

PERPUSTAKAAN HAMDAN TAHIR
UNIVERSITI SAINS MALAYSIA

**UNIVERSITI SAINS MALAYSIA
GERAN PENYELIDIKAN UNIVERSITI PENYELIDIKAN
LAPORAN AKHIR**

**UNDERSTANDING THE MECHANISM OF ACTION OF DENROPHTHOE
PENTANDRA LEAVES EXTRACT AS ANTICANCER AGENT**

PENYELIDIK

DR MOHD DASUKI SUL'AIN

PENYELIDIK BERSAMA

**DR YUSMAZURA ZAKARIA
NIK AINA SYAZANA NIK ZAINUDDIN**

2016



FINAL REPORT
FUNDAMENTAL RESEARCH GRANT SCHEME (FRGS)
Laporan Akhir Skim Geran Penyelidikan Fundamental (FRGS)
 Pindaan 1/2016

RESEARCH TITLE: UNDERSTANDING THE MECHANISM OF ACTION OF *Dendrophthoe pentandra* LEAVES EXTRACT AS ANTICANCER AGENT

PHASE & YEAR:

START DATE: 01 MAY 2013

END DATE (EXPECTED): 31 Oct 2016

EXTENSION DATE: RMC LEVEL: 31 Oct 2016

KPM LEVEL: 31 Oct 2016

PROJECT STATUS: (ACTIVE / TERMINATED / COMPLETED)

PROJECT LEADER: DR MOHD DASUKI BIN SUL'AIN

IC / PASSPORT NUMBER: 730719035605

PROJECT MEMBERS : 1. DR YUSMAZURA BINTI ZAKARIA
 (including GRA) 2. NIK AINA SYAZANA BINTI NIK ZAINUDDIN

PROJECT ACHIEVEMENT (*Prestasi Projek*)

ACHIEVEMENT PERCENTAGE

Project progress according to milestones achieved up to this period	0 - 50%	51 - 75%	76 - 100%
Percentage (please state #%)			100

RESEARCH OUTPUT

	Indexed Journal	Non-Indexed Journal
Number of articles/ manuscripts/ books (Please attach the First Page of Publication)	1. Nik Aina SNZ and Mohd Dasuki S. (2015). Phytochemical Analysis, Toxicity and Cytotoxicity Evaluation of <i>Dendrophthoe pentandra</i> Leaves Extracts. International Journal of Applied Biology and Pharmaceutical Technology. Volume 6, Issue 1, page 108 – 116. 2. Nik Aina SNZ and Mohd Dasuki S. (2015). Antiproliferative Effect of <i>Dendrophthoe pentandra</i> Leaves Extracts Towards Human Breast Adenocarcinoma Cells, MCF-7 cells. Jurnal Teknologi (Sciences & Engineering.) Special Issue: Propelling Science and Technology Through Natural Products. Volume 77, No. 2, page 35 – 39	
Conference Proceeding (Please attach the First Page of Publication)	International 1. Nik Aina SNZ, Yusmazura Z and Mohd Dasuki S. Antiproliferative and apoptosis-inducing effects of <i>Dendrophthoe pentandra</i> Methanol Extract on Human Breast Adenocarcinoma Cells, MCF-7.	National

	<p>International Conference of Biomedical and Health Sciences Research. 25th - 27th January 2015. Everly Hotel, Putrajaya.</p> <p>2. Nik Aina SNZ and Mohd Dasuki S. Antiproliferative Effect of <i>Dendrophthoe pentandra</i> Leaves Extracts Towards Human Breast Adenocarcinoma Cells, MCF-7 cells. International Conference of Natural Products. 24th – 25th March 2015. Double Tree by Hilton, Johor Bharu.</p> <p>3. Nik Aina SNZ, Yusmazura Z and Mohd Dasuki S. <i>Dendrophthoe pentandra</i> Methanol Extract (DPME) Induce Apoptosis and Cell Cycle Arrest at G1/S in Human Breast Adenocarcinoma Cells, MCF-7 via Up-Regulation of p53. International Conference of Natural Products. 15th – 17th March 2016. Permai Hotel, Kuala Terengganu.</p>	
Intellectual Property (Please specify)	No IP	

TALENT					
Talent	Number				Others (please specify)
	On-going		Graduated		
Citizen	Malaysian	Non Malaysian	Malaysian	Non Malaysian	
No. PHD STUDENT					Mohon sertakan juga Kerakyatan bagi Pelajar antarabangsa
Student Fullname: IC / Passport No: Student ID:					
No. MASTER STUDENT			1		
Student Fullname: IC / Passport No: Student ID:			1. NIK AINA SYAZANA BINTI NIK ZAINUDDIN 880423-03-6266 PSKM0009/14(R)		
No. UNDERGRADUATE STUDENT					
Student Fullname: IC / Passport No: Student ID:					
Total					

EXPENDITURE (Perbelanjaan) as Borang K1(RMC)

C	Budget Approved (Peruntukan diluluskan)	: RM 104 000 00
	Amount Spent (Jumlah Perbelanjaan)	: RM 98.458.80 =
	Balance (Baki)	: RM 5,541.20
	Percentage of Amount Spent	: 94.7 %

ADDITIONAL RESEARCH ACTIVITIES THAT CONTRIBUTE TOWARDS DEVELOPING SOFT AND HARD SKILLS

Aktiviti Penyelidikan Sampingan yang menyumbang kepada pembangunan kemahiran insaniah)

International

Activity	Date (Month, Year)	Organizer
1. International Conference of Biomedical and Health Sciences Research. Everly Hotel, Putrajaya.	1. 25 th - 27 th January 2015	1. University of Nottingham, Malaysia
2. International Conference of Natural Products 2015. Double Tree by Hilton, Johor Bharu.	2. 24 th - 25 th March 2015	2. Universiti Teknologi Malaysia (UTM)
3. International Conference of Natural Products 2016. Permai Hotel, Kuala Terengganu.	3. 15 th - 17 th March 2016	3. Universiti Malaysia Terengganu (UMT)

National

Activity	Date (Month, Year)	Organizer
(e.g : Course/ Seminar/ Symposium/ Conference/ Workshop/ Site Visit)		

PROBLEMS / CONSTRAINTS IF ANY (Masalah/ Kekangan sekiranya ada)

No problem

RECOMMENDATION (Cadangan Penambahbaikan)

For further investigation, the mechanism of DPME should be further investigated on caspase cascade pathway such as caspase-3, caspase-8 and caspase-9. By examine on caspase-9 and caspase-8, the activation of downstream executioner caspases such as caspase-3 can be activated. This can further clarify the overall pathway that takes part in apoptosis mechanism. Other than that, fractionation and purification of bioactive compound from DPME should be carried out in order to obtain pure active compound. The purification and isolation process allows exclusion of unwanted compound and help to identify the responsible compound from DPME that having anticancer properties. In addition, the anticancer activity of DPME should be examined in vivo which includes toxicity by animal testing and clinical studies.

RESEARCH ABSTRACT – Not More Than 200 Words (Abstrak Penyelidikan – Tidak Melebihi 200 patah perkataan)

Throughout medical history, herbal plants have been shown to be one of valuable sources in combating cancer such as *Dendrophthoe pentandra* (DP). However, the mechanism underlying anticancer activity is unclear and need to be explored. Therefore, DP was selected in order to evaluate its antiproliferative activity and mode of cell death in cancer treatment. The extraction of DP leaves were carried out using methanol as a solvent (DPME). Phytochemicals compound present in DPME were screened and quantified. Tannin is the most abundance phytochemical present in DPME. Further confirmation of its bioactive compound by Gas Chromatography - Mass Spectrophotometry (GC-MS) was done. Hexadecanoic acid, methyl ester (palmitic acid) and 9,12,15-octadecatrienoic acid, methyl ester (linolenic acid) were two compounds that probably contribute to antiproliferative property. The antiproliferative activities of DPME towards HeLa, HepG2, MCF-7, U2OS and MDA-MB-231 cell lines have been examined by MTT Assay and IC₅₀ values were obtained. MCF-7 cells showed the most effective growth inhibition with lowest IC₅₀ value upon treatment with DPME. The cytotoxicity activities towards normal kidney MDCK and normal connective L929 cells were evaluated to determine the cytoselectivity property of DPME. The nuclear staining by Hoechst 33258 displayed the chromatin condensation, fragmented

nuclei and formation of apoptotic bodies upon treatment with DPME according to certain period of time. Flowcytometric analysis using Annexin V/PI double staining has confirmed that DPME-treated MCF-7 arrested cell cycle distribution at G1/S phase and induced apoptosis. The mechanism of action was further confirmed by determination of protein involved in apoptosis pathway; Bcl-2, Bax, p53 and cytochrome C. The results found out that the increased of p53 was followed by an increment of Bax, pro-apoptotic and decreased of Bcl-2, anti-apoptotic. Activation of Bax and inactivation of Bcl-2 triggered release of cytochrome C which leads to apoptosis event. In conclusion, DPME demonstrated antiproliferative activity in MCF-7 cells by induction of apoptosis. Therefore, it has a promising approach for breast cancer treatment. Other than DPME, Dendrothoe pentandra ethyl acetate extract (DPEA) showed antiproliferative activity on MCF-7 of IC_{50} 4.72 ± 0.52 $\mu\text{g/mL}$. From GC-MS analysis, DPEA also showed presence of decanoic acid, palmitic acid, linolenic acid and beta-sitosterol that might contribute to DP anticancer activity.

Date : 4 OCT 2016
Tarikh

Project Leader's Signature:
Tandatangan Ketua Projek



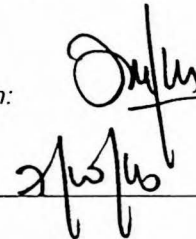
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COMMENTS, IF ANY/ ENDORSEMENT BY RESEARCH MANAGEMENT CENTER (RMC)
(Komen, sekiranya ada/ Pengesahan oleh Pusat Pengurusan Penyelidikan)

Name:
Nama:

PROF. DR LEE KEAT TEONG
Pengeran
Pejabat Pengurusan & Kreativiti Penyelidikan
Universiti Sains Malaysia

Signature:
Tandatangan:



Date:
Tarikh: