BUKU LAPORAN AKHIR
GERAN USM JANGKA PENDEK

TAJUK GERAN

An interventive study of the effects of therapeutic lifestyle changes and simvastatin on the insulin sensitivity status of non obese hyperlipidaemic subjects

NAMA PENYELIDIK UTAMA:
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NAMA CO-RESEARCHER:
Prof. Madya Aziz Al-Safi Ismail
Prof. Madya Faridah Abdul Rashid

NO.AKAUN

UNIVERSITI SAINS MALAYSIA

LAPORAN AKHIR PROJEK PENYELIDIKAN JANGKA *PENDEK*

FINAL REPORT OF SHORT TERM RESEARCH PROJECT

Sila kemukakan laporan akhir ini melalui Jawatankuasa Penyelidikan di Pusat Pengajian dan Dekan/Pengarah/Ketua Jabatan kepada Pejabat Pelantar Penyelidikan

1. **Nama Ketua Penyelidik: Dr Nor Azwany Yaacob**
   Name of Research Leader

   ☐ Profesor Madya/ *Assoc. Prof.* ☑ Dr./ *Dr.* ☐ Encik/Puan/Cik *Mr/Mrs/Ms*

2. **Pusat Tanggungjawab (PTJ): Pusat Pengajian Sains Perubatan**
   School/Department

3. **Nama Penyelidik Bersama: Prof. Madya Aziz Al-Safi Ismail**
   Prof. Madya Faridah Abdul Rashid

4. **Tajuk Projek: An interventive study of the effects of therapeutic lifestyle changes and simvastatin on the insulin sensitivity status of non obese hyperlipidaemic subjects**

   Title of Project

5. **Ringkasan Penilaian/***Summary of Assessment:*	Tidak Mencukupi *Inadequate* 1	2	Boleh Diterima *Acceptable* 3	Sangat Baik *Very Good* 4	5
i) **Pencapaian objektif projek:** *Achievement of project objectives*	☐	☐	☐	☑	☐
ii) **Kualiti output:** *Quality of outputs*	☐	☐	☐	☑	☐
iii) **Kualiti impak:** *Quality of impacts*	☐	☐	☐	☑	☐
iv) **Pemindahan teknologi/potensi pengkomersialan:** *Technology transfer/commercialization potential*	☐	☐	☑	☐	☐
v) **Kualiti dan usahasama :** *Quality and intensity of collaboration*	☐	☐	☑	☐	☐
vi) **Penilaian kepentingan secara keseluruhan:** *Overall assessment of benefits*	☐	☐	☐	☑	☐

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

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)

Please see appendix attached
Sila rujuk lampiran yang disertakan

7. **Sila sediakan laporan teknikal lengkap yang menerangkan keseluruhan projek ini.**
[Sila gunakan kertas berasingan]
Applicant are required to prepare a Comprehensive Technical Report explaning the project.
(This report must be appended separately)
Please see appendix attached
Sila rujuk lampiran yang disertakan

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

Bahasa Malaysia	*Bahasa Inggeris*
Perubahan Gaya hidup terapeutik	**Therapeutic lifestyle changes**
Sindrom Metabolik	**Metabolic Syndrome**
Sensitiviti Insulin	**Insulin sensitivity**
Hiperlipidemia	**Hyperlipidemia**
Obesiti	**Obesiti**

8. **Output dan Faedah Projek**
Output and Benefits of Project

This study proves that insulin resistance is still a problem in hyperlipidemia non obese person thus lifestyle changes is important not only to achieve ideal body weight but also in avoiding hyperlipidemia state. The therapeutic lifestyle changes proposed and tried in this study can be a model for improving the abnormalities thus preventing cardiovascular diseases.

(a)* **Penerbitan Jurnal**
Publication of Journals
(Sila nyatakan jenis, tajuk, pengarang/editor, tahun terbitan dan di mana telah diterbit/diserahkan)
(State type, title, author/editor, publication year and where it has been published/submitted)

Please see appendix attached
Sila rujuk lampiran yang disertakan

(b) **Faedah-faedah lain seperti perkembangan produk, pengkomersialan produk/pendaftaran paten atau impak kepada dasar dan masyarakat.**
State other benefits such as product development, product commercialisation/patent registration or impact on source and society.

Provide prove that the community need a well plan lifestyle changes to prevent cardiovascular diseases by modifiable risk factors namely hyperlipidemia, obesity and subsequently insulin resistant

* Sila berikan salinan/*Kindly provide copies*

(c) **Latihan Sumber Manusia**
Training in Human Resources

i) Pelajar Sarjana:

Dr Abu Khouldun Al-Mahmood
Graduates Students

(Perincikan nama, ijazah dan status) PhD BioChemistry
(Provide names, degrees and status)

ii) Lain-lain:
Others

9. Peralatan yang Telah Dibeli:
Equipment that has been purchased
Tiada

5/10/08

Tandatangan Penyelidik
Signature of Researcher

Tarikh
Date

Komen Jawatankuasa Penyelidikan Pusat Pengajian/Pusat
Comments by the Research Committees of Schools/Centres

Projek disiapkan dgn mencapai semua objektif kajian
Hasil kajian juga ditambah

22/1/09

TANDATANGAN PENGERUSI
JAWATANKUASA PENYELIDIKAN
PUSAT PENGAJIAN/PUSAT
Signature of Chairman
[Research Committee of School/Centre]

Universiti Sains Malaysia
16150 Kubang Kerian, Kelantan.

Tarikh
Date

BORANG LAPORAN HASIL PENYELIDIKAN
PPSP

Tajuk geran: An interventive study of the effects of therapeutic lifestyle changes and simvastatin on the insulin sensitivity status of non obese hyperlipidaemic subjects
Penyelidik: Dr Nor Azwany Yaacob
Jenis geran: Geran Penyelidikan Jangka Pendek USM
Tempoh geran: 2 tahun
Jenis laporan: Laporan Kemajuan [ ] Alatan di beli [ ] Ya:nyatakan.....
Laporan Akhir*: [/] [/] Tidak

OBJEKTIF SPESIFIK KAJIAN (sama spt dalam proposal)	**SECARA RINGKAS TERANGKAN PENCAPAIAN/HASIL**	**OBJEKTIF TERCAPAI ATAU TIDAK**
1. To determine effects of- i) therapeutic lifestyle changes (TLC) ii) Simvastatin on insulin sensitivity status of the non-obese-hyperlipidemic subjects.	Effects were shown by improvement of insulin parameters of both groups	Tercapai
2. To compare the insulin sensitivity status of non-obese hyperlipidemic Malay subjects after three months intervention with TLC.	16 out of 28 subjects shows significant improvement in insulin sensitivity status compared to control group	Tercapai
3. To compare insulin sensitivity status of TLC responding hyperlipidemic Malay subjects after 6 months of TLC intervention	Significant improvement in insulin sensitivity status shown by increase in HOMA%S	Tercapai
4. To compare insulin sensitivity status of TLC-non-responding hyperlipidemic Malay subjects after 6 months intervention with TLC and 3 months with Simvastatin.	Insulin sensitivity shows significant improvement among TLC plus simvastatin group after 3 months of TLC and another 3 months with simvastatin intervention shown by increase in HOMA%S	Tercapai
5. To compare insulin sensitivity status of TLC responding hyperlipidemic subjects after 6 months of TLC intervention with that of normolipidemic subjects.	Significant improvement in insulin sensitivity status shown by increase in HOMA%S	Tercapai

- *Laporan Akhir perlu disertakan salinan manuskrip dan surat yang dihantar kepada mana-mana jurnal untuk penerbitan.*

Nama Penyelidik Utama (PI): Dr Nor Azwany Yaacob t.t.:
Tarikh: 5 Oktober 2008

ABSTRACT

Obesity, hyperlipidaemia and insulin resistance are known to have relationship thus making it important to look into the insulin resistance in a group of non-obese hyperlipidaemic subjects. This study was designed to determine insulin sensitivity and secretory status of non-obese normoglycaemic subjects, and to find out the relationship between hyperlipidaemia and insulin sensitivity in a non-obese population. In addition, the second phase of this study looked at the effects of lipid lowering interventions on insulin sensitivity in hyperlipidaemic subjects. A cross sectional study involving 246 non-obese (BMI<25 kg/m^2), waist circumference male<102cm, female <88cm) and non-diabetic subjects aged between 30-60 years was carried out. The subjects underwent OGTT, LFT and RFT to exclude type 2 diabetes, IGT, IFG, renal and liver diseases. Fasting plasma glucose, fasting insulin and lipid profile were measured. Insulin sensitivity and secretory status were computed using the homeostasis model assessment (HOMA) software to obtain HOMA%S, HOMA%B and HOMA-IR. The subjects were divided into two groups according to their lipid status and their insulin sensitivity was compared between the two groups. Two groups of 28 non-obese hyperlipidaemic and 28 normolipidaemic subjects participated in the intervention study. They underwent 3 months of therapeutic lifestyle changes (TLC) regimen after which they were again divided into TLC and Simvastatin groups and for the subsequent three months went through either TLC only or TLC plus Simvastatin. Finally their insulin sensitivity and lipid status were assessed again. The hyperlipidaemic subjects showed substantially lower insulin sensitivity and higher insulin resistance in comparison to normolipidaemic subjects. The adjusted mean of HOMA%S of hyperlipidaemic and normolipidaemic subjects were 80 and 155 ($p<0.0001$) respectively. Insulin secretory status as expressed by the mean of HOMA%B were 178 and 116 for hyperlipidaemic and normolipidaemic subjects respectively. It indicates that the B cells of hyperlipidaemic subjects have to secrete more insulin to overcome the lowered insulin sensitivity. Intervention by both TLC and Simvastatin showed significant reduction of insulin resistance (62.3% improvement of HOMA-IR in TLC group and 51.44% in Simvastatin and TLC group) and improvement of insulin sensitivity (142% improvement of HOMA%S in TLC group and 122% in Simvastatin and TLC group) in hyperlipidaemic subjects with reduction of lipid levels. It can thus be concluded that, insulin sensitivity of otherwise healthy non-obese hyperlipidaemic subjects is lower than normolipidaemic subjects. Therapeutic life style changes is able to improve the insulin sensitivity in this group of subjects.

ABSTRAK

Kerintangan Insulin Bagi Subjek Melayu Tak-Obes Normoglisemic: Kesan Perubahan Gaya Hidup Terapeutik dan Simvastatin

Obesiti, hiperlipidemia dan kerintangan insulin dilaporkan mempunyai kaitan. Maka adalah penting untuk mengkaji kerintangan insulindidalam subjek yang tidak obese dengan hiperlipidemia. Kajian ini bertujuan untuk menentukan sensitiviti insulin dan status perembesan oleh subjek normoglisemik tak-obes dan untuk menentukan hubungkait di antara hiperlipidemia dan sensitiviti insulin di kalangan populasi tak-obes. Di samping itu, fasa kedua dalam kajian ini telah melibatkan perhatian pada kesan intervensi penurunan tahap lipid terhadap sensitiviti insulin di kalangan subjek hiperlipidemia. Satu kajian hirisan lintang terhadap 246 subjek tak-obes (BMI <25 kg/m^2, ukur lilit pinggang lelaki <102 cm, wanita <88 cm) dan bukan diabetik berusia dalam lingkungan 30-60 tahun telah dilakukan. Subjek menjalani OGTT, LFT dan RFT untuk tidak melibatkan pesakit yang diabetes jenis 2, IGT, IFG, renal dan hepar. Glucosa, insulin dan profil lipid plasma puasa ditentukan. Sensitiviti insulin dan status perembesan dikira dengan menggunakan perisian penilaian model homeostasis (HOMA) untuk memperoleh HOMA%S, HOMA%B, dan HOMA-IR. Subjek dibahagikan ke dua kumpulan mengikut status lipid dan sensitiviti insulin dibanding di antara dua kumpulan. Dalam Kajian intervensi, 28 subjek hiperlipidemik tak obes dan 28 normolipidemik mengambil bahagian. Mereka melalui intervensi perubahan gaya hidup (TLC) selama 3 bulan dan selepas itu mereka dibahagikan lagi ke kumpulan TLC dan Simvastatin dan tiga bulan seterusnya melalui TLC sahaja atau gabungan TLC dan Simvastatin. Akhirnya sensitiviti insulin dan status lipid mereka ditentukan semula. Subjek hiperlipidemik menunjukkan tahap sensitiviti insulin rendah dan kerintangan insulin tinggi berbanding dengan subjek normolipidemik. Mean HOMA%S diperbaiki bagi subjek hiperlipidemik dan normolipidemik adalah 80 dan 155 (P<0.001) secara berturutan. Status perembesan insulin yang diekspres melalui mean bagi HOMA%S adalah 178 dan 116 bagi subjek hiperlipidemik dan normolipidemik secara berturutan. Ini menunjukkan sel B bagi subjek ini perlu merembes lebih banyak insulin untuk mengatasi sensitiviti insulin yang menurun. Intervensi oleh kedua-dua TLC dan simvastatin menunjukkan penurunan signifikan kerintangan insulin (kemajuan HOMA-IR sebanyak 62.3% dalam kumpulan TLC dan 51.44% dalam kumpulan simvastatin dan TLC) dan pemulihan sensitiviti insulin (kemajuan HOMA%S sebanyak 142% dalam kumpulan TLC dan 122% dalam kumpulan simvastatin dan TLC) di kalangan subjek hiperlipidemik dengan penurunan tahap lipid. Sebagai kesimpulan, sensitiviti insulin bagi subjek hiperlipidemik tak-obes adalah lebih rendah berbanding normolipidemik.Perubahan gaya hidup terapeutik boleh membantu meningkatkan tahap sensitiviti insulin bagi subjek berkenaan.