UNIVERSITI SAINS MALAYSIA

Short Term Grant

Final Report

Comprehensive Technical Report

Principal Investigator: Dr Gan Siew Hua
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School of Medical Sciences.

Co-investigator: Prof Madya Dr Tan Soo Choon,

Doping Centre, USM, Penang.

March 2009

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:
Name of Research Leader

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

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

Department of Pharmacology, School of Medical Sciences

3. **Nama Penyelidik Bersama:**
Name of Co-Researcher

Assoc. Professor Dr. Tan Soo Choon

4. **Tajuk Projek:** *Title of Project*

Stereoisomer concentrations of amphetamine, amphetamine derivatives and metabolites in saliva and urine in comparison with blood plasma levels utilizing a validated stereoselective gas chromatography ion-trap mass spectrometry assay

5. Ringkasan Penilaian/*Summary of Assessment*	Tidak Memuaskan/ *Unsatisfactory*		Baik/ *Satisfactory*	Sangat Baik/ *Very Good*	
	1	2	3	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)

Appended separately

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)

Appended separately

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

Bahasa Malaysia	*Bahasa Inggeris*
stimulan jenis amfetamina	amphetamine-type stimulants
spektrografi gas – spektroskopi jisim	gas chromatography – mass spectrometry
analisa stereospesifik	stereospecific assay

8. Output dan Faedah Projek
Output and Benefits of Project

(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)

1. WAN AASIM W.A. [illegible] (2008). Development of a simultaneous liquid-liquid extraction and chiral derivatization method for stereospecific GC-MS analysis of amphetamine-type stimulants in human urine using fractional factorial design. *Biomedical Chromatography* 22, 1035-1042 (Impact factor [illegible])
2. Wan Raihana W.A. [illegible] (2008). A rapid method for stereoselective analysis of amphetamine-type stimulants using simultaneous liquid-liquid extraction and chiral derivatization. Drug Metabolism Reviews 40 (S[illegible]) [illegible] (Impact factor 6.238)

(b) **Faedah-faedah lain seperti perkembangan produk, penggunaan/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.

This research successfully developed a novel technique for sensitive and selective simultaneous extraction and derivatization of illicit amphetamine-type stimulants. The method is also applicable to future studies that involves stereoselective metabolism.

* Sila berikan salinan/*Kindly provide copies*

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

i) Pelajar Sarjana:
Graduate Students
(Berikan nama, ijazah dan status)
(Provide names, degrees and status)

Wan Rosliana binti Wan Aasim, PhD (Pharmacology)

ii) Lain-lain:
Others

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

TIADA

12 Mac 2009

Tandatangan Penyelidik
Signature of Researcher

Tarikh
Date

DR. GAN SIEW HUA
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School of Medical Sciences
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16150 Kubang Kerian, Kelantan.

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

This short term research project has been successfully completed with excellent output.

Beside human resource development and novel technique development the project has produced two publications with a cummulative Impact factor of 7.848.

This is an exemplary effort and the medical school congratulate the team for their success.

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

15/12/09
Tarikh
Date

Abstract

Amphetamine-type stimulants (ATS) are a family of drugs classified as entactogens which posses both stimulant and hallucinogenic properties. Abuse of ATS is an increasingly serious problem worldwide. The abuse of ATS results in several negative side-effects including hyperthermia, elevated heart rate and blood pressure, delirium and psychotic behavior. Long-term abuse leads to extensive hepatotoxicity and neurotoxicity. ATS are chiral molecules and metabolism of these drugs exhibits significant stereoselectivity. It has been shown that each individual ATS enantiomer exhibits a unique pharmacokinetic and pharmacodynamic profile. In this study, a novel assay for sensitive and selective stereospecific determination of amphetamine-type stimulants was developed. The assay involves a simultaneous extraction and chiral derivatization step followed by analysis by gas chromatography-mass spectrometry. THis resulted in an assay that was rapid and simple to perform. Using an fractional factorial experimental design approach, the method was optimized and validated. The method was applied to samples from known ATS abusers and the stereoselectivity for the elimination of ATS in biological samples was characterized. This study resulted in a novel method for the determination of ATS in biological samples, which will be applied in further studies on the stereoselective metabolism of ATS.

Abstrak

Stimulan jenis amfetamina (SJA) merupakan sekumpulan dadah yang diklasifikasikan sebagai entaktogen iaitu mempunyai sifat stimulan dan juga halusinogenik. Penyalahgunaan SJA merupakan suatu masalah yang bertambah serius di seluruh dunia. Penggunaan SJA membawa kepada pelbagai kesan sampingan negatif seperti hiperthermia, kadar degupan jantung dan tekanan darah yang tinggi, delirium dan tingkahlaku psikotik. Penyalahgunaan dadah SJA dalam jangkamasa panjang boleh mengakibatkan kesan toksik yang meluas pada hati dan otak. SJA adalah molekul kiral dan metabolismanya adalah secara stereoselektif. Setiap enantiomer SJA menunjukkan profil farmakokinetik dan farmakodinamik yang tersendiri. Dalam kajian ini, suatu kaedah baru yang sensitif dan selektif untuk penentuan stereoselektif bagi SJA telah dibangunkan. Kaedah ini melibatkan pengekstrakan dan langkah penerbitan kiral yang dijalankan secara serentak dan diikuti dengan analisis menggunakan kromatografi gas – spektrometri jisim. Teknik ini menghasilkan suatu kaedah analisa yang pantas dan mudah untuk dijalankan. Dengan menggunakan pendekatan rekabentuk eksperimen secara pecahan faktorial, kaedah ini telah dioptimumkan dan disahkan. Kaedah ini telah digunakan untuk menganalisa sampel-sampel yang diperolehi daripada penyalahguna dadah SJA. Berikutan ini, stereoselektiviti penyingkiran SJA di dalam sampel biologikal telah ditentukan. Kajian ini telah berjaya menghasilkan suatu kaedah baru bagi penentuan secara stereoselektif bagi SJA dalam sampel biologikal yang akan diaplikasikan dalam kajian akan datang yang berkaitan dengan metabolisma SJA.