, R. J. (2001). Fungal symbiosis from mutualism to parasitism: Who controls the outcome, host or invader? *New Phytologist, 151*(3), 705-716.

Reed, D. H., & Frankham, R. (2001). How closely correlated are molecular and quantitative measures of genetic variation? A meta-analysis. *Evolution, 55*(6), 1095-1103.

Rehman, S., Shawl, A., Kour, A., Andrabi, R., Sudan, P., Sultan, P., Verma, V., & Qazi, G. (2008). An endophytic *Neurospora* sp. from *Nothapodytes foetida* producing camptothecin. *Applied Biochemistry and Microbiology, 44*(2), 203-209.

Ren, A., Li, C., & Gao, Y. (2011). Endophytic fungus improves growth and metal uptake of *Lolium arundinaceum* Darbyshire ex. Schreb. *International Journal of Phytoremediation, 13*(3), 233-243.

Rios, J., & Recio, M. (2005). Medicinal plants and antimicrobial activity. *Journal of Ethnopharmacology, 100*(1), 80-84.

Rodrigues, K. F., & Samuels, G. J. (1990). Preliminary study of endophytic fungi in a tropical palm. *Mycological Research, 94*(6), 827-830.

Rodriguez, R., & Redman, R. (2008). More than 400 million years of evolution and some plants still can't make it on their own: Plant stress tolerance via fungal symbiosis. *Journal of Experimental Botany, 59*(5), 1109-1114.

Ruma, K., Sunil, K., Kini, K. R., & Prakash, H. S. (2015). Genetic diversity and antimicrobial activity of endophytic *Myrothecium* spp. isolated from *Calophyllum apetalum* and *Garcinia morella*. *Molecular Biology Reports, 42*(11), 1533-1543.

Saiki, R. K., Scharf, S., Faloona, F., Mullis, K. B., Horn, G. T., Erlich, H. A., & Arnheim, N. (1985). Enzymatic amplification of b-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia. *Science, 230*(4732), 1350-1354.

Saikkonen, K., Faeth, S. H., Helander, M., & Sullivan, T. (1998). Fungal endophytes: A continuum of interactions with host plants. *Annual Review of Ecology and Systematics*, *29*(1), 319-343.

Saikkonen, K., Wäli, P., Helander, M., & Faeth, S. H. (2004). Evolution of endophyte–plant symbioses. *Trends in Plant Science, 9*(6), 275-280.

Saikkonen, K. (2007). Forest structure and fungal endophytes. *Fungal Biology Reviews, 21*(2), 67-74.

Saha, K., Lajis, N., Israf, D., Hamzah, A. S., Khozirah, S., Khamis, S., & Syahida, A. (2004). Evaluation of antioxidant and nitric oxide inhibitory activities of selected Malaysian medicinal plants. *Journal of Ethnopharmacology, 92*(2), 263-267.

Sahu, N. P., Banerji, N., & Chakravarti, R. N. (1974). A new saponin of oleanolic acid from *Pereskia grandifolia*. *Phytochemistry, 13*(2), 529-530.

Sakdarat, S., Shuyprom, A., Pientong, C., Ekalaksananan, T., & Thongchai, S. (2009). Bioactive constituents from the leaves of *Clinacanthus nutans* Lindau. *Bioorganic and Medicinal Chemistry, 17*(5), 1857-1860.

Samejima, K., & Earnshaw, W. C. (2005). Trashing the genome: The role of nucleases during apoptosis. *Nature Reviews Molecular Cell Biology, 6*(9), 677-688.

Samiksha, S. (2016). Experiment to cultivate and identify a fungi. MicroBiology. Retrieved February 14, 2017 from http://www.yourarticlelibrary.com/experiments/experiment-to-cultivate-and-identify-a-fungi-with-figure-micro-biology/26696/

Samuel, A. J. S. J., Kalusalingam, A., Chellappan, D. K., Gopinath, R., Radhamani, S., Husain, H. A., Promwichit, P. (2010). Ethnomedical survey of plants used by the Orang Asli in Kampung Bawong, Perak, West Malaysia. *Journal of Ethnobiology and Ethnomedicine, 6*(1), 1-6.

Santiago, C., Fitchett, C., Munro, M. H., Jalil, J., & Santhanam, J. (2012). Cytotoxic and antifungal activities of 5-hydroxyramulosin, a compound produced by an endophytic fungus isolated from *Cinnamomum mollisimum*. *Evidence-Based Complementary and Alternative Medicine, 2012*(1) 1-6.

Sasidharan, S., Chen, Y., Saravanan, D., Sundram, K., & Latha, L. Y. (2011). Extraction, isolation and characterization of bioactive compounds from plants' extracts. *African Journal of Traditional, Complementary and Alternative Medicines, 8*(1) 1-10.

Satayavivad, J., Bunyaoraphatsara, N., Kitisiripornkul, S., & Tanasomwang, W. (1996). Analgesic and anti-inflammatory activities of extract of *Clinacanthus nutans* Lindau. *Thailand Journal of Phytopharmacology*, *3*(1), 7-17.

Satish, S., & Baker, S. (2012). Endophytes: Natural warehouse of bioactive compounds. *Drug Invention Today, 4*(11), 548-553.

Sawabe, T., Kita-Tsukamoto, K., & Thompson, F. L. (2007). Inferring the evolutionary history of vibrios by means of multilocus sequence analysis. *Journal of Bacteriology, 189*(21), 7932-7936.

Schardl, C. L., & Leuchtmann, A. (2005). The Epichloe endophytes of grasses and the symbiotic continuum. *Mycology Series, 23*, (pp. 475-503). CRC Press, Florida.

Schoch, C. L., Seifert, K. A., Huhndorf, S., Robert, V., Spouge, J. L., Levesque, C. A., & Chen W. (2012). Nuclear ribosomal internal transcribed spacer (ITS) region as a universal DNA barcode marker for fungi. *Proceedings of the National Academy of Sciences, 109*(16), 6241-6246.

Schulz, B., Wanke, U., Draeger, S., & Aust, H. J. (1993). Endophytes from herbaceous plants and shrubs: Effectiveness of surface sterilization methods. *Mycological Research, 97*(12), 1447-1450.

Schulz, B., & Boyle, C. (2005). The endophytic continuum. *Mycological Research, 109*(06), 661-686.

Seeprasert, P., Yoneda, M., Shimada, Y., & Matsui, Y. (2015). The sorption of cesium on Fungi cell: kinetic and isotherm study. *International Journal of Pharma Medicine and Biological Sciences, 4*(2), 110-114.

Sen, S., Talukdar, N. C., & Khan, M. (2015). A simple metabolite profiling approach reveals critical biomolecular linkages in fragrant agarwood oil production from *Aquilaria malaccensis*, a traditional agro-based industry in North East India. *Current Science, 108*(1), 63-71.

Shaanker, R. U., Ramesha, B., Ravikanth, G., Gunaga, R., Vasudeva, R., & Ganeshaiah, K. (2008). Chemical profiling of *Nothapodytes nimmoniana* for camptothecin, an important anticancer alkaloid: Towards the development of a sustainable production system *Bioactive molecules and medicinal plants* (pp. 197-213). Springer Publisher, New York.

Shang, X., Pan, H., Li, M., Miao, X., & Ding, H. (2011). *Lonicera japonica* Thunb.: Ethnopharmacology, phytochemistry and pharmacology of an important traditional Chinese medicine. *Journal of Ethnopharmacology, 138*(1), 1-21.

Shanmugam, S., Annadurai, M., & Rajendran, K. (2011). Ethnomedicinal plants used to cure diarrhoea and dysentery in Pachalur hills of Dindigul district in Tamil Nadu, Southern India. *Journal of Applied Pharmaceutical Science, 1*(8), 94-97.

Sharma, R., Sharma, C. L., & Kapoor, B. (2005). Antibacterial resistance: Current problems and possible solutions. *Indian Journal of Medical Sciences, 59*(3), 120.

Shaw, J. J., Spakowicz, D. J., Dalal, R. S., Davis, J. H., Lehr, N. A., Dunican, B. F., Orellana, E. A., Narvaez-Trujillo, A., & Strobel, S. A. (2015). Biosynthesis and genomic analysis of medium-chain hydrocarbon production by the endophytic fungal isolate *Nigrograna mackinnonii* E5202H. *Applied Microbiology and Biotechnology, 99*(8), 3715-3728.

Shivaprakash, M., Jain, N., Gupta, S., Baghela, A., Gupta, A., & Chakrabarti, A. (2009). Allergic fungal rhinosinusitis caused by *Neosartorya hiratsukae* from India. *Medical Mycology, 47*(3), 317-320.

Shweta, S., Gurumurthy, B. R., Ravikanth, G., Ramanan, U. S., & Shivanna, M. B. (2013). Endophytic fungi from *Miquelia dentata* Bedd., produce the anti-cancer alkaloid, camptothecine. *Phytomedicine, 20*(3), 337-342.

Siddiquee, S., Al Azad, S., Bakar, F. A., Naher, L., & Kumar, S. V. (2015). Separation and identification of hydrocarbons and other volatile compounds from cultures of *Aspergillus niger* by GC–MS using two different capillary columns and solvents. *Journal of Saudi Chemical Society, 19*(3), 243-256.

Sidjui, L., Toghueo, R., Zeuko'o, E., Mbouna, C., Mahiou-Leddet, V., Herbette, G., & Folefoc, G. (2016). Antibacterial activity of the crude extracts, fractions and compounds from the stem barks of *Jacaranda mimosifolia* and *Kigelia africana* (*Bignoniaceae*). *Pharmacologia, 7*(1), 22-31.

Sieber, T. N., & Grunig, C. R. (2006). Biodiversity of fungal root-endophyte communities and populations, in particular of the dark septate endophyte *Phialocephala fortinii* sl. *Microbial Root Endophytes* (pp. 107-132): Springer Publisher, New York.

Siegel, R. L., Miller, K. D., & Jemal, A. (2015). Cancer statistics, 2015. *CA: A Cancer Journal for Clinicians, 65*(1), 5-29.

Sikes, B. A., Hawkes, C. V., & Fukami, T. (2016). Plant and root endophyte assembly history: Interactive effects on native and exotic plants. *Ecology, 97*(2), 484-493.

Sim, K., Nurestri, A. S., Sinniah, S., Kim, K., & Norhanom, A. (2010). Acute oral toxicity of *Pereskia bleo* and *Pereskia grandifolia* in mice. *Pharmacognosy Magazine, 6*(21), 67-70.

Sim, K., Nurestri, A. S., & Norhanom, A. (2010). Phenolic content and antioxidant activity of *Pereskia grandifolia* Haw.(Cactaceae) extracts. *Pharmacognosy Magazine, 6*(23), 248-254.

Sim, J. H., Khoo, C. H., Lee, L. H., & Cheah, Y. K. (2010). Molecular diversity of fungal endophytes isolated from *Garcinia mangostana* and *Garcinia parvifolia*. *Journal of Microbiology and Biotechnology, 20*(4), 651-658.

Singh, S. V., Herman-Antosiewicz, A., Singh, A. V., Lew, K. L., Srivastava, S. K., Kamath, R., Brown, K. D., Zhang, L., & Baskaran, R. (2004). Sulforaphane-induced G_2/M phase cell cycle arrest involves checkpoint kinase 2-mediated phosphorylation of cell division cycle 25C. *Journal of Biological Chemistry, 279*(24), 25813-25822.

Singh, S., Krishna, V., Mankani, K., Manjunatha, B., Vidya, S., & Manohara, Y. (2005). Wound healing activity of the leaf extracts and deoxyelephantopin isolated from *Elephantopus scaber* Linn. *Indian Journal of Pharmacology, 37*(4), 238-242.

Singh, S. B., & Barrett, J. F. (2006). Empirical antibacterial drug discovery-foundation in natural products. *Biochemical Pharmacology, 71*(7), 1006-1015.

Singh, S., Singh, S. K., & Yadav, A. (2013). A review on Cassia species: Pharmacological, traditional and medicinal aspects in various countries. *American Journal of Phytomedicine and Clinical Therapeutics, 1*(3), 291-312.

Smithee, S., Tracy, S., Drescher, K. M., Pitz, L. A., & McDonald, T. (2014). A novel, broadly applicable approach to isolation of fungi in diverse growth media. *Journal of Microbiological Methods, 105*, 155-161.

Song, Y., Li, H., Ye, Y., Shan, C., Yang, Y., & Tan, R. (2004). Endophytic naphthopyrone metabolites are co-inhibitors of xanthine oxidase, SW1116 cell and some microbial growths. *FEMS Microbiology Letters, 241*(1), 67-72.

Srinivasan, G., Ranjith, C., & Vijayan, K. (2008). Identification of chemical compounds from the leaves of *Leea indica*. *Acta Pharmaceutica, 58*(2), 207-214.

Srinivasan, G., Sharanappa, P., Leela, N., Sadashiva, C., & Vijayan, K. (2009). Chemical composition and antimicrobial activity of the essential oil of *Leea indica* (Burm. f.) Merr. flowers. *Natural Product Radiance, 8*(5), 488-493.

Srivastava, V., Negi, A. S., Kumar, J., Gupta, M., & Khanuja, S. P. (2005). Plant-based anticancer molecules: A chemical and biological profile of some important leads. *Bioorganic and Medicinal Chemistry, 13*(21), 5892-5908.

Stackebrandt, E., Liesack, W., & Witt, D. (1992). Ribosomal RNA and rDNA sequence analyses. *Gene, 115*(1), 255-260.

Stansbury, J., Saunders, P. R., & Zampieron, E. R. (2013). The use of lobelia in the treatment of asthma and respiratory illness. *Journal of Restorative Medicine, 2*(1), 94-100.

Stępniewska, Z., & Kuzniar, A. (2013). Endophytic microorganisms promising applications in bioremediation of greenhouse gases. *Applied Microbiology and Biotechnology, 97*(22), 9589-9596.

Stierle, A., Strobel, G., & Stierle, D. (1993). Taxol and taxane production by *Taxomyces andreanae*, an endophytic fungus of Pacific yew. *Science, 260*(5105), 214-216.

Stierle, A., Strobel, G., Stierle, D., Grothaus, P., & Bignami, G. (1995). The search for a taxol-producing microorganism among the endophytic fungi of the pacific yew, *Taxus brevifolia*. *Journal of Natural Products, 58*(9), 1315-1324.

Stierle, A. A., Stierle, D. B., & Bugni, T. (1999). Sequoiatones A and B: Novel antitumor metabolites isolated from a redwood endophyte. *The Journal of Organic Chemistry, 64*(15), 5479-5484.

Stinson, M., Ezra, D., Hess, W. M., Sears, J., & Strobel, G. (2003). An endophytic *Gliocladium* sp. of *Eucryphia cordifolia* producing selective volatile antimicrobial compounds. *Plant Science, 165*(4), 913-922.

Stone, J., & Petrini, O. (1997). Endophytes of forest trees: A model for fungus-plant interactions *Plant Relationships Part B,* (pp. 129-140). Springer Publisher, New York.

Stone, J. K., Bacon, C. W., & White, J. (2000). An overview of endophytic microbes: endophytism defined. *Microbial Endophytes,* (pp. 29-33). Marker Dekker Incorporation, New York.

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

Strobel, G., Yang, X., Sears, J., Kramer, R., Sidhu, R. S., & Hess, W. (1996). Taxol from *Pestalotiopsis microspora*, an endophytic fungus of *Taxus wallachiana*. *Microbiology, 142*(2), 435-440.

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

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

Strobel, G., Daisy, B., Castillo, U., & Harper, J. (2004). Natural products from endophytic microorganisms. *Journal of Natural Products, 67*(2), 257-268.

Strobel, G., Daisy, B., & Castillo, U. (2005). Novel natural products from rainforest endophytes *Natural Products* (pp. 329-351): Springer Publisher, New York.

Sudi, I. Y., Ksgbiya, M., Muluh, E. K., & Clement, A. (2011). Nutritional and phytochemical screening of *Senna obtusifolia* indigenous to Mubi, Nigeria. *Advances in Applied Science Research, 2*(3), 432-437.

Suffness, M., & Pezzuto, J. M. (1990). Assays related to cancer drug discovery. Methods Plant Biochemistry: Assays for Bioactivity. (pp. 71-133) London: Academic Press, England.

Sultana, M. J., & Ahmed, F. R. S. (2014). Biological characterization of crude extract & pure compound isolated from *Swertia chirata* Ham. *Biomedical Science and Engineering, 2*(1), 1-4.

Sumner, L. W., Mendes, P., & Dixon, R. A. (2003). Plant metabolomics: Large-scale phytochemistry in the functional genomics era. *Phytochemistry, 62*(6), 817-836.

Sun, S., Tian, L., Wang, Y., Wu, H., Lu, X., & Pei, Y. (2009). A novel natural product from the fermentation liquid of marine fungus *Trichoderma atroviride* G20-12. *Asian Journal of Traditional Medicines, 4*(3), 123-127.

Sun, X., & Guo, L. D. (2012). Endophytic fungal diversity: Review of traditional and molecular techniques. *Mycology, 3*(1), 65-76.

Talbot, G. H., Bradley, J., Edwards, J. E., Gilbert, D., Scheld, M., & Bartlett, J. G. (2006). Bad bugs need drugs: An update on the development pipeline from the antimicrobial availability task force of the infectious diseases society of America. *Clinical Infectious Diseases, 42*(5), 657-668.

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

Tan, M., Sulaiman, S., Najimuddin, N., Samian, M., & Muhammad, T. T. (2005). Methanolic extract of *Pereskia bleo* (Kunth) DC.(Cactaceae) induces apoptosis in breast carcinoma, T47-D cell line. *Journal of Ethnopharmacology, 96*(1), 287-294.

Tedersoo, L., & Nilsson, R. H. (2016). Molecular identification of fungi. *Molecular Mycorrhizal Symbiosis* (pp. 301-322): Wiley Publisher, New Jersey.

Tejesvi, M. V., Kini, K. R., Prakash, H. S., Subbiah, V., & Shetty, H. S. (2007). Genetic diversity and antifungal activity of species of *Pestalotiopsis* isolated as endophytes from medicinal plants. *Fungal Diversity, 24*(3), 37-54.

Tejesvi, M., Nalini, M., Mahesh, B., Prakash, H., Kini, K. R., Shetty, H. S., & Subbiah, V. (2007). New hopes from endophytic fungal secondary metabolites. *Boletin de la Sociedad Quimica de Mexico, 1*(1), 19-26.

Teles, H. L., Sordi, R., Silva, G. H., Castro-Gamboa, I., da Silva Bolzani, V., Pfenning, L. H., de Abreu, L. M., Costa-Neto, C .M., Young, M. C. M., & Araujo, A.R. (2006). Aromatic compounds produced by *Periconia atropurpurea*, an endophytic fungus associated with *Xylopia aromatica*. *Phytochemistry, 67*(24), 2686-2690.

Tenover, F. C., Arbeit, R. D., & Goering, R. V. (1997). How to select and interpret molecular strain typing methods for epidemiological studies of bacterial infections a review for healthcare epidemiologists. *Infection Control and Hospital Epidemiology, 18*(06), 426-439.

Tindall, K. R., & Kunkel, T. A. (1988). Fidelity of DNA synthesis by the *Thermus aquaticus* DNA polymerase. *Biochemistry, 27*(16), 6008-6013.

Tomsheck, A. R., Strobel, G. A., Booth, E., Geary, B., Spakowicz, D., Knighton, B., Floerchinger, C., Sears, J., Liarzi, O., & Ezra, D. (2010). *Hypoxylon* sp., an endophyte of *Persea indica*, producing 1, 8-

cineole and other bioactive volatiles with fuel potential. *Microbial Ecology, 60*(4), 903-914.

Tonial, F., Maia, B. H., Gomes-Figueiredo, J. A., Sobottka, A. M., Bertol, C. D., Nepel, A., Savi, D. C., Vicente, V. A., Gomes, R. R., & Glienke, C. (2016). Influence of culturing conditions on bioprospecting and the antimicrobial potential of endophytic fungi from *Schinus terebinthifolius*. *Current Microbiology, 72*(2), 173-183.

Toofanee, S. B., & Dulymamode, R. (2002). Fungal endophytes associated with *Cordemoya integrifolia*. *Fungal Diversity, 11*(1), 169-175.

Tsai, C. C., & Lin, C. C. (1998). Anti-inflammatory effects of Taiwan folk medicine 'Teng-Khia-U'on carrageenan and adjuvant-induced paw edema in rats. *Journal of Ethnopharmacology, 64*(1), 85-89.

Turbyville, T. J., Wijeratne, E. K., Liu, M. X., Burns, A. M., Seliga, C. J., Luevano, L. A., David, C. L., Faeth, S. H., Whitesell, L. & Gunatilaka, A. A. L. (2006). Search for Hsp90 inhibitors with potential anticancer activity: isolation and SAR studies of radicicol and monocillin I from two plant-associated fungi of the sonoran desert 1. *Journal of Natural Products, 69*(2), 178-184.

Tyagi, A. K., Singh, R. P., Agarwal, C., Chan, D. C., & Agarwal, R. (2002). Silibinin strongly synergizes human prostate carcinoma DU145 cells to doxorubicin-induced growth Inhibition, G2-M arrest, and apoptosis. *Clinical Cancer Research, 8*(11), 3512-3519.

Udagawa, S., Tsubouchi, H., & Horie, Y. (1991). *Neosartorya hiratsukae*, a new species of food-borne Ascomycetes. *Transactions of the Mycological Society of Japan (Japan)*, *(32)*1, 23-9.

Vaara, M. (1992). Agents that increase the permeability of the outer membrane. *Microbiological Reviews, 56*(3), 395-411.

Vaidya, A. D., & Devasagayam, T. P. (2007). Recent advances in Indian herbal drug, current status of herbal drugs in India: An Overview. *Journal of Clinical Biochemistry and Nutrition, 41*(1), 1-11.

Van der Sar, S. A., Blunt, J. W., & Munro, M. H. (2006). Spiro-Mamakone A: A unique relative of the spirobisnaphthalene class of compounds. *Organic Letters, 8*(10), 2059-2061.

Van Oppen, M. J., Klerk, H., Olsen, J. L., & Stam, W. T. (1996). Hidden diversity in marine algae: Some examples of genetic variation below the species level. *Journal of the Marine Biological Association of the United Kingdom, 76*(01), 239-242.

Vanparys, C., Maras, M., Lenjou, M., Robbens, J., Van Bockstaele, D., Blust, R., & De Coen, W. (2006). Flow cytometric cell cycle analysis allows for rapid screening of estrogenicity in MCF-7 breast cancer cells. *Toxicology In Vitro, 20*(7), 1238-1248.

Venugopalan, A., & Srivastava, S. (2015). Endophytes as *in vitro* production platforms of high value plant secondary metabolites. *Biotechnology Advances, 33*(6), 873-887.

Verpoorte, R. (2000). Pharmacognosy in the new millennium: Lead finding and biotechnology. *Journal of Pharmacy and Pharmacology, 52*(3), 253-262.

Wachira, F. N., Waugh, R., Powell, W., & Hackett, C. (1995). Detection of genetic diversity in tea (*Camellia sinensis*) using RAPD markers. *Genome, 38*(2), 201-210.

Wachsmuth, K. (1985). Genotypic approaches to the diagnosis of bacterial infections: Plasmid analyses and gene probes. *Infection Control, 6*(03), 100-109.

Wagele, J., & Rodding, F. (1998). Origin and phylogeny of metazoans as reconstructed with rDNA sequences *Molecular Evolution: Towards the Origin of Metazoa* (pp. 45-70): Springer Publisher, New York.

Waheeda, K., & Shyam, K. (2017). Formulation of novel surface sterilization method and culture media for the isolation of endophytic actinomycetes from medicinal plants and its antibacterial activity. *Journal of Plant Pathology and Microbiology, 8*(399), 1-9.

Wang, S., Li, X. M., Teuscher, F., Li, D. L., Diesel, A., Ebel, R., Proksch, P. and Wang, B. G. (2006). Chaetopyranin, a benzaldehyde derivative, and other related metabolites from *Chaetomium globosum*, an endophytic fungus derived from the marine red alga *Polysiphonia urceolata*. *Journal of Natural Products, 69*(11), 1622-1625.

Wang, J. J., Liu, S. M., Chen, R., Li, L., Guo, X. S., Xue, B., & Hu, W. C. (2007). A novel effect of lobeline on vascular smooth muscle cell: inhibition of proliferation induced by endothelin-1. *Die Pharmazie-An International Journal of Pharmaceutical Sciences, 62*(8), 620-624.

Wang, C., Tian, X., Yang, Q., Lu, Y., Ma, L., Huang, H., & Fan, C. (2014). Diversity of secondary metabolites from two Antarctic microbes *Rhodococcus* sp. NJ-008 and *Pseudomonas* sp. NJ-011. *Open Journal of Marine Science, 4*(3), 1-7

Wani, M. C., Taylor, H. L., Wall, M. E., Coggon, P., & McPhail, A. T. (1971). Plant antitumor agents. VI. Isolation and structure of taxol, a novel antileukemic and antitumor agent from *Taxus brevifolia*. *Journal of the American Chemical Society, 93*(9), 2325-2327.

Wani, M. A., Sanjana, K., Kumar, D. M., & Lal, D. K. (2010). GC–MS analysis reveals production of 2–Phenylethanol from *Aspergillus niger* endophytic in rose. *Journal of Basic Microbiology, 50*(1), 110-114.

Wanikiat, P., Panthong, A., Sujayanon, P., Yoosook, C., Rossi, A. G., & Reutrakul, V. (2008). The anti-inflammatory effects and the inhibition of neutrophil responsiveness by *Barleria lupulina* and *Clinacanthus nutans* extracts. *Journal of Ethnopharmacology, 116*(2), 234-244.

Welsh, J., & McClelland, M. (1990). Fingerprinting genomes using PCR with arbitrary primers. *Nucleic Acids Research, 18*(24), 7213-7218.

Welsh, J., Petersen, C., & McClelland, M. (1991). Polymorphisms generated by arbitrarily primed PCR in the mouse: Application to strain identification and genetic mapping. *Nucleic Acids Research, 19*(2), 303-306.

Welsh, J., Chada, K., Dalal, S. S., Cheng, R., Relph, D., & McClelland, M. (1992). Arbitrarily primed PCR fingerprinting of RNA. *Nucleic Acids Research, 20*(19), 4965-4970.

Wennström, A. (1994). Endophyte: The misuse of an old term. *Oikos, 71*(3), 535-536.

Wijeratne, E. K., Paranagama, P. A., Marron, M. T., Gunatilaka, M. K., Arnold, A. E., & Gunatilaka, A. L. (2008). Sesquiterpene quinones and related metabolites from *Phyllosticta spinarum*, a fungal strain endophytic in *Platycladus orientalis* of the Sonoran Desert (1). *Journal of Natural Products, 71*(2), 218-222.

Williams, J. G., Kubelik, A. R., Livak, K. J., Rafalski, J. A., & Tingey, S. V. (1990). DNA polymorphisms amplified by arbitrary primers are useful as genetic markers. *Nucleic Acids Research, 18*(22), 6531-6535.

Wilson, D. (1995). Endophyte: The evolution of a term, and clarification of its use and definition. *Oikos*, *73*(2), 274-276.

Wiyakrutta, S., Sriubolmas, N., Panphut, W., Thongon, N., Danwisetkanjana, K., Ruangrungsi, N., & Meevootisom, V. (2004). Endophytic fungi with anti-microbial, anti-cancer and anti-malarial activities isolated from Thai medicinal plants. *World Journal of Microbiology and Biotechnology, 20*(3), 265-272.

White, T. J., Bruns, T., Lee, S., & Taylor, J. (1990). Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics. *PCR Protocols: A Guide to Methods and Applications,* (pp. 315-322). Academic Press, Massachusetts.

WHO, Traditional medicine. (2003, May) *World Health Organisation*. Retrieved July 31, 2016, from http://www.who.int/mediacentre/factsheets/2003/fs134/en/

WHO, Antimicrobial resistance (2016, September) *World Health Organisation* Retrieved December 05, 2016, from http://www.who.int/mediacentre/ factsheets/fs194/en/

Wright, G. D. (2012). Antibiotics: A new hope. *Chemistry and Biology, 19*(1), 3-10.

Won, H., & Renner, S. S. (2005). The internal transcribed spacer of nuclear ribosomal DNA in the gymnosperm *Gnetum*. *Molecular Phylogenetics and Evolution, 36*(3), 581-597.

Wong, M. M. (2012). The reproductive biology and cytotoxic activity of *Persicaria chinensis* (L.) H. *gross* var. chinensis (Polygonaceae), PhD Thesis, University of Malaya.

Xiong, J., Li, S., Wang, W., Hong, Y., Tang, K., & Luo, Q. (2013). Screening and identification of the antibacterial bioactive compounds from *Lonicera japonica* Thunb. leaves. *Food chemistry, 138*(1), 327-333.

Yaacob, N. S., Hamzah, N., Kamal, N. N. N. M., Abidin, S. A. Z., Lai, C. S., Navaratnam, V., & Norazmi, M. N. (2010). Anticancer activity of a sub-fraction of dichloromethane extract of *Strobilanthes crispus* on human breast and prostate cancer cells *in vitro*. *BioMed Central Complementary and Alternative Medicine, 10*(1), 42-56.

Yamauchi, K., Isshiki, Y., Zhou, Z. X., & Nakahiro, Y. (1990). Scanning and transmission electron microscopic observations of bacteria adhering to ileal epithelial cells in growing broiler and White Leghorn chickens. *British Poultry Science, 31*(1), 129-137.

Yang, X., Zhang, L., Guo, B., & Guo, S. (2003). Preliminary study of a vincristine-producing endophytic fungus isolated from leaves of *Catharanthus roseus*. *Chinese Traditional and Herbal Drugs, 35*(1), 79-81.

Yasunaka, K., Abe, F., Nagayama, A., Okabe, H., Lozada-Perez, L., Lopez-Villafranco, E., Muniz, E. E., Aguilar, A., & Reyes-Chilpa, R. (2005). Antibacterial activity of crude extracts from Mexican medicinal plants and purified coumarins and xanthones. *Journal of Ethnopharmacology, 97*(2), 293-299.

Yogeswari, L. (1948). Trace element nutrition of fungi. *Proceedings: Plant Sciences, 28*(6), 177-201.

Yong, Y. K., Tan, J. J., Teh, S. S., Mah, S. H., Ee, G. C. L., Chiong, H. S., & Ahmad, Z. (2013). *Clinacanthus nutans* extracts are antioxidant with antiproliferative effect on cultured human cancer cell lines. *Evidence-Based Complementary and Alternative Medicine, 2013*(1), 1-8

Yu, H., Zhang, L., Li, L., Zheng, C., Guo, L., Li, W., Sun, P., & Qin, L. (2010). Recent developments and future prospects of antimicrobial metabolites produced by endophytes. *Microbiological Research, 165*(6), 437-449.

Yurkonis, K. A., Maherali, H., Bolton, K. A., Klironomos, J. N., & Newman, J. A. (2012). Cultivar genotype, application and endophyte history affects community impact of *Schedonorus arundinaceus*. *Journal of Applied Ecology, 49*(5), 1094-1102.

Zaidan, M., Noor Rain, A., Badrul, A., Adlin, A., Norazah, A., & Zakiah, I. (2005). *In vitro* screening of five local medicinal plants for antibacterial activity using disc diffusion method. *Tropical Biomedicine, 22*(2), 165-170.

Zareisedehizadeh, S., Tan, C. H., & Koh, H. L. (2014). A review of botanical characteristics, traditional usage, chemical components, pharmacological activities, and safety of *Pereskia bleo* (Kunth) DC. *Evidence-Based Complementary and Alternative Medicine, 2014*(1), 1-11.

Zhang, D. X., Nagabhyru, P., & Schardl, C. L. (2009). Regulation of a chemical defense against herbivory produced by symbiotic fungi in grass plants. *Plant Physiology, 150*(2), 1072-1082.

Zhang, H. Y., Liu, X. Z., He, C. S., & Yang, Y. M. (2008). Genetic diversity among flue-cured tobacco cultivars based on RAPD and AFLP markers. *Brazilian Archives of Biology and Technology, 51*(6), 1097-1101.

Zhao, J., Mou, Y., Shan, T., Li, Y., Zhou, L., Wang, M., & Wang, J. (2010). Antimicrobial metabolites from the endophytic fungus *Pichia guilliermondii* isolated from *Paris polyphylla* var. yunnanensis. *Molecules, 15*(11), 7961-7970.