"THE EFFECTS OF ADJUVANT HONEY THERAPY ON DISEASE ACTIVITY, LYMPHOCYTE FUNCTION AND LYMPHOCYTE SUBSETS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)"

RESEARCH UNIVERSITY GRANT (RU)
FINAL REPORT

Assoc. Prof Kamaliah Mohd Daud

June 2010

UNIVERSITY RESEARCH GRANT

FINAL REPORT

UNIVERSITI SAINS MALAYSIA

UNIVERSITY RESEARCH GRANT FINAL REPORT
Geran Penyelidikan Universiti Laporan Akhir

A.	**TITLE OF RESEARCH:** *Tajuk penyelidikan:* The Effects Of Adjuvant Honey Therapy On Disease Activity, Lymphocyte Function And Lymphocyte Subsets In Patients With Systemic Lupus Erythematosus (SLE).
B.	**PERSONAL PARTICULARS OF RESEARCHER** / *MAKLUMAT PENYELIDIK:*
(i)	**Name of Research Leader:** *Nama Ketua Penyelidik:* Prof Madya Dr Kamaliah Mohd Daud
	Name of Co-Researcher *Nama Penyelidik Bersama:* 1. Prof Madya Siti Amrah Bte Sulaiman 2. Dr Wan Syamimee Wan Ghazali 3. Dr Che Maraina Bt Che Hussin 4. Dr Azreen Syazril Bin Adnan
(ii)	**School/Institute/Centre/Unit :** *Pusat Pengajian /Institut/Pusat/Unit :* School of Medical Sciences (PPSP)

C. **Research Platform (Please tick (/) the appropriate box):**
Pelantar Penyelidikan (Sila tanda (/) kotak berkenaan):

☐	**A. Life Sciences** *Sains Hayat*
☐	**B. Fundamental** *Fundamental*
☐	**C. Engineering & Technology** *Kejuruteraan & Teknologi*
☐	**D. Social Transformation** *Transformasi Sosial*
☐	**E. Information & Communications Technology (ICT)** *Teknologi Maklumat & Komunikasi*
☑	**F. Clinical Sciences** *Sains Klinikal*
☐	**G. Biomedical & Health Sciences** *Bioperubatan Sains Kesihatan*

D. **Duration of this research :**
Tempoh masa penyelidikan ini :

***Duration :** 2 Years
Tempoh :

From : Oct 2007 **To** : Sept 2009
Dari: *Ke :*

E. **ABSTRACT OF RESEARCH**

(An abstract of between 100 and 200 words must be prepared in **Bahasa Malaysia and in English**. This abstract will be included in the Annual Report of the Research and Innovation Section at a later date as a means of presenting the project findings of the researcher/s to the University and the community at large)

Abstrak Penyelidikan

(Perlu disediakan di antara 100 - 200 perkataan di dalam **Bahasa Malaysia dan juga Bahasa Ingge** Abstrak ini akan dimuatkan dalam Laporan Tahunan Bahagian Penyelidikan & Inovasi sebagai satu ca untuk menyampaikan dapatan projek tuan/puan kepada pihak Universiti & masyarakat luar).

ABSTRACT

Objectives: To compare the effects of adjuvant tualang honey therapy versus conventional therapy alone on disease activity, lymphocyte functions and lymphocyte subsets in SLE patients.
Methodology: Sixty SLE patients from Hospital Universiti Sains Malaysia were randomized into two equal groups, group 1 receiving conventional treatment with low dose steroid and cyclophosphamide or azathioprim, group 2 receiving same treatment in addition to tualang honey 20 gm twice a day. Disease activity was measured in all patients every 3 months by SLEDAI score, the function of T lymphocyte was determined at baseline and after 6 months by measuring the expression of 3 lymphocyte activation markers (HLADR, CD45RO and CD25). Enumeration of lymphocyte subsets (CD3, CD4, CD8, CD19, and CD16/56) was done at baseline and after 6 months.
Results: The SLEDAI score was significantly decreased in honey group compared to non honey group after 3 and 6 months of follow up. There was a significant decrease in the expression of CD8CD45RO and CD8CD25 in honey group.There was a significant increase in CD3 and CD16/56 percentage in honey group after 6 months follow up.
Conclusion: The use of honey therapy as adjuvant to conventional treatment in patients with SLE was found to be useful in suppressing disease activity and enhancing lymphocyte function and lymphocyte subsets.

ABSTRAK

Objektif: Untuk membandingkan kesan terapi tambahan madu tualang dan terapi konvensional terhadap aktiviti penyakit, fungsi dan subset limfosit dikalangan pesakit SLE.
Prosedur:
Enam puluh pesakit SLE dari Hospital Universiti Sains Malaysia dibahagikan kepada dua kumpulan secara rawak, kumpulan pertama menerima rawatan secara konvensional dengan dos steroid yang rendah dan cyclophosphamide atau azathioprim, kumpulan kedua menerima rawatan yang sama dengan tambahan madu tualang sebanyak 20 gm dua kali sehari. Aktiviti penyakit diukur untuk semua pesakit setiap 3 bulan menggunakan skor SLEDAI, fungsi T-limfosit ditentukan pada permulaan kajian dan selepas 6 bulan dengan mengukur ekspresi 3 penanda pengaktifan limfosit (HLADR, CD45RO dan CD25) Pengiraan subset limfosit (CD3, CD4, CD45, CD19, dan CD16/56) dilakukan pada permulaan kajian dan selepas 6 bulan.

Keputusan: Skor SLEDAI menunjukkan penurunan yang signifikan dalam kumpulan terapi tambahan madu dibandingkan dengan kumpulan terapi konvensional.
Terdapat penurunan yang signifikan dalam ekspresi CD8CD45RO dan CD8CD25 dalam kumpulan terapi madu setelah 6 bulan susulan.Terdapat kenaikan yang signifikan untuk peratus CD3 dan CD16/56 dalam kumpulan terapi madu setelah 6 bulan.
Kesimpulan: Penggunaan terapi tambahan madu keatas rawatan konvensional di kalangan pesakit SLE didapati bermanfaat di dalam mengurangkan aktiviti penyakit dan menambahbaik fungsi dan subset limfosit.

F. SUMMARY OF RESEARCH FINDINGS
Ringkasan dapatan Projek Penyelidikan

1. The use of honey therapy as adjuvant to conventional treatment in patients with systemic lupus erythematosus (SLE) was found to be useful in suppressing disease activity..
2. Honey also enhanced lymphocyte function as our study showed a significant decrease in the expression of CD8CD45RO and CD8CD25 within honey group compared to non honey group after 6 months follow up.
3. In addition honey improved lymphocyte subsets as we found a significant increase in CD3 and CD16/56 percentage in honey group after 6 months follow up compared with non honey group.

G. COMPREHENSIVE TECHNICAL REPORT
Laporan Teknikal Lengkap
Applicants are required to prepare a comprehensive technical report explaining the project.
(This report must be attached separately)
Sila sediakan laporan teknikal lengkap yang menerangkan keseluruhan projek ini.
[Laporan ini mesti dikepilkan] – Please refer to attached sheet (G).

List the key words that reflectour research:
Senaraikan kata kunci yang mencerminkan penyelidikan anda:

English	Bahasa Malaysia
Systemic lupus erythematosus	Sistemik lupus eritematosus
Lymphocyte subset and function	Subset dan fungsi limfosit
Tualang Honey	Madu tualang
Disease activity	Aktiviti penyakit

H. **a) Results/Benefits of this research**
Hasil Penyelidikan

No. *Bil:*	Category/Number: *Kategori/ Bilangan:*	Promised	Achieved
1.	**Research Publications (Specify target journals)** *Penerbitan Penyelidikan (Nyatakan sasaran jurnal)*	3	2
2.	**Human Capital Development**		
	a. Ph. D Students		
	b. Masters Students	1	1
	c. Undergraduates (Final Year Project)		
	d. Research Officers		
	e. Research Assisstants		
	f. Other: Please specify		
3.	**Patents** *Paten*	-	-
4.	**Specific / Potential Applications** *Spesifik/Potensi aplikasin*	-	-
5.	**Networking & Linkages** *Jaringan & Jalinan*	-	-
6.	**Possible External Research Grants to be Acquired** *Jangkaan Geran Penyelidikan Luar Diperoleh*	-	-

- Kindly provide copies/evidence for Category 1 to 6.

b) Equipment used for this research.
Peralatan yang telah digunakan dalam penyelidikan ini.

Items *Perkara*	Approved Equipment	Approved Requested Equipment	Location
Specialized Equipment Peralatan khusus			
Facility Kemudahan			
Infrastructure Infrastruktur			

- Please attach appendix if necessary.

I. **BUDGET** / *BAJET*

Perbelanjaan :Expenditure

Project Account No.	:
Total Approved Budget	:
Total Additional Budget	:
Grand Total of Approved Budget	:
Total Expenditure	:
Balance	:

- **Please attach final account statement from Treasury**

30/06/2010

Signature of Researcher
Tandatangan Penyelidik

Date
Tarikh

H. COMMENTS OF PTJ'S RESEARCH COMMITTEE
KOMEN JAWATANKUASA PENYELIDIKAN PERINGKAT PTJ

General Comments:
Ulasan Umum:

The project has been completed successfully and objectives achieved. The output include two manuscript submitted and a MSc thesis. The report has been checked and approved by the PTJ Evaluation committee.

.....
Signatu
Tandata

J's Evaluation Committee
sa Penilaian PTJ

PROFESSOR AHMAD SUKARI HALIM
Chairman of Research Commitee
School of Medical Sciences
Health Campus
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.

Date : .....
Tarikh : .....

Signature and Stamp of Dean/ Director of PTJ
Tandatangan dan Cop Dekan/ Pengarah PTJ

Date : .....
Tarikh : .....

PROFESOR ABDUL AZIZ BABA
Dekan
Pusat Pengajian Sains Perubatan
Kampus Kesihatan
Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.

27/12/09

Submission Confirmation

Thank you for submitting your manuscript to *International Journal of Rheumatic Diseases.*

Manuscript ID: APLAR-0074-2010

Title: Effects of adjuvant Tualang honey therapy on circulating lymphocyte subsets in patients with systemic lupus erythematosus

Authors: Mohd Daud, Kamaliah
Mohamad, Wathik
Wan Ghazali, Wan Syamimee
Bachok, Norsaadah
Che Maraina, Che Hussin

Date Submitted: 13-Apr-2010

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Submission Confirmation

Thank you for submitting your revised manuscript to *International Journal of Rheumatic Diseases*.

Manuscript ID: APLAR-0074-2010.R1

Title: Effects of adjuvant Tualang honey therapy on circulating lymphocyte subsets in patients with systemic lupus erythematosus

Authors: Mohd Daud, Kamaliah
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Wan Ghazali, Wan Syamimee
Bachok, Norsaadah
Che Maraina, Che Hussin

Date Submitted: 27-May-2010

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Effects of adjuvant *Tualang* honey therapy on circulating lymphocyte subsets in patients with systemic lupus erythematosus

Kamaliah MOHD DAUD[1], Wathik M. MOHAMAD[1], Wan Syamimee WAN GHAZALI[1], Che Maraina CHE HUSSIN[2], Norsa'adah BACHOK [3].

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Running title:

Effects of adjuvant honey therapy on lymphocyte subsets in SLE patients.

Author's Contribution

Author	Contribution
1. Kamaliah Mohd Daud	Principle investigator Preparation of study protocol and involved in data collection.
2. Wathik M. Mohamad	Preparation of study protocol and involved in data collection.
3. Wan Syamimee Wan Ghazali	Involved in data collection and input into immunological aspects.
4. Che Maraina Che Hussin	Input into immunological aspects of the study.
5. Norsa'adah Bachok	Advice on study design and statistical analysis.

Abstract

Aims: To compare the effects of adjuvant *Tualang* honey therapy versus conventional therapy alone on circulating lymphocyte subsets (CD3+ T-cells, CD4+ T-cells, CD8+ T-cells, CD19+ B-cells, and CD16/56+ natural killer cells) in systemic lupus erythematosus (SLE) patients.

Methods: This was a prospective randomized study involving sixty SLE patients who were randomized into two equal groups. Group 1 received maintenance treatment with low dose prednisolone alone or in combination with second line immunosuppressive drugs such as cyclophosphamide or azathioprine; group 2 receiving the same maintenance treatment together with oral *Tualang* honey 20 gm twice a day. In both groups, the percentages of circulating lymphocyte subsets (CD3+ T-cells, CD4+ T-cells, CD8+ T-cells, CD19+ B-cells, and CD16/56+ natural killer cells) were measured by immunophenotyping method using flow cytometer at baseline and after 6 months.

Results: There was a significant increase in the percentages of circulating CD3+ T-cells and CD16/56+ natural killer cells in honey treated group after 6 months follow up compared with non honey group ($p = 0.021, 0.038$ respectively). A pattern of increment for the percentages of circulating CD4+ T-cell and decrement for circulating CD8+ T-cell and CD19+ B-cell were observed in honey group but it was not statistically significant.

Conclusion: The use of adjuvant honey therapy increases the percentages of circulating CD3+ T-cells and CD16/56+ natural killer cells in SLE patients.

KEYWORDS

Honey, T-lymphocyte subsets, B-lymphocytes, natural killer cells, systemic lupus erythematosus.