



MINGGU PENYELIDIKAN PERUBATAN DAN KESIHATAN KE -14

16 - 20 JULAI 2012

AUDITORIUM

Kompleks Pendidikan Perubatan
Canselor Tuanku Ja'afar UKM
Cheras

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PENGENALAN

Minggu Penyelidikan ini telah dianjurkan sejak tahun 1999. Ia melibatkan Fakulti Perubatan, Fakulti Pergigian, Fakulti Sains Kesihatan, Fakulti Farmasi dan Institut Perubatan Molekul (UMBI) UKM. Minggu ini merupakan minggu di mana ketrampilan penyelidikan, prasarana dan suasana penyelidikan di fakulti dilihat, dalam usaha untuk meningkatkan pencapaian dalam dunia penyelidikan, latihan dalam kaedah dan pengurusan penyelidikan selain daripada mengukuhkan hubungan antara fakulti di kampus kesihatan UKM.

OBJEKTIF

- Memaparkan sebahagian daripada hasil penyelidikan.
- Menemukan para penyelidik bagi merangsangkan minda dan menambahkan pemikiran untuk menghasilkan lebih banyak idea dan kolaborasi penyelidikan.
- Meningkatkan pembudayaan dan aktiviti penyelidikan di Fakulti Perubatan.

**KATA ALU-ALUAN
DEKAN FAKULTI PERUBATAN & PENGARAH PUSAT PERUBATAN
UNIVERSITI KEBANGSAAN MALAYSIA**

Assalamualaikum Warahmatullahi Wabarakatuh dan Salam Sejahtera

Alhamdulillah, syukur ke hadrat Allah SWT, Minggu Penyelidikan Perubatan & Kesihatan kali ke-14 dapat diadakan dengan jayanya. Tahniah dan syabas kepada Pusat Perubatan Universiti Kebangsaan Malaysia, Fakulti Sains Kesihatan, Fakulti Pergigian, Fakulti Farmasi serta Institut Perubatan Molekul UKM (UMBI) di atas kerjasama yang murni ini. Ini merupakan tahun ke-14 aktiviti tahunan ini diadakan dan saya percaya ianya amat menepati misi dan objektif UKM dalam menghasilkan lebih banyak penyelidikan yang membanggakan yang boleh membawa UKM hingga ke persada antarabangsa.

Kerjasama yang telah terjalin harus diteruskan agar menjadi satu pemangkin kepada kecemerlangan penyelidikan. Apa juga jenis penyelidikan sama ada dalam bidang perubatan, kesihatan, pergigian, farmasi mahupun dalam bidang molekul, ianya harus merupakan kaedah paling berkesan untuk menghasilkan pengetahuan baru atau untuk mengisi jurang-jurang ilmu yang akan memberi manfaat kepada manusia sejagat serta memberi sumbangan yang tidak ternilai kepada pembangunan insan dan negara.

Saya yakin program ini dapat mencetuskan idea bagi menambah siri penyelidikan cemerlang dalam suasana persekitaran akademik yang mendorong dan mendukung ke arah penyelidikan yang kreatif dan inovatif. Saya berharap usaha ini akan dimanfaatkan oleh semua peserta terutamanya oleh semua pascasiswazah dalam mendalami ilmu penyelidikan.

Akhir kata, tahniah kepada jawatankuasa bengkel dan semua yang terlibat dalam program ini dan saya amat menghargai usaha yang dilakukan dan berharap usaha sebegini dapat diteruskan pada masa hadapan.

Sekian, terima kasih.



PROFESOR DATO' DR RAYMOND AZMAN ALI
Dekan Fakulti Perubatan
& Pengarah Pusat Perubatan
Universiti Kebangsaan Malaysia

**KATA ALU-ALUAN
PENGARAH INSTITUT PERUBATAN MOLEKUL (UMBI)
UNIVERSITI KEBANGSAAN MALAYSIA**

Assalamualaikum Warahmatullahi Wabarakatuh dan Salam Sejahtera

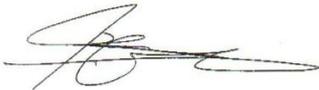
Saya ingin mengucapkan tahniah kepada jawatankuasa penganjur Minggu Penyelidikan Perubatan dan Kesihatan ke-14 atas kejayaan menganjurkan program ini. Kerjasama Fakulti Perubatan dengan Fakulti Sains Kesihatan, Fakulti Pergigian, Fakulti Farmasi dan UMBI mencerminkan semangat keserakanan penyelidikan yang semakin mantap.

Nic Teknologi Kesihatan dan Perubatan (TKP) terus bergerak melalui kelompok dan kumpulan penyelidikan serta menekankan *output* penyelidikan dalam bentuk penerbitan berimpak serta produk yang berpotensi untuk dikomersialkan. Program ini menyediakan peluang untuk para penyelidik memaparkan hasil penyelidikan mereka serta berkongsi idea dan pengalaman bagi merealisasikan potensi yang ada dalam nic TKP ini.

Penyelidikan perubatan dan kesihatan masa kini telah menjadi lebih mencabar dengan peningkatan prevalens penyakit kronik serta penyakit yang disebabkan gaya hidup yang tidak sihat. Fokus penyelidikan seharusnya menjurus kepada impak maksimum terhadap perubahan status kesihatan komuniti. Teknologi canggih dalam era perubatan genomik ini harus digembeling sepenuhnya supaya kita terus menjadi relevan. Justeru, para penyelidik harus sentiasa mengikuti perkembangan terbaru dalam dunia sains perubatan dan kesihatan.

Saya berharap peserta akan memanfaatkan program ini dengan sepenuhnya.

Sekian, terima kasih.



PROFESOR DATUK DR. A RAHMAN A JAMAL
Pengaroh
Institut Perubatan Molekul UKM (UMBI)

**KATA ALU-ALUAN
DEKAN FAKULTI SAINS KESIHATAN
UNIVERSITI KEBANGSAAN MALAYSIA**

Assalamualaikum Warahmatullahi Wabarakatuh dan Salam Sejahtera

Alhamdulillah, bersyukur saya ke hadrat Illahi kerana dengan limpah kurnianya, sekali lagi Fakulti Sains Kesihatan bersama-sama Fakulti Farmasi, Fakulti Pergigian, Institut Perubatan Molekul UKM (UMBI) dan Pusat Perubatan UKM dapat menganjurkan Minggu Penyelidikan Perubatan & Kesihatan yang ke-14 ini. Dalam era yang serba kompetitif ini, pencapaian dalam aspek penyelidikan telah menjadi ukuran bagi kecemerlangan sesebuah institusi pengajian tinggi. Oleh yang demikian, penekanan harus diberi sebaiknya kepada semua warga UKM amnya dan Gugusan Kesihatan khususnya untuk menuju ke arah penyelidikan bertaraf antarabangsa.

Saya amat berharap program ini mampu mencetuskan idea-idea baru dalam menghasilkan produk inovasi yang boleh dikomersialkan bagi penjenamaan semula serta meningkatkan kemahiran para penyelidik dalam memaparkan hasil-hasil penyelidikan yang bermutu sekaligus menyemarakkan budaya penyelidikan.

Akhir kata, saya ucapkan tahniah kepada semua yang terlibat dalam menjayakan program ini. Semoga Minggu Penyelidikan Perubatan & Kesihatan ini dapat diadakan secara berterusan bagi memberi manfaat kepada setiap warga UKM sama ada Gugusan Kesihatan ataupun di Fakulti dan Institut yang lain.

Sekian, terima kasih.



PROFESOR DR SALMAAN HUSSAIN INAYAT HUSSAIN
Dekan Fakulti Sains Kesihatan
Universiti Kebangsaan Malaysia

**KATA ALU-ALUAN
DEKAN FAKULTI PERGIGIAN
UNIVERSITI KEBANGSAAN MALAYSIA**

Assalamualaikum Warahmatullahi Wabarakatuh dan Salam Sejahtera

Sepertimana yang sedia maklum, objektif Bengkel Minggu Penyelidikan ini adalah satu aktiviti untuk meningkatkan kemahiran dan membudayakan aktiviti penyelidikan didalam pengajaran dan pembelajaran. Ia bertujuan membolehkan para peserta menambah ilmu pengetahuan serta berpeluang berkongsi hasil penyelidikan masing-masing. Adalah diharapkan agar penyelidikan yang dijalankan adalah bermutu tinggi dan hasilnya nanti dapat diterbitkan di jurnal yang diiktiraf.

Saya ingin mengucapkan syabas dan tahniah kepada Jawatankuasa dan Urusetia Minggu Penyelidikan Perubatan & Kesihatan pada tahun ini, yang telah berusaha untuk menjayakan program tahunan ini.

Saya berharap agar kita semua dapat memanfaatkan pengetahuan yang diperolehi melalui Minggu Penyelidikan ini dan seterusnya merealisasikan lagi UKM sebagai Universiti penyelidikan.

Terima kasih



PROFESOR DATO' DR. GHAZALI MAT NOR
Dekan Fakulti Pergigian
Universiti Kebangsaan Malaysia

**KATA ALU-ALUAN
DEKAN FAKULTI FARMASI
UNIVERSITI KEBANGSAAN MALAYSIA**

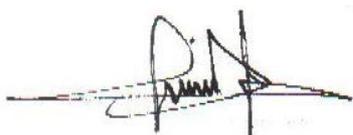
Assalamualaikum Warahmatullahi Wabarakatuh dan Salam Sejahtera

Alhamdulillah, bersyukur saya ke hadrat Allah S.W.T. kerana dengan izin, limpah dan kurnia-Nya jua dapat saya menyampaikan sepatah dua kata-kata aluan sempena Minggu Penyelidikan Perubatan & Kesihatan Ke-14 pada kali ini.

Tahniah dan syabas diucapkan kepada Jawatankuasa Induk Minggu Penyelidikan Perubatan & Kesihatan Ke-14 kerana sekali lagi telah berjaya menganjurkannya pada tahun ini. Sepertimana lazimnya, program ini adalah merupakan program tahunan yang melibatkan penyelidikan di bawah empat fakulti yang berpayung di bawah Gugusan Sains Kesihatan. Gugusan ini pula diletakkan di bawah NIC Teknologi Perubatan & Kesihatan yang merupakan salah satu daripada 7 NIC penyelidikan yang telah dikenalpasti di UKM. Kesemua kumpulan penyelidikan daripada keempat-empat fakulti ini berkumpul pada hari tersebut untuk mempamerkan kekuatan dan penemuan-penemuan terbaru dalam bidang penyelidikan masing-masing.

Akhir kata, saya sekali lagi bagi pihak seluruh warga Fakulti Farmasi mengucapkan syabas dan tahniah kepada Jawatankuasa Induk Minggu Penyelidikan Perubatan & Kesihatan Ke-14 kerana telah berjaya menganjurkan program ini.

Sekian, terima kasih.



PROFESOR DR. IBRAHIM JANTAN
Dekan Fakulti Farmasi
Universiti Kebangsaan Malaysia

**KATA ALU-ALUAN
PENGERUSI
MINGGU PENYELIDIKAN PERUBATAN & KESIHATAN KE-14
PUSAT PERUBATAN UNIVERSITI KEBANGSAAN MALAYSIA**

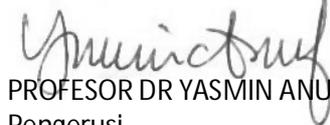
Assalamualaikum Warahmatullahi Wabarakatuh dan Salam Sejahtera

Syukur ke hadrat Ilahi kerana dengan limpah kurniaNya maka sekali lagi Minggu Penyelidikan Perubatan & Kesihatan ke-14 (MP14) dapat diadakan pada tahun ini. MP14 ini adalah merupakan salah satu agenda tahunan yang penting dalam kalendar aktiviti di Pusat Perubatan UKM dan ianya sentiasa mendapat penyertaan dari pelajar UKM mahupun dari luar UKM yang sangat memberangsangkan. Program ini adalah satu aktiviti dalam mencerap budaya penyelidikan selaras dengan wawasan Universiti kita sebagai memastikan UKM terus menjadi Universiti Penyelidikan seiring dengan universiti yang lain. Objektif bengkel seperti ini bertujuan membolehkan para peserta meningkatkan pengetahuan dan memantapkan ilmu penyelidikan agar metodologi yang digunakan adalah bermutu tinggi bertaraf antarabangsa di samping memenuhi keperluan etika di mana hasilnya nanti dapat diterbitkan dalam jurnal-jurnal berimpak tinggi serta mampu menghasilkan suatu produk yang boleh dikomersialkan.

Di kesempatan ini, saya ingin merakamkan setinggi-tinggi penghargaan kepada Dekan Fakulti Perubatan & Pengarah Pusat Perubatan UKM, Y. Bhg Profesor Dato' Dr Raymond Azman Ali dan Y. Bhg. Profesor Dr. Musalmah Mazlan, Timbalan Dekan (Penyelidikan & Inovasi), selaku penasihat Minggu Penyelidikan Ke-14, Dekan-Dekan daripada Fakulti Sains Kesihatan, Fakulti Pergigian, Fakulti Farmasi dan Pengarah UMBI serta pihak pengurusan atas sokongan yang telah diberikan dalam menjayakan Minggu Penyelidikan Ke-14 ini. Penghargaan khusus juga buat para penceramah dan fasilitator di atas keikhlasan meluangkan masa untuk berkongsi ilmu dan juga kepada para peserta di atas kesudian kalian meluangkan masa untuk turut serta menjayakan Minggu Penyelidikan ini. Seterusnya ucapan ribuan terima kasih yang tidak terhingga dan tahniah kepada semua Ahli jawatankuasa, pihak urusetia dan individu-individu yang terlibat secara langsung mahupun tidak langsung dalam memastikan kejayaan dan kelancaran Minggu Penyelidikan ini.

Saya berharap agar kita semua dapat memanfaatkan dan seterusnya mempraktikkan pengetahuan yang diperolehi melalui Minggu Penyelidikan ke-14 ini, dalam usaha meningkatkan kualiti penyelidikan yang beretika, cemerlang dan seterusnya diiktiraf di peringkat global. Saya percaya dengan izin Allah dan kerjasama kita semua, InsyaAllah objektif Minggu Penyelidikan ini dapat dicapai dengan jayanya.

Terima kasih.



PROFESOR DR YASMIN ANUM MOHD YUSOF

Pengerusi

Minggu Penyelidikan Perubatan & Kesihatan ke-14
Pusat Perubatan Universiti Kebangsaan Malaysia

JAWATANKUASA PENGANJUR & URUSETIA MINGGU PENYELIDIKAN KE-14

Penasihat: Profesor Dato' Dr Raymond Azman Ali (Dekan Fakulti Perubatan & Pengarah Pusat Perubatan UKM)
Profesor Datuk Dr A. Rahman A. Jamal (Pengarah Institut Perubatan Molekul, UMBI)
Profesor Dr Salmaan Hussain Inayat Hussain (Dekan Fakulti Sains Kesihatan Bersekutu)
Profesor Dato' Dr Ghazali Mat Nor (Dekan Fakulti Pergigian)
Profesor Dr Ibrahim Jantan (Dekan Fakulti Farmasi)
Profesor Dr Musalmah Mazlan (Timbalan Dekan, Penyelidikan & Inovasi)

Pengerusi: Profesor Dr Yasmin Anum Mohd Yusof
Jabatan Biokimia
Pusat Perubatan UKM

Ahli Jawatankuasa Penganjur Minggu Penyelidikan ke-14:

- Profesor Madya Dr Mohd Rizal Abdul Manaf
Jabatan Kesihatan Masyarakat
Pusat Perubatan UKM
- Profesor Madya Dr Sabarul Afian Mokhtar
Jabatan Ortopedik
Pusat Perubatan UKM
- Profesor Madya Dr Ahmad Nazrun Shuid
Jabatan Farmakologi
Pusat Perubatan UKM
- Profesor Madya Dr Azmi Mohd Tamil
Jabatan Kesihatan Masyarakat
Pusat Perubatan UKM
- Dr Petrick @ Ramesh A/L K Periyasamy
Jabatan Perubatan
Pusat Perubatan UKM
- Dr Jemaima Che Hamzah
Jabatan Oftalmologi
Pusat Perubatan UKM
- Dr Isa Naina Mohamed
Jabatan Farmakologi
Pusat Perubatan UKM
- Dr Goon Jo Aan
Jabatan Biokimia
Pusat Perubatan UKM
- Profesor Madya Dr Norfilza M. Mokhtar
Institut Perubatan Molekul (UMBI)
Pusat Perubatan UKM
- Prof esorMadya Dr Rohaya Megat Abdul Wahab
Jabatan Ortodontik
Fakulti Pergigian
UKM
- Profesor Madya Dr Siti Balkis Budin
Jabatan Sains Bioperubatan
Fakulti Sains Kesihatan
UKM
- Dr Malina Jasamai
Fakulti Farmasi
UKM

Urusetia:

- Sekretariat Penyelidikan Perubatan & Inovasi
- Jabatan Perhubungan Awam
- Jabatan Multimedia & Penyiaran
- Jabatan Pengurusan Bangunan
- Jabatan Keselamatan
- Jabatan Teknologi Maklumat

PENCERAMAH-PENCERAMAH JEMPUTAN

Profesor Dr Musalmah Mazlan

Profesor Dr Rahimah Abdul Kadir

Profesor Dr Zarina Abdul Latiff

Profesor Dr Baharudin Omar

Profesor Dr Nor Azmi Kamaruddin

Profesor Madya Dr Roslan Harun

Profesor Madya Dato' Dr Fuad Ismail

Profesor Madya Dr Shamsul Azhar Shah

Profesor Madya Dr Mohd Hasni Jaafar

Profesor Madya Dr Sabarul Afian Mokhtar

Profesor Madya Dr Mohd Cairul Iqbal Mohd Amin

Profesor Madya Dr Rahmah Mohd Amin

Profesor Madya Dr Mohd Rizal Abdul Manaf

Profesor Madya Dr Azmi Mohd Tamil

Dr Azmawati Mohammed Nawi

Dr Norfazilah Ahmad

FASILITATOR-FASILITATOR JEMPUTAN

BIL	NAMA	JABATAN	NO. KUMPULAN	LOKASI DISKUSI
1	Dr Norzana Abd. Ghafar	Anatomi	1	Bilik Kuliah 1, Jabatan Kesihatan Masyarakat, Tingkat 1 Blok Klinikal
2	Dr Azimatun Noor Aizuddin	Kesihatan Masyarakat		
3	Prof. Madya Dr Goh Bee See	Otorinolaringologi	2	Bilik Kuliah 2, Jabatan Kesihatan Masyarakat, Tingkat 1 Blok Klinikal
4	Dr Khin Pa Pa Hlaing @ Farida Hussan	Anatomi		
5	Prof. Madya Dr Kanaheswari a/p Yoganathan	Pediatrik	3	Bilik Siswazah Lanjutan, Jabatan Anaesthesiologi, Tingkat 2, Blok Pendidikan
6	Dr Goon Jo Aan	Biokimia		
7	Dr Zakiah Jubri	Biokimia	4	Bilik Mesyuarat, Sekretariat Penyelidikan Perubatan & Inovasi, Tingkat 1, Blok Klinikal
8	Dr Rizuana Iqbal Hussein	Radiologi		
9	Prof. Madya Dr Abdul Halim Abd. Rashid	Ortopedik	5	Bilik DKSP, Jabatan Kesihatan Masyarakat, Tingkat 1 Blok Klinikal
10	Dr Qodriyah Hj Mohd Saad	Farmakologi		
11	Dr Shamsuriani Md Jamal	Perubatan Kecemasan	6	Bilik Mesyuarat, Jabatan Perubatan Kecemasan, Aras Bawah, Blok Klinikal
12	Dr Isa bin Naina Mohamed	Farmakologi		
13	Profesor Madya Dr. Azlin Baharudin	Psikiatri	7	Bilik Monitor, Wad Penyelidikan Klinikal, Tingkat 1, Blok Klinikal
14	Dr Siti Fatimah Ibrahim	Fisiologi		
15	Dr Mohamad Radzniwan A. Rashid	Perubatan Keluarga	8	Bilik Kuliah 1, Jabatan Kejururawatan, Tingkat 5, Blok Pendidikan
16	Prof. Madya Ho Siew Eng	Kejururawatan		
17	Prof. Madya Raja Lexshimi Raja Gopal	Kejururawatan	9	Bilik Kuliah 2, Jabatan Kejururawatan, Tingkat 5, Blok Pendidikan
18	Prof. Madya Dr Shareena Ishak	Pediatrik		

19	Ran Santhara Pradagam	Kéjuurawatan	10	Bilik Kuliah 3, Jabatan Kéjuurawatan, Tingket 5 Bok Perodden
20	D/Anavati Mohamed Navv	Kesihatan Masyarakat		
21	Prof. Maja D/Abul Halim Abul Gafur	Perubatan	11	Bilik Tjangan, Perpustakaan, Tingket 3, Bok Perodden
22	D/Azirah Zaham	Anastesidologi		
23	D/Rafiah Aklan	FSK	12	Bilik Mesyuarat, Jabatan Maklumat Kesihatan, Basement, Bok Klinik
24	D/Uhrikom @ Sarah Ali	Mikrobiologi & Imunologi Perubatan		
25	D/Zairah Nail	Mikrobiologi & Imunologi Perubatan	13	Bilik Mesyuarat, Perpustakaan, Tingket 3, Bok Perodden
26	Prof. Maja D/Amad Zain Shaban	FSK		
27	D/Abul Karim Abul Karim	Ostetrik & Ginekologi	14	Dewan Penyelidikan, Tingket 4, Bok Perodden
28	D/Zahirah Zairah Aich	Fakulti Perguruan		
29	D/Muhammad Saif	Ostetrik & Ginekologi	15	Bilik Seminar, Jabatan Patologi, Basement, Bok Klinik
30	D/Noh Hui Min	UNB		
31	D/Ghazalza Ghman	Otoridologi	16	Bilik Kuliah 4, Jabatan Kéjuurawatan, Tingket 5 Bok Perodden
32	Prof. Maja D/Salinar Abdullah	Otoridologi		
33	Prof. Maja D/Muhammad Akbar Bakry	Fakulti Farmasi	17	Dewan Penyelidikan, Tingket 4, Bok Perodden
34	Prof. Maja D/Muhammad Akbar Bakry	Patologi		
35	D/Amad Farid Salan	Fakulti Perguruan		
36	D/Tan Chai Eng	Perubatan Keluarga	18	Bilik Tutorial, Jabatan Patologi, Atas Basah, Bok Klinik
37	Prof. Maja D/Rhiana Abul Gari	Perubatan		
38	Prof. D/Phong Bekon	FSK		

39	Dr. Agus Slam	Pendidikan Perubatan	19	Etilikseminar, Jabatan Pendidikan Perubatan Atas Bawah, Blok Pendidikan
40	Profesor Madya Dr. Susan Tan	Psikiatri		
41	Dr. Saifiah M. Athidus Athasi	Radologi		
42	Dr. Zuhari Ghman	UMB	20	Etilik Mesyuarat, Institut Perubatan Molekul (UMB), Tingkat 7, Blok Klinikal
43	Prof. Madya Dr. Christopher H. Cheek Kong	Surgei		
44	Dr. Ching Hong	Surgei		

PROGRAM SEPANJANG MINGGU PENYELIDIKAN PERUBATAN & KESIHATAN KE-14

TARIKH	MASA	AKTIVITI	TEMPAT
16 Jul 2012 (ISNIN)	0800 – 0830	Pendaftaran	Auditorium
	0830 - 1030	Majlis Perasmian Ketibaan Tetamu Jemputan Ketibaan Dekan & Pengarah PPUKM Bacaan Doa <ul style="list-style-type: none"> • Ucapan oleh Pengerusi Minggu Penyelidikan 14 • Ucapan oleh Dekan & Pengarah PPUKM • Tokoh Penyelidik – Profesor Dato' Dr Raymond Azman Ali Penyampaian Cenderahati Sesi Bergambar	Auditorium
	1030 – 1100	Minum Pagi / Pengadil Poster	Foyer Blok Pendidikan
	PAGI	PENGERUSI: Profesor Madya Dr Mohd Rizal Abd Manaf	
	1100 – 1145	Concepts of Research University – The Present Status oleh Profesor Dr Musalmah Mazlan	Auditorium
	1145 – 1230	Ethics in Clinical Research oleh Profesor Madya Dato' Dr Fuad Ismail	Auditorium
	1230 – 1400	Makan Tengahari/ Solat / <i>Viewing</i> Poster	Foyer Blok Pendidikan
	PETANG	PENGERUSI: Profesor Madya Dr Ahmad Nazrun Shuid	
	1400 – 1445	Developing & Submitting a Project Proposal oleh Profesor Madya Dr Sabarul Afian Mokhtar	Auditorium
	1445 – 1530	Designing, Validating & Pre-Testing A Questionnaire oleh Dr Azmawati Mohammed Nawi	Auditorium
	1530 – 1545	Taklimat Kerja Kumpulan	Auditorium
	1545 – 1630	Sesi Pengenalan dan Suai Kenal dalam Kumpulan (Semua Fasilitator)	Bilik-bilik Kumpulan
	1630 – 1700	Minum Petang	Foyer Blok Pendidikan

TARIKH	MASA	AKTIVITI	TEMPAT
17 Jul 2012 (SELASA)	PAGI	PENGERUSI: Profesor Madya Dr Rohaya Megat Abd Wahab	
	0800 – 0840	Cross Sectional Study oleh Profesor Madya Dr Mohd Hasni Jaafar	Auditorium
	0840 – 0920	Case-Control Study oleh Profesor Madya Dr Shamsul Azhar Shah	Auditorium
	0920 – 1000	Cohort Study oleh Profesor Madya Dr Shamsul Azhar Shah	Auditorium
	1030 – 1100	Minum Pagi	Foyer Blok Pendidikan
	1100 – 1145	Sample Size Calculation oleh Profesor Madya Dr Azmi Mohd Tamil	Auditorium
	1145 – 1230	Meta Analysis oleh Profesor Madya Dr Roslan Harun	Auditorium
	1230 – 1400	Makan Tengahari/ Solat / <i>Viewing</i> Poster	Foyer Blok Pendidikan
	PETANG	PENGERUSI: Profesor Madya Dr Siti Balkis Budin	
	1400 – 1445	Avoiding & Controlling for Biases oleh Profesor Dr Rahimah Abdul Kadir	Auditorium
	1445 – 1530	Clinical Disagreement and The Kappa oleh Dr Norfazilah Ahmad	Auditorium
	1530 – 1550	Critical Appraisal I (Semua Fasilitator)	Bilik-bilik Kumpulan
	1550 – 1630	Perbincangan Proposal (Semua Fasilitator)	Bilik-bilik Kumpulan
	1630 – 1700	Minum Petang	Foyer Blok Pendidikan

TARIKH	MASA	AKTIVITI	TEMPAT
18 Jul 2012 (RABU)	0800 – 0930	Clinical Pathological Conference	
	PAGI	PENGERUSI: Profesor Madya Dr Azmi Mohd Tamil	Auditorium
	0930 – 1030	Clinical Trial oleh Profesor Dr Nor Azmi Kamaruddin	Auditorium
	1030 – 1100	Minum Pagi	Foyer Blok Pendidikan
	1100 – 1145	Screening in Clinical Research oleh Profesor Dr Zarina Abdul Latiff	Auditorium
	1145 – 1230	Sampling Method oleh Profesor Madya Dr Azmi Mohd Tamil	Auditorium
	1230 – 1400	Makan Tengahari/ Solat / <i>Viewing</i> Poster	Auditorium
	PETANG	PENGERUSI: Dr Malina Jasamai	
	1400 – 1445	Manuscript Writing oleh Profesor Madya Dr Mohd Cairul Iqbal Mohd Amin	Auditorium
	1445 – 1530	Qualitative Research & Analysis oleh Profesor Madya Dr Rahmah Mohd Amin	Auditorium
	1530 – 1550	Critical Appraisal II (Semua Fasilitator)	Bilik-bilik Kumpulan
	1550 – 1630	Perbincangan Proposal (Semua Fasilitator)	Bilik-bilik Kumpulan
	1630 – 1700	Minum Petang	Foyer Blok Pendidikan

TARIKH	MASA	AKTIVITI	TEMPAT
19 Jul 2012 (KHAMIS)	PAGI	PENGERUSI: Profesor Madya Dr Azmi Mohd Tamil	
	0800 – 0900	Statistic I: Data Collection & Handling oleh Profesor Madya Dr Azmi Mohd Tamil	Auditorium
	0900 – 1000	Statistic II: Testing Hypothesis oleh Profesor Madya Dr Azmi Mohd Tamil	Auditorium
	1000 – 1030	Minum Pagi	Foyer Blok Pendidikan
	1030 – 1130	Statistic III: Chi-Square Test oleh Profesor Madya Dr Mohd Rizal Abdul Manaf	Auditorium
	1130 – 1230	Statistic IV: t test and ANOVA oleh Profesor Madya Dr Mohd Rizal Abdul Manaf	Auditorium
	1230 – 1400	Makan Tengahari/ Solat / <i>Viewing</i> Poster	Foyer Blok Pendidikan
	PETANG	PENGERUSI: Profesor Madya Dr Sabarul Afian Mokhtar	
	1400 – 1445	Statistic V: Correlation and regression oleh Dr Norfazilah Ahmad	Auditorium
	1445 – 1530	Statistic VII: Non-Parametric Tests oleh Profesor Dr Baharudin Omar	Auditorium
	1530 - 1550	Critical Appraisal III (Semua Fasilitator)	Bilik-bilik Kumpulan
	1550 - 1630	Perbincangan Proposal (Semua Fasilitator)	Bilik-bilik Kumpulan
	1630 – 1700	Minum Petang	Foyer Blok Pendidikan

TARIKH	MASA	AKTIVITI	TEMPAT
20 Jul 2012 (JUMAAT)		PENGERUSI: Profesor Madya Dr Norfilza Mokhtar	
	0800 – 1000	Pembentangan Proposal Kumpulan	Auditorium
	1030 – 1100	Minum Pagi	Foyer Blok Pendidikan
	1100 – 1200	Pembentangan Proposal Kumpulan - Sambungan	Auditorium
	1200 – 1230	Penyampaian Hadiah dan Penutup	Auditorium

Abstrak (kategori klinikal)

PATTERN OF UPPER LIMBS MUSCLE STRENGTH IN PATIENT WITH UNILATERAL SACRAL ILIAC JOINT (SIJ) INSTABILITY

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Introduction: The sacroiliac joint (SIJ) joins the sacrum to the pelvis and it is essential for stability. Dysfunction of SIJ can cause low back pain and/or leg pain since greater burden is placed on SIJ ligaments during activities that involve the distribution of weight between the upper limbs and lower limbs. This study was aimed at evaluating whether instability of SIJ may affect upper limbs function and contribute to the shoulder dysfunction.

Methods: The study design used is a cross sectional study consisting of 31 subjects with mean age of ± 39.39 ; 16 (52%) males and 15 (48%) females. Subjects with positive hip flexion test (Gillet test) were considered to have SIJ instability. Explanation was given to the subjects about procedures to perform task prone hip extension with shoulder external rotation and the placement of hand-held dynamometer. In order to get accurate results, all the qualified subjects are requested to complete the task with 3 repetitions. The mean Wilcoxon rank test was used to find the relationship between upper limbs muscles strength with affected and non affected SI joints.

Results: The results showed significant differences in affected and non affected SIJ with $p < 0.001$ with upper limb muscle strength. There were significant differences between affected SIJ (4.9355) and muscle strength of upper limb versus non affected SIJ (3.6129).

Conclusion: In conclusion, the SIJ dysfunction will affect the upper limbs muscle strength while performing the assigned task using upper limb.

COMPARISON BETWEEN HOME-BASED AND HOSPITAL-BASED PULMONARY REHABILITATION PROGRAMME AMONG CHRONIC LUNG DISEASES PATIENTS

^aCF Ng, ^aR Ayiesah

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Introduction: Pulmonary rehabilitation is still considered new in Malaysia and is usually carried out in hospital setting for patients suffering from Chronic Lung Disease (CLD). Recently the direction of the rehabilitation had switched from traditionally hospital-based to home-based or community-based programme due to overcrowding and increment of patient visit to hospitals. This study investigates and compares the effect of hospital based (HsPR) rehabilitation compare to Home Based (HmPR) for exercise tolerance, dyspnoea coping and Quality of Life (QoL).

Methods: 20 subjects was involved in the study with 11 subjects in HbPR and 9 subjects in HsPR. Both groups underwent a 6-week programme. The HmPR consists of home visit twice, exercise training, telephone call each weeks and patient education while HsPR patients underwent the usual routine of exercise in the physiotherapy department.

Results: Findings showed significant ($p < 0.05$) improvement in 6 minute walking test distance and QoL using St George Respiratory Questionnaire. For HsPR, improvement was observed in QoL (using COPD assessment test (CAT)) as well as on domains of SGRQ impact ($p = 0.016$, $p < 0.05$) and total score ($p = 0.011$, $p < 0.05$). In both settings, no significant improvement in dyspnoea coping was seen. All the groups show significant improvement clinically.

Conclusion: HmPR and HsPR showed improvement in QoL but the improvement in exercise tolerance was better in HmPR. Clinically there were improvements shown in both group in all the aspect being tested. Therefore, both HmPR and HsPR are just as effective for patient management.

RETINAL NERVE FIBER LAYER THICKNESS MEASUREMENT USING OPTICAL COHERENCE TOMOGRAPHY IN MIGRAINE HEADACHE PATIENTS

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Objective: The purpose of this study was to compare the retinal nerve fiber layer (RNFL) thickness between migraine headache patients in UKM Medical Centre and normal control population.

Methodology: This was a case-control study. A total of 117 participants were recruited where 39 were migraine patients (recruited from Neuromedical Clinic UKMMC) and 78 participants were normal control. All participants underwent an interview of demographic data, visual acuity test, slit lamp examination, intraocular pressure (IOP) measurements and Optical Coherence Tomography (OCT) measurements of RNFL thickness.

Results: Average mean RNFL thickness in migraine group was $99.88 \pm 13.22 \mu\text{m}$, significantly thinner from control group by 6.29%. There was statistically significant difference in 360° RNFL thickness except for nasal quadrant in migraine patients compared to normal control. There was a weak correlation between severity and duration of migraine with RNFL thickness measurements. RNFL decayed with increasing age with fair correlation in the superior quadrant, ($r = -0.446$, $p = 0.004$) in migraine patients. The inferior and nasal quadrant RNFL did not decay with increasing age in normal control. Higher IOP in migraine compared to normal population by 10.2% difference was detected ($p=0.001$).

Conclusion: Peri-papillary RNFL was significantly thinner in migraine patients. Significantly higher IOP in migraine patients may suggest relation with glaucoma. Any amount of RNFL thinning in the inferior and nasal quadrant may suggest pathologic features that careful monitoring should be borne in mind.

VISUAL AND ANATOMICAL OUTCOME OF ARTISAN IRIS-CLAW LENS FOR CORRECTION OF APHAKIA FOLLOWING VITRECTOMY SURGERY

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Introduction: To review the visual and anatomical outcomes of Artisan iris-claw lenses for correction of aphakia following vitrectomy

Methods: Retrospective review of all patients utilizing the Artisan lens

Results: There were 9 eyes implanted with the lens from May 2011 to February 2012 for correction of aphakia. Six of these were implanted in vitrectomised eyes secondarily or as part of combined 23G vitrectomy by one surgeon. Age range was 23 years to 70 years. All were male. History included eye trauma in one case and glaucoma in 3 eyes. Anterior chamber depth preoperatively was at least 3.2 mm. Follow-up was 12 months to 6 months. Preoperative visual acuity was 6/18 to hand motions. Best corrected post-operative visual acuity (BCVA) at final review was 6/6 to 6/60. Improvement in BCVA was seen in all (100%). There was no corneal decompensation, pupillary block or lens dislocation. Two patients had slit like pupil distortion prior to pupillary dilatation. Hence BCVA following refraction through dilated pupil was better than undilated BCVA. These had undergone combined vitrectomy-lens implantation. One patient had poor VA due to diabetic macular ischaemia.

Conclusion: The Artisan lens provides stable visual rehabilitation for aphakia in selected cases. It is relatively easy to implant in vitrectomised eyes. However, residual pupil dilatation despite discontinuation of adrenaline in vitrectomy fluid and injection of miochrome may result in postoperative pupil distortion to an "almond shape" in the undilated state. Secondary lens implantation at a later date is an option in such cases.

INSULIN EYE DROPS FOR NORMALIZATION OF THE HEALING OF DIABETIC EPITHELIAL DEFECT INDUCED DURING OCULAR SURGERY IN MALAYSIAN PATIENTS

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Introduction: To investigate the rate of healing of corneal epithelial erosions in diabetics who underwent ocular surgery with topical insulin as compared with diabetics and non-diabetic eyes treated conventionally

Method: We retrospectively reviewed 14 eyes of 13 patients who underwent corneal epithelial debridement during various vitreoretinal surgeries to improve surgeon's view over a 10 month period at our centre in 2010.

Results: Three groups were identified: DTI, which comprised diabetics who had received topical insulin 1 unit qds post-operatively (n=5); DCT which comprised diabetics who had been treated with conventional post-operative medications only (n=5) and NDCT comprising non diabetic patients on conventional post operative therapy (n=5). Only eyes in which the corneal epithelial defect had been serially photographed at time, t= 0, 12, 24, 36, 48, 60, 72 and 120 hours following commencement of topical medications were included in the analysis. The size of the defect was calculated using local software. DTI eyes had a significantly smaller defect size at t= 24 (p=0.008), 36 (p=0.008), 48 (p=0.016) and 60 hours (p=0.008) compared to DCT eyes and had no statistical difference from NDCT eyes at all times in the Mann-Whitney test (p>0.05). In the diabetic operated bilaterally, the insulin treated eye re-epithelialised by 48 hours whereas the fellow eye treated conventionally re-epithelialised in 72 hours.

Conclusion: Topical insulin 1 unit qds may be applied to the corneal surface to normalize the rate of healing of epithelial defects in diabetic patients who have undergone epithelial debridement to improve the surgeon's view.

A RETROSPECTIVE REVIEW OF PAEDIATRIC RETINAL SURGERIES AT UNIVERSITI KEBANGSAAN MALAYSIA MEDICAL CENTER OVER A TWENTY-THREE MONTH PERIOD

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Objective: To review clinical features, surgical and visual outcomes of pediatric retinal surgeries in UKMMC.

Methods: Retrospective review of 178 retinal surgeries performed at UKMMC from January 2008 to November 2009

Results: Five eyes of 5 patients (2.8%) operated were from age group 0-18 years. Mean patient age was 10.6 years. Four were male.

Indications for surgery were rhegmatogenous retinal detachment (RRD) (n=3) and vitreous haemorrhage (VH) (n=2). Underlying etiology for RRD was familial vitreoretinopathy, post-surgical capsulotomy and blunt trauma. VH was secondary to posterior uveitis and shaken baby syndrome. Two eyes with RRD underwent combined 23 G vitrectomy with 360° scleral buckle and silicone oil and 1 had 360° scleral buckle (SB) for retinal dialysis. For the VH cases, one had 20 G.

Overall postoperative anatomic reattachment was 100%. Average post-op follow-up was 11.7 months (range 8 to 15 months). Three eyes developed secondary glaucoma; 2 associated with silicone oil. Final recordable visual acuity was 6/12 to 6/60. There was one case of anterior proliferative vitreoretinopathy (PVR).

Conclusion: Paediatric retinal surgery is rare and trauma being the most common etiology. Successful repair can be achieved with single surgery provided effects of PVR are anticipated including

placement of SB. Secondary glaucoma was the most common post-operative complication related to silicone oil.

VITRECTOMY FOR BREAKTHROUGH BLEEDING IN AGE RELATED MACULAR DEGENERATION AND POLYPOIDAL CHOROIDAL VASCULOPATHY: A CASE SERIES

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Introduction: Subretinal haemorrhage in age-related macular degeneration (AMD) or polypoidal choroidal vasculopathy (PCV) is an important sight-threatening condition. A massive intraocular haemorrhage due to breakthrough bleeding (BTB) is a devastating event, which often requires surgical intervention. The purpose of this study was to review the risk factors and clinical outcomes of patients undergoing pars planar vitrectomy (PPV) for BTB from AMD and PCV.

Methods: Retrospective review of medical records of 346 patients who underwent PPV at UKMMC from January 2008 - June 2011.

Results: Eight eyes of 8 patients with AMD/PCV-related BTB who underwent PPV were included. Mean age of patients was 64.4 years (range 41-80 years) with 5 males. Five (62.5%) were Chinese. 6 patients (75%) had hypertension and 4 patients (50%) were on anticoagulant/antiplatelet (AC/AP) therapy. Two had history of prior photodynamic therapy (PDT). There were five cases of PCV and three cases of AMD. Mean follow-up period was 13.12 months (range 2 – 28 months). All cases reported improvement in visual acuity and 3 cases with extrafoveal lesions achieved final visual acuity of 6/18 or better. Postoperative complications included retinal tear and detachment in one case, reattached on reoperation.

Conclusion: Our small series found PCV as the predominant diagnosis compared to AMD. Hypertension seems to be a significant risk factor for BTB. Usage of AC/AP and previous PDT may be other predisposing factors. Better visual prognosis occurs with extrafoveal lesions, which tend to be of PCV type.

***Helicobacter pylori* DETECTION USING IN-HOUSE RAPID UREASE TEST (iRUT) FROM GASTRIC ANTRAL BIOPSIES**

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Introduction: We developed an in-house rapid urease test (iRUT) and evaluate the efficacy of the iRUT with culture and histology for the detection of *H. pylori* infection.

Methods: Antral biopsies from 29 patients who underwent oesophagogastroduodenoscopy (OGDS) were diagnosed for *H. pylori* infection by culture, histology and iRUT. A positive result was determined by culture and histological examination and / or iRUT being positive. The result of iRUT was read within 10 min, at 1 h and up to 24 h for each specimen.

Results: *H. pylori* was detected in antral biopsies by histology, culture and iRUT with 10.3% (n=3), 10.3% (n=3) and 24.2% (n=7), respectively. The sensitivity of the iRUT result at 10 min, 1 h and 24 h was 100%, 100% and 57.14%, respectively. iRUT result showed 100% specificity for 10 min, 1 h and 24 h. Six iRUT specimens that initially negative became positive by iRUT within 24 hours. Positive predictive value of iRUT was 100% at 10 min, 1 h and 24 h. Negative predictive value of iRUT was 100% at 10 min and 1 h, and 88% at 24 hours.

Conclusion: We concluded that iRUT has a high specificity and may used as a rapid and cheap method to diagnose *Helicobacter pylori* infection. The most appropriate time point to read the result of iRUT was within 10 minutes and 1 hour when there was an agreement between sensitivity and specificity.

A TRANSGRESSIVE BROWN RICE MEDIATES FAVOURABLE GLYCAEMIC AND INSULIN RESPONSES

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Introduction: The potential use of the glycaemic index (GI) in foods to optimize blood glucose control in patients with diabetes receives favourable support from expert medical opinion. Controlling rice intake is an issue in therapeutic dietary prescription given its value as a staple in Asian diets. Our study aims to evaluate the GI and Insulin Index (II) potential of a new brown rice variant developed by the National University of Malaysia (UKM) and the Malaysian Agricultural Research Development Institute (MARDI).

Method: We evaluated glycaemic response of a brown rice variant (BR) developed by cross-breeding. Subjects (n=9) consumed 50g carbohydrate equivalents of BR, white rice (WR) and the polished brown rice (PR) in comparison to 50g glucose reference (GLU) in a cross-over design with one week of washout period. Subjects were fasted overnight (12 hours of fasting) with only plain water was allowed before challenging with the tested rice. Blood plasma was first obtained at baseline with venous puncture by phlebotomist. The subjects then challenged with tested rice and blood plasma had further taken at 15, 45, 60, 90, 120 and 180 minutes. Plasma glucose and insulin at each time points were measured and incremental area under the curve (IAUC) and indices for glucose (GI) and insulin were calculated.

Results: BR compared to PR or WR produced the lowest postprandial glycaemia (GI:51 vs. 79 vs. 86) and insulinaemia (II:39 vs 63 vs 68) irrespective of amylose content (19% vs. 23% vs. 26.5%). Only BR was significantly different from GLU for both plasma glucose (p=0.012) and insulin (p=0.013) as well as IAUC_{glu} (p=0.045) and IAC_{ii} (p=0.031). Glycaemic and insulinaemic responses correlated positively (r=0.550, p<0.001). Linear trends for IAUC_{glu} and IAUC_{ii} indicated a greater secretion of insulin tied with a greater glycaemic response for WR (r²=0.848), moderate for PR (r²=0.302) and weakest for BR (r²=0.122).

Conclusion: The brown rice variant had the lowest GI and II values but these advantages were lost with polishing.

IDENTIFYING PREDICTORS FOR PROTEIN-ENERGY WASTING IN HEMODIALYSIS PATIENTS

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Introduction: Protein-energy wasting (PEW) signified by inflammation-related muscle wasting is an issue in hemodialysis (HD) patients. PEW assessment remains unclear in literature. Our objective was to evaluate predictors for muscle wasting.

Methods: We enrolled 98 HD patients (63 men, 35 women; mean ± SD, age: 51.13 ± 12.7yrs; dialysis duration: 8.5 ± 7.2yrs). Lean tissue mass (LTM) was measured by bioimpedance absorptiometry. Assessments included International Physical Activity Questionnaire (IPAQ), modified-Subjective Global Assessment (mSGA), Malnutrition-Inflammation Score (MIS), 24-hour diet recall and laboratory data. Physical function (PF) testing evaluated endurance, strength and balance.

Results: PEW was identified in 61.1% (n=58) of patients. PEW patients had significantly lower post-dialysis weight (p<0.001), dry weight (p=0.003), BMI (p<0.001), MAC (p<0.001), MAMC (p=0.03),

MAMA ($p=0.01$) and TSF ($p=0.002$) as well as energy ($p=0.01$) and protein ($p=0.04$) intakes. Laboratory, IPAQ and PF testing could not discriminate between PEW and non-PEW patients. LTM correlated with MIS ($r=-2.7$, $p=0.02$) and ser.creatinine ($p<0.001$) but not mSGA ($r=-0.16$, $p>0.05$), Kt/V ($p>0.05$), ser.Urea ($p>0.05$) nor ser.Albumin ($p>0.05$). LTM did not correlate to IPAQ scores ($p>0.05$) but did with most PF tests ($p<0.01$). Hand grip (HG) best correlated with LTM ($p<0.001$, $r=0.75$) followed by back-leg chest dynamometry (BLC) ($p=0.001$, $r=0.68$) and high stool (HS, $p<0.001$, $r=0.51$). MIS better correlated to PF tests than mSGA. Regression analysis indicated MAMA ($p=0.04$), BMI ($p<0.001$), protein and energy ($p=0.01$) intakes and HG ($p=0.004$) correlated with LTM.

Conclusion: MIS identified PEW better than mSGA whilst HG, HS, Ser.Creatinine and MAC appropriately detected muscle wasting in HD patients.

ADVERSE DRUG REACTION REPORTING AMONG GENERAL PRACTITIONERS IN KUALA LUMPUR: THE PREDICTIVE VALUE OF KNOWLEDGE AND ATTITUDE

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Introduction: In Malaysia, general practitioners (GPs) contributed less than 5% of adverse drug reaction (ADR) reports to the National Centre for Adverse Drug Reactions Monitoring since 2008. This figure reflects a lower reporting practice among them compared to their Western counterparts. This study aims to determine the role of knowledge and attitude in the practice of ADR reporting among GPs in Kuala Lumpur.

Methods: A cross-sectional survey was done among GPs in Kuala Lumpur. The questionnaire used two scales to measure knowledge and attitude towards ADR reporting, both with good internal reliability. Retrospective ADR reporting status was based on self-report. Nonprobability quota sampling method was employed, with 36.9% participation rate. A hierarchical logistic regression analysis was performed to predict the ADR reporting status based upon the attitude and knowledge scales, with adjustment of the length of practice.

Results: 66 GPs participated in the study, among whom 63.6% were males and 62.1% were clinic-owners. Their mean length of practice was 24 years (SD: 12). Only 11 GPs reported ADR, at least once, throughout their practice. The hierarchical logistic regression model was valid, with 100.0% positive predictive value and 85.9% negative predictive value. Based on the hierarchical logistic regression, ADR reporting status was significantly predicted by the attitude scale (odds ratio: 1.4, $p<0.05$). However, the knowledge scale was not a significant predictor, even after the length of practice was adjusted.

Conclusion: Among Malaysian GPs, the practice of ADR reporting is more influenced by their attitude towards it, rather than their knowledge.

PREVALENCE AND RISK FACTORS ASSOCIATED WITH *Entamoeba histolytica*/*Entamoeba dispar*/*Entamoeba moshkovskii* COMPLEX INFECTION AMONG DIFFERENT TRIBES OF MALAYSIAN ABORIGINES

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Introduction: Amoebiasis is defined as an intestinal or extraintestinal infection with the protozoan parasite *Entamoeba histolytica*. It is prevalent in rural Malaysia especially among aboriginal communities.

Methods: A series of community-based surveys to determine the prevalence and risk factors associated with *E. histolytica*/*E. dispar*/*E. moshkovskii* complex (*Entamoeba* complex) infection was carried out among three different aboriginal tribes (Proto-Malay, Negrito and Senoi) in selected

villages of Negeri Sembilan, Perak and Pahang, Peninsular Malaysia. Socioeconomic data were collected using a pre-tested questionnaire. Faecal specimens were examined by formalin-ether concentration and trichrome staining techniques.

Results: Out of 500 individuals, 8.7% of Proto-Malay (13/150), 29.5% of Negrito (41/139) and 18.5% of Senoi (39/211) were found positive for *Entamoeba* complex infection. The prevalence of *Entamoeba* complex infection showed an age dependency relationship, with significantly higher rates observed among those aged less than 15 years. Multivariate analysis confirmed that failure to wash their hands after playing with soil or gardening and the presence of other family members infected with *Entamoeba* complex were identified as significant risk factors among all tribes. However, eating with hands, eating raw vegetables and close contact with domestic animals were identified as significant predictors of infection among Senoi. Overall, Negrito tribe presented a greater risk of *Entamoeba* complex infection than Proto-Malay and Senoi tribes.

Conclusion: Further studies on molecular approaches are needed to distinguish the morphologically identical species of pathogenic, *E. histolytica* from the non-pathogenic, *E. dispar* and *E. moshkovskii*. As highlighted by this study, the dynamic of transmission are most probably due to improper hygienic practice and contaminated vegetables. This study also showed that human to human contact is a possible mode of transmission. However, the role of domestic animals in the transmission of *Entamoeba* complex infection needs further investigation. The establishment of such data will be beneficial for the public health authorities to plan and implement specific prevention and control strategies to reduce amoebiasis significantly in different aboriginal tribes in Malaysia.

EFFICACY, ADVERSE EFFECTS AND COST EFFECTIVENESS OF AMPHOTERICIN B COLLOIDAL DISPERSION COMPARED TO AMPHOTERICIN B-DEOXYCHOLATE IN INVASIVE FUNGAL INFECTIONS AMONG PAEDIATRIC PATIENTS

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Introduction: Amphotericin B is the first line agent for treatment of invasive fungal infections (IFI) among paediatric patients. Amphotericin B deoxycholate (AmBD) and amphotericin B colloidal dispersion (AmBCD) are the two most commonly used antifungals for IFI. The objective of this pilot study was to compare the efficacy (resolution of IFI), adverse effects (AEs) and cost effectiveness between AmBD and AmBCD in the treatment of IFI among paediatric patients admitted at Universiti Kebangsaan Malaysia Medical Centre.

Methods: This was a clinical observational study that involved secondary data analysis of paediatric medical records, using an internally validated data collection form.

Results: Between July 1, 2006 and June 30, 2011, 35 patients received AmBD only treatment and five patients received AmBCD only treatment. 24 were males, mean age 7.18 (SD 4.59) years. On average, the AmBCD treatment course was significantly more expensive than AmBD ($p < 0.01$), RM4476 (SD RM3440) versus RM136 (SD RM188). There was a significant difference in the presence of AEs between the two treatment groups ($p < 0.05$), odds ratio of AE for AmBD compared to AmBCD was 15.43. Patients on AmBD had more AEs compared to those on AmBCD (average of two AEs compared to one, respectively). However, there was no significant difference in severe AEs (hepatotoxicity and nephrotoxicity) or efficacy between these groups.

Conclusion: These findings implied that the use of AmBD in IFI treatment among paediatric patients is justified, as it is cost-effective and there was no significant difference in the efficacy and severe AEs between these two treatments.

Keywords: Amphotericin B colloidal dispersion, Amphotericin B deoxycholate, Paediatrics, Invasive Fungal Infections (IFI).

WITHDRAWAL OF ALPHA BLOCKER THERAPY FOLLOWING INITIAL COMBINATION THERAPY WITH 5 ALPHA-REDUCTASE INHIBITOR (5ARI) DUTASTERIDE FOR BENIGN PROSTATIC HYPERPLASIA: A RANDOMISED CONTROLLED TRIAL ON EFFICACY

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Introduction: The objective was to compare the efficacy of withdrawing alpha blocker following initial combination therapy with dual 5 alpha-reductase inhibitor (Dutasteride) in benign prostate hyperplasia (BPH) patients.

Methods: 103 BPH patients, who had been on combination therapy for 52 weeks, were randomised to either continuation of alpha blocker and dutasteride (DT64) or withdrawal of alpha blocker for another 12 weeks (DT52+D12) from January 2010 to June 2011. Patients' assessment of symptoms based on International Prostate Symptom Score (IPSS) and peak urinary flow rate (Qmax) were evaluated at the end of 4, 8 and 12 weeks from baseline.

Results: 89% patients with an IPSS<20 who changed to dutasteride monotherapy at week 52, switched without a noticeable deterioration in their symptoms. In the 26% of men with severe baseline symptoms (IPSS≥20) who had withdrawal of alpha-blocker therapy at week 52, 34% reported a worsening of their symptoms compared with 20% in the DT64 group. Peak urinary flow measurements (Qmax) among both DT52+D12 and DT64 groups showed significant improvements (72.5% and 89.2% respectively). Among the patients with improved IPSS, only 77% and 94% of patients in DT52+D12 and DT64 groups showed concurrent improvement in Qmax. There were no significant associations between both the groups in terms of clinical BPH progression as assessed by IPSS (moderate symptoms p=0.12, severe symptoms p=0.33) and Qmax (moderate symptoms p=0.45, severe symptoms p=0.28).

Conclusion: Alpha-blocker can be stopped safely after 52 weeks of combination therapy without any significant deterioration in symptoms and flow rate.

FACTORS OF NOT REPORTING ADVERSE DRUG REACTION AMONG GENERAL PRACTITIONERS IN KUALA LUMPUR

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Introduction: Adverse drug reaction (ADR) reporting is the cornerstone of pharmacovigilance. This study was aimed to determine the attitudes and perceptions of general practitioners (GPs) towards ADR reporting to the national pharmacovigilance centre (MADRAC), and to determine the reason for lack of ADR reporting among general practitioners. In order to stress this issue, we attempted to provide a recommendation to MADRAC for improving ADR reporting among general practitioners in Malaysia.

Methods: A cross-sectional survey was conducted for a period of 5 months, from December 2011 through April 2012. The questionnaire sought the demographics of the private general practice, their knowledge and attitude to ADR reporting and the factors that they perceived may influence their ADR reporting.

Results: The total response rate was 66 out of 220 questionnaires (30.0%). Seventy four of the 220 approached but refuse to participate, and the remaining practices refused to meet. The majority of respondents (83.3%) had not report ADR throughout their practice. Factors most influencing GPs not reporting an ADR to MADRAC from most influencing were: lack of information on ADR reporting (55%), lack of time (33%) and level of clinical knowledge regarding ADR (28.8%).

Conclusion: Lack of information about how to report an ADR is the most common factor influencing GPs not to report an ADR. Findings of this study are useful for MADRAC to improve reporting rates.

Recommendation to MADRAC would be to increase awareness on ADR reporting with regular communication between MADRAC and GPs to explain about reporting procedures.

PREVALENCE OF *Clostridium difficile*-ASSOCIATED DIARRHEA (CDAD) AMONG ANTIBIOTIC-ASSOCIATED DIARRHEA (AAD) IN UNIVERSITI KEBANGSAAN MALAYSIA MEDICAL CENTER (UKMMC)

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Introduction: Antibiotic-associated diarrhea (AAD) is unexplained diarrhea associated with the administration of antibiotics. *Clostridium difficile* accounts for 10-20% of AAD cases. There was limited prevalence data of *C. difficile*-associated diarrhea (CDAD) especially in Asian countries. This study has been proposed to study prevalence of CDAD among AAD patients in Universiti Kebangsaan Malaysia Medical Center (UKMMC).

Methods: From November 2011 to April 2012, hospitalized patients who had a history of antibiotic usage within the prior 2 months and developed diarrhea without another identified etiology were classified as having AAD. The diagnosis of CDAD was established using *Wampole™ Tox A/B Quik Chek* kit. Clinical information was obtained from Medical Information Department. Data were analyzed using Fisher's exact test for categorical variables and Mann-Whitney test for continuous variables. $P < 0.05$ was considered significant.

Results: Of 30 non-repeated samples investigated, only 3 samples were toxin positive. CDAD rate were 0 case per 10 000 inpatient-days in November 2011, 0.56 (December 2011), 1.25 (January 2012) and no case was detected from February to April 2012. The average test positivity rates were 10%. The average CDAD incidences were 0.3 cases per 10 000 inpatient-days. All 3 toxin positive cases were categorized as healthcare facility-onset, healthcare facility associated CDAD. There was statistically significant difference between AAD and duration of hospitalization ($P=0.012$).

Conclusion: The rate of CDAD in UKMMC was relatively low. This study is useful as benchmark data for UKMMC. A continuous surveillance is needed for better understanding of the epidemiology of CDAD in our population.

IS THERE AN INFLUENCE OF DIETARY HABITS TO BREAST DENSITY AS SEEN ON DIGITAL MAMMOGRAMS?

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Introduction: The purpose of this study was to evaluate the influence of dietary habit on breast density, which is an important risk factor for breast cancer.

Methods: This cross-sectional study was performed on 64 healthy Malaysian women of all races between the age of 35 to 70 years. All subjects underwent mammography and the breast density was analyzed from the images using BI-RADS by two independent radiologists. A self administered food-frequency questionnaire with validation by expert in the field was used to evaluate the nutrient intake.

Results: The data were analyzed using Chi-square test to evaluate the association of dietary habits to breast density. Based on the results, mutton, pork, vegetables, sweets, snacks, soy bean and eggs intake showed associations with increased breast density ($p < 0.05$) while grains, meat, beverages, oil and fruits, did not show any association ($p > 0.05$).

Conclusion: Further study needs to be undertaken to look at the association between dietary habit, breast density and breast cancer.

THE PREVALENCE AND PROGNOSTIC SIGNIFICANCE OF LYMPH NODE MICROMETASTASES AMONG STAGES I AND II COLORECTAL CANCER

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Introduction: Stage II colorectal carcinomas remain a major management challenge as 20 - 30% of patients will eventually develop recurrence. It is postulated that these patients may harbour nodal micrometastases which is imperceptible by routine histopathological evaluation. The aim of our study is to evaluate (1) the feasibility of multilevel sectioning method utilizing routine haematoxylin and eosin (H&E) stain and immunohistochemistry technique with the epithelial marker cytokeratin (CK) AE1/AE3, in detecting micrometastases in histologically-negative lymph nodes and (2) correlation of nodal micrometastases with various clinicopathological parameters.

Methods: Sixty two stages I and II colorectal carcinomas diagnosed at Universiti Kebangsaan Malaysia Medical Centre (UKMMC) from 2003 to 2008 were reviewed. Multilevel sectioning with H&E stain and immunohistochemical study with CK AE1/AE3 were performed on all lymph nodes retrieved to detect micrometastases and isolated tumour cells. The findings were correlated with various clinicopathological parameters by statistical methods.

Results: Only one lymph node (1.6%) was found to harbour micrometastasis detected by both methods. In addition, CK AE1/AE3 successfully identified five patients (7.9%) with isolated tumour cells, but none through multilevel sectioning method. The presence of micrometastasis was not associated with larger tumour size, poorly differentiated tumour, higher depth of tumour invasion and poorer outcome.

Conclusion: Both immunohistochemistry and multilevel sectioning techniques are feasible methods in detecting nodal micrometastases. Immunohistochemical detection for isolated tumour cells is superior to multilevel sectioning method. However, there was no statistical significant correlation between nodal micrometastases and various clinicopathological parameters studied.

GENE REARRANGEMENTS IN DIFFUSE LARGE B-CELL LYMPHOMA: THE CORRELATION WITH CLINICOPATHOLOGICAL FEATURES

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Introduction: Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous group of disease and less than half of patients are cured with conventional chemotherapy. Studies have shown that some genetic abnormalities found in DLBCLs may influence the behaviour. This study aims to investigate the presence of **BCL-2**, **BCL-6**, **MYC**, **BCL-10**, and **MALT-1** gene rearrangements in a series of diffuse large B-cell lymphomas in a Malaysian population.

Methods: We analysed 141 cases of formalin-fixed paraffin-embedded tissues of diffuse large B-cell lymphoma from UKM Medical Centre using interphase fluorescent *in situ* hybridization with commercially available probes for split-signal targeting **BCL-2**, **BCL-6**, **MYC**, **BCL-10**, and **MALT-1**.

Results: A total of 13 cases (9.22%) showed the presence of gene rearrangements. **BCL-6** gene rearrangement was present with the highest frequency involving 10/13 cases (76.9%), followed by two cases by **MYC** gene rearrangement in 2/13 cases (15.4%) and **BCL-2** gene rearrangement in 1/13 case (7.7%). No **BCL-10** and **MALT-1** rearrangements were found in this study. Multiple rearrangements were not detected in any case. In addition, 11/141 cases (7.8%) were identified with gene amplification pattern. **BCL-2** gene amplification was observed in 6/11 cases (54.5%), **MALT-1** gene amplification in 3/11 cases (27.3%) and **MYC** gene amplification showed 2/11 cases (18.2%).

Conclusion: Our results produced relatively lower rate of gene rearrangements in this population of DLBCLs, in comparison with previous study by Grazia *et al*, 2009. These findings may suggest that DLBCL found in our population could be biologically different from that found in the Western population.

IDENTIFICATION OF UNCLASSIFIED VARIANTS IN *CHEK2* GENE AMONG MALAYSIAN PATIENS WITH HIGH RISK BREAST CANCER

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Introduction: Breast cancer is the most frequent cancer affecting women. Checkpoint Kinase 2 (*CHEK2*) is an important signal transducer of cellular responses to DNA damage, whose defects have been associated with an increase in breast cancer risk. The aim of this study is to investigate the patterns of *CHEK2* gene sequence changes in Malaysian patients with high-risk breast cancer.

Methods: Fifty nine high risk breast cancer patients were selected from UKM Medical Centre (UKMMC), Hospital Kuala Lumpur (HKL) and Hospital Putrajaya (HPJ). All the patients selected were non-*BRCA1* and *BRCA2* carriers. Ten milliliters of peripheral blood was obtained from each fully informed, consented patient. Isolation of genomic DNA was done using standard protocol. Mutational analysis for all coding regions and intron-exon junctions of the *CHEK2* gene was performed using direct DNA sequencing.

Results: We identified four *CHEK2* sequence variants in our cohort which consists of two missense and two synonymous mutations. The missense mutations (I160M and R180C) classified as variant of uncertain significance whilst the synonymous mutations (252A>G and 387G>A) are polymorphisms. Both variants (I160M and R180C) were detected in one Malay patient which accounts for 1.7% of total samples. Variant I160M was detected in a 43-years old patient with family history of breast cancer and variant R180C was detected in a 15-years old patient with a history of ovarian cancer.

Conclusion: The results of this study indicate that *CHEK2* mutations are rare in high-risk Malaysian breast cancer patients but may play a contributing role in breast cancer.

STUDY OF HEAVY METALS EXPOSURE AMONG FARMERS IN BACHOK AND TUMPAT, KELANTAN

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Introduction: Heavy metals in the environment may be toxic to human. Pesticides and chemical fertilizer are used in agricultural activities to increase crop production and protect from pests. The use of pesticides and chemical fertilizers is one of the main sources of heavy metals (lead, cadmium, arsenic, nickel and cobalt) release into the environment, that can increase the risk of heavy metal exposure to the farmers.

Methods: A total of 128 farmers were involved in this study. The inclusion criteria were at least one year of working experience and age less than 70 years old. All the samples were collected using universal sampling. The fingernails, toenails and hair samples were collected from farmers in Bachok and Tumpat, Kelantan. The concentration levels of heavy metals (lead, arsenic, cadmium, nickel and cobalt) were measured using Inductively Coupled Plasma Spectrometry (ICP-MS)

Results: The results showed that there were significant differences in the lead, arsenic, nickel and cobalt levels between fingernails, toenails and hair samples. However, there was no significant difference in the cadmium level between fingernails, toenails and hairs samples. There were no significant differences in the lead, cadmium, arsenic, nickel and cobalt levels between the different genders of the farmers. In correlation test, there were significant correlations in the lead, arsenic and cobalt levels in the toenails and the lead level in the hair with age of the farmers. There were also significant correlations in the lead and cobalt levels in the toenails with working periods.

Conclusion: The higher levels of heavy metals in the nails compared to hair could be due to failure to implement protective measures when handling the pesticide. The lead, arsenic and cobalt levels in

the nail and hair were significantly correlated with age and working experience. Therefore, the authorities should promote the use of safety equipment to control exposure to heavy metals especially among elderly farmers.

QUALITY OF LIFE AMONGST END STAGE RENAL FAILURE AT A DIALYSIS CENTER IN KLANG VALLEY, MALAYSIA

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Introduction: End Stage Renal Disease (ESRD) is one of the leading causes of morbidity and mortality that impinge on quality of life amongst haemodialysis patients. The main aim of the study was to examine the quality of life amongst the ESRD haemodialysis patients.

Methods: A cross sectional descriptive study was conducted on 72 ESRD patients at a Dialysis Centre in Klang valley of Malaysia. The modified KDQOL-SF™ subscales, kidney disease targeted scale and 36 item health survey scale questionnaires were used.

Results: The findings showed an overall health rating of good quality of life (66.73±11.670). There was no significant difference between quality of life in the domains with gender of the respondents with p value > 0.05. However, there were significant differences between quality of life in the domain of burden of kidney disease. Ethnic groups, local Malays were noted to have better quality of life in the domain of burden of kidney disease (p=0.015), cognitive function (p=0.014), quality of social interaction (p=0.026), emotional well being (p=0.047), and energy/fatigue (p=0.029) compared to non-Malays. Physical functioning deteriorated significantly with age (p=0.012) while social functioning was lowest in the 50-65 years age group (p=0.037). Those who had no co-morbidities had significantly better scores on effects of kidney (p=0.036), burden of kidney disease (p=0.011) and physical functioning (p=0.025).

Conclusion: The ESRD haemodialysis patients possessed good quality of life. It is opined that co-morbid conditions may influence the individual's kidney disease condition and quality of life.

Abstrak (kategori makmal)

DEVELOPMENTAL RATE OF *Chrysomyamegacephala* (FABRICIUS) AND *Hemipyrellialigurriens* (WIEDEMANN) (DIPTERA:CALLIPHORIDAE) ON DIFFERENT TYPES OF FOOD SOURCE REARED AT ENVIRONMENTAL TEMPERATURE AND HUMIDITY AND ITS EFFECT ON POST MORTEM INTERVAL (PMI) ESTIMATION

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Introduction: Laboratory rearing of flies to establish their developmental rate usually utilizes liver as the main source of food although it is known that the nutritional contents of different food vary from one another and could affect growth rates of larvae.

Method: This study was conducted in 3 sets at different time range, temperature and relative humidity to determine the differences in the developmental rate of *Chrysomyamegacephala*(Fabricius) and *Hemipyrellialigurriens*(Wiedemann) (Diptera: Calliphoridae) reared on beef muscle, liver and stomach at fluctuating natural environmental temperature and humidity. Eggs were collected freshly from the oviposition site (bait) and then equally distributed into 3 different containers, each containing 150g of muscle, liver and stomach respectively.

Results: Results indicated that the type of food did not significantly influence the size of *C. megacephala* larvae in set 1. This was inconsistent with the results obtained for *H. ligurriens* in set 2 and set 3. In set 2 and 3, there was a significant difference in size between larvae reared in stomach, muscle and liver. Muscle indicated higher growth rates compared to liver and stomach in both sets. In set 2, significant differences in size of larvae were recorded between stomach-muscle and stomach-liver. In set 3, significant differences were recorded between muscle-liver and muscle-stomach. This means that the type of food influenced the growth rate of *H. ligurriens* larvae significantly.

Conclusion: Different species have different preference for food source and this can affect the duration of their life cycle, developmental rate and hence PMI.

Keywords: type of food, growth rate, species, *Chrysomyamegacephala* (Fabricius), *Hemipyrellialigurriens* (Wiedemann), PMI

***Piper betle* INDUCED NRF2 SIGNALING VIA ANTIOXIDANT RESPONSE ELEMENT-MEDIATED PATHWAY**

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Introduction: Nuclear factor-erythroid 2 p45 related factor 2 (Nrf2) is a primary transcription factor, protecting cells from oxidative stress by regulating a number of endogenous antioxidants and phase II detoxifying enzymes. Previous studies have shown that *Piper betle* (sirih) extract increased the levels of glutathione (GSH) and glutathione S-transferase activity in Swiss albino mice subjected to benzo[a]pyrene. However the association between the Nrf2/ARE signalling pathway and the detoxification enzymes was unclear. Thus, the aim of this study is to elucidate the involvement of PB in the Nrf2 signaling pathway by determining the expression of genes and proteins of the phase II detoxification enzymes.

Methods: Two types of cells were used; mouse embryonic fibroblasts (MEFs) derived from wild-type (WT) and Nrf2 knockout (NO) mice. The cells were treated with PB (5 and 10 µg/ml) for 24h to determine the gene and protein expressions of Nrf2, HO-1 and NQO1. Luciferase reporter gene

activity was performed in HCT116 in order to determine the antioxidant response element (ARE)-induction by PB.

Results: Western blot analysis showed significant increase in the expressions of HO-1 and NQO1 proteins ($p < 0.05$) in WT, but not in N0 cells. Real time PCR results showed significant increase in the expression of NQO1 gene ($p < 0.05$) but not Nrf2 gene in WT cells. ARE/luciferase activity was increased by PB in HCT116 cells.

Conclusion: PB is involved in Nrf2-ARE signaling pathway by inducing the expressions of cytoprotective genes and proteins.

Keywords: Nrf2, PB, ARE, NQO1, antioxidant

AGE RELATED CHANGES OF Nrf2/ARE SIGNALING PATHWAY BY *Chlorella vulgaris* IN C57BL/6 MICE

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Introduction: Supplementation of natural products with high antioxidant capacity can alter the age related changes. The aim of this study was to investigate the effects of antioxidants *Chlorella vulgaris* (CV) on modulating the Nrf2/ARE signalling pathway associated with the production of endogenous antioxidants (SOD, GPx, CAT) and phase II detoxifying enzyme (NQO1) during ageing in mice.

Methods: The mice were divided into three groups according to their age, young (6 months old), middle (12 months old) and old age (18 months old). The mice were sub-divided into control and treatment group of CV (50mg/kg). Heart tissues were collected for determination of genes and proteins expression of antioxidants and phase II detoxifying enzyme via Nrf2/ARE signalling pathway by Quantigene Plex 2.0 Assay and Western Blot Analysis.

Results: CV down-regulated Nrf2, NQO1, GPx1 and CAT genes in young age group, and down-regulated GPx1, and CAT genes in old age group ($p < 0.05$). In contrast to the gene expressions, CV increased protein expression of Keap1 and NQO1 in young and middle age group and increased NQO1 expression in old age group ($p < 0.05$).

Conclusion: CV supplementation is unable to induce the expression of cytoprotective genes through the Nrf2/ARE signalling pathway.

MODULATION OF CELL CYCLE PROFILE BY *Chlorella vulgaris* PREVENTS REPLICATIVE SENEESCENCE OF HUMAN DIPLOID FIBROBLASTS

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Introduction: As ageing is directly related to genetic and environment, scientists believe that the event can be prevented or delayed with natural or synthetic compound. In this study, we evaluated the effects of *Chlorella vulgaris* (CV) algae in preventing replicative senescence of human diploid fibroblasts (HDFs) by determining several ageing biomarkers.

Method: Hot water extract of CV was used to treat HDFs at passage 6, 15 and 30 which represent young, pre-senescence and senescence ages, respectively. The level of DNA damage was determined by Comet assay while apoptosis and cell cycle profile were determined using FACs Calibur Flowcytometer.

Results: Our results showed increased level of damaged DNA and apoptosis with senescence of HDFs ($p < 0.05$) while cell cycle profile showed increased population of cells in G_0/G_1 phase and decreased S phase cells ($p < 0.05$). Treatment with CV caused a significant reduction in the level of damaged DNA and apoptosis of HDFs ($p < 0.05$). Cell cycle analysis showed that treatment with CV

significantly increased the S phase and G2/M phase of senescent HDFs and decreased population of cells in G₀/G₁ phase ($p < 0.05$).

Conclusion: Hot water extract of *Chlorella vulgaris* decrease the biomarkers of ageing indicating its potential as an anti ageing compound. However further study is needed before it can be introduced as an effective anti-ageing supplement.

REVERSAL OF AGING ON POST-TREATED HUMAN SKELETAL MUSCLE SATELLITE CELLS WITH TOCOTRIENOL RICH FRACTION

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Introduction: Skeletal muscle and the quality of human life are closely related. Aging of skeletal muscle leads to the progressive loss in muscle strength and muscle mass, slower regenerative capacity and eventually disabilities. Skeletal muscle satellite cells are heavily involved in the regeneration of skeletal muscle in response to the deterioration of the skeletal muscle due to aging or damage. Stress-induced premature senescence (SIPS) in the skeletal muscle is associated with the generation of reactive oxygen species through hydrogen peroxide (H₂O₂).

Methods: Human skeletal muscle satellite cells were isolated from a biopsy of a 5-day-old infant quadriceps muscle and were cultured as myoblasts. SIPS model was developed through 1 mM H₂O₂ inducement. The morphology of the cells was observed via immunocytochemistry assay. The development of SIPS model and the effect of tocotrienol rich fraction (TRF) towards the SIPS model were evaluated through senescence-associated β -galactosidase (SA- β -gal) activity.

Results: H₂O₂-induced the myoblasts to develop the morphology of senescence. The myoblasts exhibited a large flattened morphology and prominent intermediate filaments. H₂O₂-induced senescence in myoblasts significantly accumulated the SA- β -gal activity in the cells ($p < 0.05$). Interestingly, post-treatment with TRF reversed the accumulation of the SA- β -gal activity in the H₂O₂-treated myoblasts ($p < 0.05$). However, pre-treatment with TRF failed to protect the myoblasts from the induction of H₂O₂ in presenting the accumulation of SA- β -gal activity.

Conclusion: We suggest that TRF may reverse the aging of the skeletal muscle cells. Mechanism of the action of the TRF in reversing the aging of skeletal muscle is under investigation.

TOCOTRIENOL-RICH FRACTION MODULATES THE EXPRESSION OF GENES IN NRF2-ARE SIGNALING PATHWAY IN PREVENTING CELLULAR SENESCENCE OF HUMAN DIPLOID FIBROBLASTS

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Introduction: Human diploid fibroblasts (HDFs) undergo a limited number of cell divisions in culture which is known as cellular senescence. Oxidative stress caused damage to cellular macromolecules and contributed to ageing. Nrf2-antioxidant response element (ARE) signaling pathway acts as a cellular defense against oxidative stress. Vitamin E has shown beneficial effects on human health and prevents ageing. The aim of this study was to determine the molecular mechanism of TRF in preventing cellular ageing focusing on the modulation of genes expression involved in Nrf2- ARE signaling pathway.

Methods: HDFs were divided into young control, young TRF-treated, senescent control, senescent TRF-treated, siRNA of CDKN2a, TRF-treated pre-siRNA of CDKN2a and TRF-treated post-siRNA of CDKN2a. HDFs were treated with TRF at a dose of 500 μ g/ml for 24 hours. Gene expression

associated with NRF-2 ARE signaling pathway such as NRF2, KEAP, NF- κ B and PKC δ was analysed using quantitative real time RT-PCR technique.

Results: NRF2 was down regulated in cellular senescence but was up regulated in senescent TRF-treated HDFs and in senescent HDF treated with TRF post siRNA of CDKN2a ($p < 0.05$). KEAP1 was up regulated in cellular senescence and HDFs with siRNA of CDKN2a and HDFs treated with TRF pre- and post-siRNA of CDKN2a ($p < 0.05$). No significant difference was observed on the expression of NF- κ B and PKC δ genes.

Conclusion: TRF exerted protection against cellular ageing of HDFs by modulating the expression of genes involved in Nrf2- ARE signaling pathway. These findings indicate that modulation of inflammation signaling pathways by TRF may prevent cellular senescence of HDFs.

MODULATION OF PI3K/AKT AND MAPK/ERK PATHWAYS BY TOCOTRIENOL-RICH FRACTION (TRF) PREVENTS REPLICATIVE SENESENCE IN HUMAN DIPLOID FIBROBLASTS

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Introduction: Normal somatic cells have finite cellular divisions. When exhausted the limitation, cells undergo irreversible growth arrest or replicative senescence which is thought to be the underlying cause of aging. Tocotrienol has been reported as an effective antioxidant and genes modulator in previous studies. However, the effects of tocotrienols on genes expression during aging remain unclear. Therefore, this study determined the modulation of TRF on the expression of genes involved in PI3K/AKT and MAPK/ERK pathways.

Methods: Circumcision foreskins from 8 to 10 years old boys were used to isolate the fibroblast cells. The cells were cultured until passage 6 (young), passage 15 (pre-senescent) and passage 30 (senescent) and treated with 0.5 mg/ml TRF for 24 hours. Expression of genes AKT, forkhead box O3 (FOXO3), cyclin dependent kinase inhibitor 1A (CDKN1A), extracellular signal-regulated kinase (ERK), ELK1, ribosomal protein S6 kinase 90 kDa (RSK1), FBJ murine osteosarcoma viral oncogene homolog (FOS) and sirtuin1 (SIRT1) were determined by quantitative real-time polymerase chain reaction.

Results: AKT, FOXO3, RSK1 and CDKN1A in senescent HDFs were up regulated as compared to young HDFs ($p < 0.05$) while ELK1, FOS and SIRT1 were down regulated. Treatment with TRF caused down regulation of AKT, FOXO3, RSK1 and ERK in senescent cells but similar effects was not observed in young HDFs. ELK1, FOS and SIRT1 were up regulated with TRF treatment in senescent HDFs.

Conclusion: Replicative senescence in HDFs can be prevented by TRF through modulation of genes expression in pathways that regulate cell cycle and SIRT1.

ANTIOXIDANT AND ANTIPROLIFERATIVE ACTIVITIES OF *Quassia borneensis* NOOT. ON HL-60 HUMAN PROMYELOCYTIC LEUKEMIA CELLS

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Introduction: The family of Simaroubaceae is known to contain quassinoids, a group of compounds that have been reported to possess numerous biological activities such as anticancer and antimalarial activities. This study was carried out to evaluate the antioxidant capacity and inhibition of HL-60 cells proliferation of various extracts from *Quassia borneensis*, an unexplored indigenous Simaroubaceae plant from Sabah.

Methods: The bark and root of *Q. borneensis* were extracted by Soxhlet and maceration in methanol and further partitioned with hexane, chloroform and water. Twelve different extracts obtained were named as Q1 to Q12. The antioxidant capacity of *Q. borneensis* extracts was measured using Ferric

Reducing Antioxidant Power (FRAP) assay with or without the presence of HL-60 cells, while antiproliferative activity was determined by MTT assay.

Results: Among all the extracts, the highest antioxidant capacity was shown by bark maceration chloroform extract (Q5) with or without the presence of HL-60 cells, where the FRAP value were $125.45 \pm 9.1 \mu\text{M FeSO}_4 \cdot 7\text{H}_2\text{O}$ and $181.55 \pm 3.45 \mu\text{M FeSO}_4 \cdot 7\text{H}_2\text{O}$ respectively. Meanwhile, bark Soxhlet chloroform extract (Q7) exhibited the highest antiproliferative activity on HL-60 cells with the IC_{50} of $5.0 \mu\text{g/mL}$.

Discussion: The high antioxidant and antiproliferative activities shown by chloroform extracts may be contributed by the high quassinoids or other phytochemicals contents.

Conclusion: *Q. borneensis* possessed both antioxidant and antiproliferative activities on HL-60 cells where the highest activities were shown by chloroform extracts.

GELAM HONEY ACTS AS A RADIOPROTECTANT AGENT IN IRRADIATED HUMAN DIPLOID FIBROBLAST (HDFs)

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Introduction: Radiation involves in production of free radicals that may attack and lead to DNA or cellular damages. The aim of this study was to determine the potential of gelam honey as a radioprotectant agent.

Methods: The antioxidant properties of irradiated gelam honey were determined by DPPH and FRAP assays. While, cytotoxicity of gelam honey on human diploid fibroblasts (HDFs) was evaluated using MTT assay. Effects of gelam honey against radiation-induced DNA damage and cell survival rate on HDFs was evaluated by Comet and Clonogenic assay respectively. Furthermore, effects of gelam honey treatment on antioxidant defense system were determined via gene and protein expression, cell cycle, apoptosis and antioxidant enzyme activities.

Results: The degree of DNA damage was decreased, whereas cell survival rate was significantly increased when HDFs were exposed to 1 Gray of gamma-rays ($p < 0.05$). Results of Real-time RT-PCR and Western Blot analysis revealed that DNA damage increased expression of ATM, subsequently activated p73/p53 which initiated cell cycle inhibition at G0/G1 phase. The up-regulation of p73 leads to apoptosis induction in HDFs. Pre-treatment with 6 mg/ml of gelam honey was showed to down-regulate *ATM*, *p53* and *p16^{INK4A}* genes allowing cell progression to enter S phase and decreased apoptosis in HDFs ($p < 0.05$). Gamma-irradiation also decreased the expression of genes and specific activities of SOD, CAT and GPx antioxidant enzymes ($p < 0.05$). Our results showed that SOD and CAT activities were increased when HDFs were treated with gelam honey before exposure to gamma-radiation.

Conclusion: Gelam honey maintained cell defense system against radiation-induced injuries and acts as a radioprotectant agent.

HISTOLOGICAL OBSERVATION ON HIPPOCAMPUS AND FRONTAL CORTEX OF RATS DUE TO LEAD INGESTION IN A DOSE-RELATED MANNER

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Introduction: In recent times, lead poisoning cases have been on the rise. This might be due to an increased pollutant levels in the environment. This study aimed to look into the changes that may occur in the rat brain as the result of lead ingestion.

Methods: Eighteen male *Sprague-Dawley* rats weighing 150-200 g were randomly divided into 3 groups. A control (CTRL) group was fed with distilled water. The PB2 and PB4 groups were fed with 0.2% and 0.4% lead acetate in distilled water respectively, for 30 days. At the end of the study the rat brains were harvested and preserved. The hippocampus and frontal cortex were subjected to histological observation.

Results: It was observed that there were apoptosis of the neurons in the hippocampus and frontal cortex that occurred in a dose-related manner after 30 days of lead ingestion. Compared to CTRL, PB2 showed the presence of apoptotic neurons accompanied by disorganized neuronal cells. PB4 showed a significant increase of apoptotic cells in both hippocampus and frontal cortex compared with CTRL. Thus, histological changes observed in PB2 and PB4 might be due to 0.2% and 0.4% lead acetate consumption, respectively. However, there was no significant difference in the histological changes that occurred in both groups.

Conclusion: Dose-related lead ingestion is capable of causing histopathological changes in the hippocampus and frontal cortex of experimental rats. Caution should be taken to avoid poisoning especially for those exposed to lead.

RISK ASSESSMENT OF LOCAL BELACAN (SHRIMP PASTE) INTAKE

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Introduction: Shrimp paste is one of the staple food condiments in Malaysia. This research was conducted to evaluate the mutagenic activity of local shrimp paste and to estimate the actual intake among Malaysian population.

Methods: Two types of shrimp paste produced from factory and small scale industry (SSI) were sampled from Melaka, Malaysia and extracted with aqueous and methanol solvent. Ames Test was used to determine the mutagenicity potential of shrimp paste using *Salmonella thyphimurium* TA98 and TA100 bacterial strains. Semi quantitative Food Frequency Questionnaire (FFQ) was used to evaluate the actual intake of shrimp paste among population using multistage random sampling. Heavy metal analyses were also determined by ICP-MS.

Results: There were mutagenic activities in methanol extracts of shrimp paste from SSI at 25 mg/ml and 50 mg/ml without the presence of metabolic activator S9 in TA98 strain. In the presence of metabolic activation, the same extract showed mutagenic response at 50 mg/ml in TA 98 strain. The mean daily intake of shrimp paste was 1.41 ± 0.27 g/day. Arsenic (As) and Lead (Pb) were found exceeded the limit of Malaysian Food Act 1983 and Food Regulation 1985.

Conclusion: From this study, it has been observed that the daily intakes of As, Pb, Cd and Hg in shrimp paste is much lower than the provisional tolerable weekly intakes (PTWI) given by FAO/WHO and could not be considered harmful to the population. The outcome of this research can be used as baseline data for safe intake of shrimp paste as daily condiment.

HISTOLOGICAL CHANGES IN LIVER DUE TO ACETAMINOPHEN INDUCED HEPATIC INJURY IN MALE SPRAGUE DAWLEY RATS

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Introduction: Most of the drugs are metabolized in the liver for excretion. During metabolism process, reactive oxygen species and potentially harmful metabolites are produced. However, innate antioxidant substances like glutathione neutralize the metabolites. Depletion of these substances in drug overdose leads to cellular damage and more severely causes acute liver failure. In this study,

the cellular changes in drug induced liver toxicity were identified. The impact of acetaminophen on liver toxicity was assessed histopathologically.

Methods: Thirty male Sprague Dawley rats (200-250g) were randomly divided into baseline group (n=6) and acetaminophen induced liver toxicity groups (n=24). After one week of acclimatization, the experimental groups were given acetaminophen orally with the dose of 1000mg/kg body weight at day 0. The baseline group which was not induced with acetaminophen was sacrificed on day 0. The animals in group D1, D3, D5 and D7 were sacrificed on day 1, 3, 5 and 7 accordingly.

Results: Histological changes of liver tissue were determined and analyzed. Derangement in the liver histology was discovered such as distorted hepatic cellular cords, narrowing of sinusoidal spaces, enlarged hepatocytes with loss of cell membrane forming binucleated cells and inflammatory cells infiltration in all the experimental groups.

EFFECT OF *Plantago major* L. ON ACETAMINOPHEN-INDUCED LIVER TOXICITY OF RATS: HISTOLOGICAL ANALYSIS

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Introduction: Acetaminophen is a commonly used agent to induce acute liver toxicity in rats. It is metabolized in the liver for excretion. During metabolism, reactive oxygen species and potentially harmful metabolites are produced. The innate antioxidants like glutathione neutralize these harmful substances. Depletion of the antioxidants leads to liver cellular damage. *Plantago major*, known as *Ekor Anjing* in Malaysia were known to have antioxidant properties. In this study, the effects of the methanol extract of *Plantago major* leaves on acetaminophen-induced liver injury were observed.

Methods: Forty four male Sprague Dawley rats (200-250gm) were randomly divided into 6 groups, namely: BSL group as the baseline group (n=6), group A (n=6) was given vehicle (5% DMSO) orally and group B, C, D and E received acetaminophen on day 0 (n=8 each). From day 1 until day 7, group C and D received per oral plant extract 1000mg/kg and 1500mg/kg respectively and group E received 900mg/kg of N-acetylcysteine. The rats in the BSL group were sacrificed on day 0. Rats in group A, B, C, D and E were sacrificed on day 8 and the liver tissue was collected for histological analysis.

Result: Normal liver histology was found in BSL and group A. However, the derangement of liver histology was revealed such as distorted hepatic cellular cords, narrowing of sinusoidal spaces, enlarged hepatocytes with loss of cell membrane forming binucleated cells and inflammatory cells infiltrations in group B. In group C and D, the liver histology showed liver architecture similar to BSL and group A. The recovery effect was more prominent in group D which received 1500 mg/kg of plant extract.

Conclusion: The methanol extract of *Plantago major* L. possesses recovery effect on the acetaminophen-induced liver injury.

Key words: acetaminophen, *Plantago major*, liver toxicity

***Labisia pumila* PREVENTS OSTEOPOROSIS COMPLICATIONS BY INCREASING THE BONE STRENGTH OF POSTMENOPAUSAL OSTEOPOROSIS RAT MODEL**

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Introduction: Estrogen Replacement Therapy (ERT) is the main treatment of postmenopausal osteoporosis. However, ERT causes serious side effects, such as cancers and thromboembolic problems. *Labisia pumila* var. *alata* (LPva) is a herb with the potential as ERT alternative to prevent

osteoporosis complications especially fragility fractures. This study was conducted to determine the effects of LPva on the biomechanical strength of the femora exposed to osteoporosis due to estrogen deficiency using the postmenopausal rat model.

Methods: Thirty two female rats were randomly divided into 4 groups: Sham operated (Sham), ovariectomized control (OVXC), ovariectomized with *Labisia pumila* var. *alata* (LP) and ovariectomized with ERT (Premarin®) (ERT). The LPva and ERT were administered through the route of oral gavage daily at the dose of 17.5 mg/kg and 64.5 µg/kg respectively. Following 2 months of treatment, rats were euthanized and the right femora were prepared for bone biomechanical test.

Results: Ovariectomy had compromised the femoral strength, while LPva supplementation to the ovariectomized rats was able to improve the femoral strength.

Conclusion: LPva was as effective as ERT in preventing fractures due to estrogen deficient-osteoporosis.

EFFECTS OF TOCOPHEROL AND TOCOTRIENOL ON BONE FRACTURE HEALING IN POSTMENOPAUSAL OSTEOPOROSIS RAT MODEL (BIOMECHANICAL ANALYSIS)

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Introduction: Osteoporosis causes bone loss, leading to fragile bone which fractures under slight trauma. This study investigated the effects of α-tocopherol and tocotrienol supplementations on bone fracture healing in postmenopausal osteoporosis rats.

Methods: 32 female Sprague-Dawley rats were divided into four groups. The first group was sham-operated (SO), while the others were ovariectomised. After 2 months, the right femora were fractured under anaesthesia and fixed with K-wire. The SO and ovariectomised-control rats (OVXC) were given olive oil (vehicle), while both the alpha-tocopherol (ATF) and tocotrienol-enriched fraction (TEF) groups were given alpha tocopherol and tocotrienol-enriched fraction respectively, at the dose of 60 mg/kg via oral gavages 6 days per week for 8 weeks. The rats were then euthanized and the femora dissected out for bone biomechanical testing to assess their strength.

Results: The callous of the TEF group had significantly higher Stress parameter than the SO and OVXC groups. Only the SO group showed significantly higher Strain parameter compared to the other treatment groups. The Load parameter of the OVXC and ATF groups was significantly lower than the SO group. There was no significant difference in the Young's Modulus between the groups.

Conclusion: Tocotrienol is better than α-tocopherol in improved the biomechanical properties of the fracture callous in postmenopausal osteoporosis rat model.

Eurycoma longifolia AND OSTEOPOROSIS: THE TRABECULAR BONE ASSESSMENT USING MICROCOMPUTED TOMOGRAPHY

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Introduction: Recent studies suggested that *Eurycoma longifolia* (Tongkat Ali) is a potential herbal plant for the treatment of osteoporosis in elderly male, due to their testosterone-enhancing effects. The trabecular bone connectivity density and microarchitecture changes in osteoporosis can be assessed more accurately using microcomputed tomography (microCT) imaging system. The aim of this study was to determine the effects of *Eurycoma longifolia* supplementation on the trabecular bone connectivity density and microarchitecture of orchidectomized rats (androgen-deficient osteoporosis model).

Methods: 32 aged (12 months old) Sprague Dawley rats were divided into four groups of sham-operated (SHAM), orchidectomized-control (orxC), orchidectomized + testosterone enanthate (orx + TE) and orchidectomized + *Eurycoma longifolia* (30 mg/kg) (orx + EL). Rats were sacrificed after six weeks of treatment. The left femora were used to measure the trabecular bone connectivity density and microarchitecture using microCT.

Results: Orchidectomy decreased ($p < 0.05$) connectivity density, trabecular bone volume and trabecular number; and did not change the trabecular number and trabecular separation in comparison to the SHAM and orx + TE groups. Testosterone was able to reverse all orchidectomy-induced changes in the microCT parameters. EL was not able to reverse the orchidectomy-induced changes; instead it further worsened the trabecular separation in orchidectomized rats.

Conclusion: The microCT analysis has shown that EL supplementation was not able to prevent androgen-deficient osteoporosis and may further worsen the trabecular separation.

VIRGIN COCONUT OIL IMPROVES BONE OXIDATIVE STATUS IN POSTMENOPAUSAL OSTEOPOROTIC RAT MODEL

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Introduction: Virgin coconut oil (VCO) was found to have antioxidant property due to its high polyphenol content. The aim of this study was to investigate the effect of the virgin coconut oil on lipid peroxidation in the bone of an osteoporotic rat model.

Methods: Normal female Sprague Dawley rats aged 3 months old were randomly divided into 5 groups, with 8 rats in each group: Baseline, sham, ovariectomised (OVX) control group, OVX given calcium, and OVX given 8% VCO in the diet for six weeks. The oxidative status of the bone was assessed by measuring the index of lipid peroxidation, which is malondialdehyde (MDA) concentration, as well as the endogenous antioxidant enzymes glutathione peroxidase (GPX) and superoxide dismutase (SOD) in the tibia at the end of the study.

Result: The results showed that there was a significant decrease in MDA levels the OVX-VCO group compared to control group. Ovariectomised rats treated with VCO also had significantly higher GPX concentration. The SOD level seemed to be increased in the OVX-VCO group compared to OVX-control group.

Conclusion: VCO prevented lipid peroxidation and increased the antioxidant enzymes in the osteoporotic rat model; therefore VCO has the potential to be used in prevention and treatment of postmenopausal osteoporosis.

BONE BIOMECHANICAL STRENGTH OF GLUCOCORTICOID-INDUCED OSTEOPOROTIC MALE RATS GIVEN *Piper sarmentosum* LEAF EXTRACT

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Glucocorticoid-induced osteoporosis is the most common cause of secondary osteoporosis. Glucocorticoids have profound impact on bone, predominantly through modulation of bone formation but also through the effects on bone resorption. Long-term glucocorticoid therapy is associated with rapid bone loss and deterioration of bone quality. *Piper sarmentosum* (Ps) extract is known to possess antioxidant and anti-inflammatory activities. In this study, we determined the effects of *Piper sarmentosum* leaves on the bone biomechanical strength of glucocorticoid-induced osteoporotic rats. Three-month old male Sprague-Dawley rats (250-300g) were adrenalectomized to remove the main source of circulating glucocorticoids. They were divided into three groups: sham; adrenalectomized control group and adrenalectomized group treated with *Piper sarmentosum*. The glucocorticoid deficiency in adrenalectomized rats was replaced with intramuscular dexamethasone 120µg/kg/day. Treatment with water-based *Piper sarmentosum* leaf extract 125mg/kg body weight was given for 2

months. The right femora were dissected out for biomechanical assessment. Three biomechanical parameters were measured for analysis (flexure modulus, flexure stress and energy at maximum flexure load). The results showed that *Piper sarmentosum* leaf extract had significantly improved the flexural modulus, flexure stress and energy ($p < 0.05$) of the femoral bones of adrenalectomised rats. The results showed that *Piper sarmentosum* leaf extract was able to prevent bone weakness due to long-term glucocorticoid therapy. Thus *Piper sarmentosum* may have the potential to be used as prophylaxis against osteoporosis and fracture in patients on long-term glucocorticoid treatment.

EFFECTS OF GLUCOSE AND PYRUVATE IN THE CULTURE MEDIUM ON *IN VITRO* MATURATION OF BOVINE OOCYTES

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Introduction: Glucose and pyruvate are energy substrate essential for the growth of oocytes *in vitro*. Hence, this study was conducted to investigate the effects of energy substrate in the culture medium on *in vitro* maturation of bovine oocytes.

Methods: Modified TCM199 medium (M-7528) used to mature bovine oocytes *in vitro*. Supplementation of different glucose (1.5, 5.6, 20.0 mM) and pyruvate (0.1, 0.2, 0.4 mM) concentrations were incubated for 48 hours at 38.5°C under 5% CO₂ atmosphere with 95% humidity. After 48 hours, the denuded oocytes were stained with fluorescence dye JC1 (5,5',6,6'-tetrachloro-1,1,3,3'-tetraethylbenzimidazolcarbocyanine iodide), incubated for 30 minutes and examined under fluorescence microscope. The maturation and mitochondrial organization of oocytes at different stages of development were examined. A mean of two measurements of oocyte diameter was measured and made perpendicular to each other using Image-J software.

Results: There is significant difference of oocytes diameter of glucose (1.5, 5.6 and 20.0 mM) compared to control. No significant difference was observed in oocytes diameter of pyruvate (0.1, 0.2 and 0.4 mM) concentrations compared to control. The supplementation of pyruvate (0.2 mM) significantly promoted oocytes maturation to metaphase II (MII) stage much faster and produced matured oocytes with a diameter of $\geq 120 \mu\text{m}$. In comparison, 5.6 mM glucose was able to mature up to 115 μm only. All changes were significant at the level of $p < 0.05$.

Conclusion: Pyruvate at 0.2 mM is the optimum concentration for in-vitro maturation and produced matured bovine oocytes with a diameter larger than 120 μm .

THE EFFECT OF *Ficus deltoidea* LEAVES AQUEOUS EXTRACT VARIATION DELTOIDEA AND ANGUSTIFOLIA ON RAT UTERUS CONTRACTION

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Introduction: *Ficus deltoidea* is a herbal plant that usually used by women after parturition. This study was carried out to investigate the effects of *F. deltoidea* leaves aqueous extracts variation Deltoidea and Angustifolia on the rat uterus contraction.

Methods: Twelve Sprague dawley female rats were pretreated with diethylstilbestrol to induce the estrus phase. The uterine horns were taken out after 24 hours, cut into 2 cm length and put into the organ bath which was connected to the Powerlab apparatus. Both extracts with the cumulative concentration (10 $\mu\text{g/ml}$ to 1280 $\mu\text{g/ml}$) were injected into the organ bath separately. The synergistic effects between both extracts in combination and between oxytocin (0.01 IU/ml) and the extracts in combination were determined.

Results: All extracts were found to induce significant ($p < 0.05$) uterine contraction. The contraction increased proportionately to the concentration of extract. However, it ceased to increase after the maximum contraction was elicited even after higher extract concentration was injected. *F. deltoidea* aqueous extract variation Deltoidea and variation Angustifolia produced maximum uterine contraction at 320 $\mu\text{g/ml}$ ($3.492 \pm 0.244\text{g}$) and 1280 $\mu\text{g/ml}$ ($3.407 \pm 0.148\text{g}$) respectively. For the synergistic effect of both variations, the maximum uterine contraction was produced at 640 $\mu\text{g/ml}$ ($3.630 \pm 0.097\text{g}$). While

for the synergistic effect of both *F. deltoidea* variations and oxytocin, the maximum contraction was produced with the lower concentration for both extracts which are 320µg/ml (6.694±0.153g) for *Angustifolia* variation and 80µg/ml (3.979±0.058g) for *Deltoidea* variation.

Conclusion: The *F. deltoidea* leaves aqueous extract possessed significant contractile effect on rat uterus.

PHOSPHOLIPIDS AND PROTEIN CHARACTERIZATION OF BULL SPERMATOZOA FOLLOWING ELECTROPHORETIC SEPARATION

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Spermatozoa preparations are essential before any assisted reproduction techniques. Conventional spermatozoa preparation of either swim up or density gradient centrifugation produces damaged spermatozoa through ROS generation pathways. Thus, electrophoretic separation technique is studied as an alternative. This study used fresh semen from adult bulls which were acquired by artificial vagina and was conducted in two phases. Phase one involved voltage and separation time optimization. The voltages were 10, 20, 30, 40, 50 and 60V while separation time involved was 2, 4, 6, 8, 10 and 12 minutes. Result showed that optimum setting was 20V and 6 minutes for this system. This produced a spermatozoa population fraction of more than 80% viable and 70% motile with minimal DNA damage. In phase two, optimized setting are used. Phospholipids and protein from the fractions were extracted. Phospholipids composition were identified by using gas-chromatography mass spectrometry. While the extracted protein were purified by 2D-electrophoresis and identified by MALDI-TOF-TOF. Phospholipids concentrations and protein composition results were then compared with its negative and positive controls. Result indicated that test group had a higher concentration of phosphatidylinositol and phosphatidylcholine compared to both control groups. Two types uniquely expressed protein were identified - spermatozoa equatorial segment protein and lamin A/C. As a conclusion, this system is able to fractionate high quality spermatozoa at 20V and 6 minutes. The expressions of both phospholipids and proteins could be involved in this separation process.

DENSITY GRADIENT CENTRIFUGATION: EFFECTS ON SPERM KINETIC AND DNA INTEGRITY

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The goal of this study was to identify an alternative method of sperm separation using density gradient centrifugation in producing yields of select spermatozoa befitting for cryopreservation. Ejaculates from four mature bulls were extracted using artificial vagina for assessment of viability, motion of sperm trajectory and fertility potential through sperm kinetics study. Collection of spermatozoa samples from Charolais cross Kedah-Kelantan bulls were carried out at IBVK Pahang, Malaysia. The ejaculates were aliquoted into 2 equal groups: control and treatment. The control group proceeded with cryopreservation without initial sperm separation process. The treatment group were separated using a commercially available density gradient centrifugation (DGC) system. Bioxcell® (IMV, L'Aigle, France) was used as an extender for both control and treatment groups. Prior to analysis, samples from both groups were thawed at 37°C for 30 seconds. All samples were analysed for sperm kinetic parameters, viability and severity of DNA fragmentation. The kinetics assessment involved velocity and progression analysed by computer aided sperm analysis (CASA). Eosin-Nigrosin Staining technique was used to assess the percentage of retrieved viable spermatozoa. Results indicated that the changes in kinetic parameter values were significant except for spermatozoa straightness (STR) Spermatozoa viability had also increased by 26.2% following the treatment. DNA Fragmentation Index (DFI, %) revealed the treatment group recorded a significantly

small DFI value. Our findings suggest that the use of commercial DGC before cryopreservation would increase the probability of obtaining higher quality spermatozoa after cryopreservation.

SPERM KINETIC: EFFECT OF THAWING RATES ON POST-THAWED MAGNETIC-ACTIVATED SPERM SORTED

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Sperm preparation and thawing rates contribute to the overall outcome of post-thawed semen quality. Preselected sperm using Magnetic-Activated-Cell-Sorting System (MACS) was studied against various thawing rates. A total of six fresh ejaculates obtained from adult bulls Piedmontese-breed. The semen were pooled, diluted in Bioexcel, incubated and subjected to MACS semen preparation before cryopreserved. Sperm kinetic and viability of pre and post-thawed semen was conducted using Computer-Assisted Semen Analysis (CASA) System and eosin-nigrosin staining respectively. Cryopreserved semen was divided into equal groups for five thawing rates. These thawing rates include 20°C 13sec, 37°C 30 sec, 40°C 7sec, 60°C 6sec and 80°C 5sec. Results indicated that thawing rates did not significantly changed motility percentage but influenced progression (wobble-WOB, straightness-STR, linearity-LIN), velocity (average path velocity-VAP, straight line velocity-VSL, curvilinear velocity-VCL) and viability. The contribution of magnetic separation and various thawing rates were more on progression compared to velocity. Increased thawing rates has increased WOB (37°C 30sec- 7.85%, 80°C 5 sec - 11.87%) and LIN (37°C 30sec- 6.79%, 80°C 5 sec - 12.8%) but reduced STR (40°C 7sec - 2.78%, 60°C 6sec - 2.48%). Velocity (VCL) was changed significantly at 37°C 30 sec only. Increasing thawing rates has reduced sperm viability (20°C 13sec - 31.38%; 40°C 7sec - 18.6%) too. As a conclusion, optimum thawing rates and magnetic-activated sperm sorting determine sperm kinetic. A suitable combination of sperm kinetic parameters would ensure a higher percentage of fertilisation rates.

THE CHEMOPREVENTIVE EFFECT OF *Piper betle* IN AZOXYMETHANE-INDUCED COLON CANCER RATS

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Introduction: Many herbal plants in Malaysia have been shown to have chemopreventive effect which is mainly attributed to antioxidant compounds they contain. In this study, we investigated the chemopreventive effect of *Piper betle* (PB) or known as "sireh" in rats induced with colon cancer using azoxymethane (AOM). AOM is known to induce the development of aberrant crypt foci (ACF) in mice and rats indicating an early lesion of colon cancer. Several biomarkers are expressed during the early stages of colon cancer including β -catenin protein.

Methods: Rats were divided into four groups : control (normal saline, NS + dH₂O), AOM, PB, and AOM + PB. AOM group was administered with 15mg/kg azoxymethane while control group was administered with 1ml/kg NS once weekly for two weeks. PB (75mg/kg body weight) was forced-fed to rats a week after the second dose of AOM and NS. Rats were sacrificed at week 8. Colon tissues were removed and immunohistochemistry staining of β -catenin protein was performed.

Results: β -catenin is highly expressed in AOM group (75% of cells were stained strongly) but treatment with PB suppressed the expressions of β -catenin (33%) when compared to control and AOM groups.

Conclusion: PB may be a potential chemopreventive agent against colon cancer at the early stage by suppressing the expressions of β -catenin.

Keywords: colon cancer, azoxymethane (AOM), *Piper betle* (PB), chemopreventive, β -catenin

INTERACTIONS OF DIETARY PHYTOCHEMICALS ON PROLIFERATION OF HUMAN COLON CANCER CELLS

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Introduction: Recently, evidence is emerging that combination of dietary phytochemicals may be more effective than isolated compounds. However, there is only little information regarding the possible interaction among these bioactive compounds in cancer prevention. Thus, the objective of this study is to determine the effect of [6]-gingerol, γ -tocotrienol (GTT), epigallocatechin gallate (EGCG) and hydroxychavicol (HC) combinations on human colon cancer cell lines, HT 29 (Stage II), COLO 320 (Duke's C), and SW 837 (Stage IV).

Methods: MTS assay was performed to determine the antiproliferative and cytotoxicity effect of each compound on cells. Then the cells were treated with the respective compounds under a certain range namely, HC and GTT at 0-100 μ g/ml while EGCG and [6]-gingerol at 0 – 300 μ g/ml. The treatment mixture was prepared based on the IC₅₀ of each isolated compound. The interaction value was calculated based on analysis with isobologram.

Results: We obtained IC₅₀ of all compounds on all cell lines, except for EGCG on SW 837. Combination of [6]-gingerol: GTT showed synergistic effect (0.89 ± 0.02 , $P < 0.05$), while the rest of the combination showed antagonistic effect ($P < 0.05$). For COLO 320, combination of [6]-gingerol: EGCG showed additive effect (1.00 ± 0.01 , $P < 0.05$) and the other five combinations showed antagonistic effect ($P < 0.05$). Interaction value for combination of HC:GTT and [6]-gingerol:GTT showed synergistic effect (0.81 ± 0.19 and 0.77 ± 0.10 , $P < 0.05$).

Conclusion: Synergistic effects were shown by combination of [6]-gingerol:GTT on HT 29 and SW 837 and HC:GTT on SW 837. Meanwhile, additive interaction was observed in [6]-gingerol: EGCG combination on COLO 320. Other combinations showed antagonistic effect. Thus, we conclude that combining compounds does not only guarantee synergism, but also may diminish the efficacy of certain compounds on cells.

A GENOME-WIDE METHYLATION ANALYSIS OF BREAST CANCER

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Introduction: Breast cancer is the commonest cancer among women for the last ten years in Malaysia. It is a serious health concern and the prevalent cause of death among women which accounts for more than 410,000 deaths each year. DNA methylation is a known epigenetic marker which plays a critical role in controlling genes activities. Previous studies showed that DNA methylation is one of the early events that will contribute to the tumour progression. Hypermethylation is associated with gene repression and genomic instability through silencing of the DNA repair genes and compaction of chromatin. Hypomethylation is related with gene reactivation and chromosomal instabilities. This study is carried out to investigate DNA methylation landscapes in breast cancer.

Methods: DNA was extracted from representative fresh frozen primary breast tumours tissues and normal breast tissues followed by bisulphite conversion that converts unmethylated cytosine to uracil. DNA methylation profiling was carried out using the Illumina Infinium® HumanMethylation27 BeadChip (Illumina, USA).

Results: A total of 1270 significant CpG islands sites with aberrant DNA methylation were identified. Among these sites, 1255 of the CpG loci were found to be hypermethylated whereas 15 CpG loci are hypomethylated. Pathway analysis showed that most of these genes are involved in cell cycle regulation including DNA repair, chromatin remodelling, DNA replication, kinetochore assembly and chromosome separation that may lead to tumour formation and progression.

Conclusion: This study has successfully characterised breast cancer through identification of the epigenetic profile of significant methylated genes. These genes may be potential biomarkers for the early detection of breast cancer.

ANTIOXIDANT AND ANTI-TUMOUR PROPERTIES OF *Zingiber officinale* AGAINST HEPATOMA CELLS

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Introduction: Ginger oleoresin was shown previously by our group to have antioxidant, anti-tumour, and anti-inflammatory properties in liver cancer-induced rats. The objective of this study was to determine the antioxidant and anti-tumour properties of water based ginger extract on hepatoma HepG₂ cells.

Methods: The antioxidant effect of water based ginger extract was tested using DPPH (1,1-diphenyl-2-picryl-hydrazyl) assay. The ability of ginger extract at various concentrations (0 - 9 mg/ml) to inhibit the growth of hepatoma HepG₂ cells was conducted using MTS tetrazolium assay.

Results: Water based ginger extract was able to scavenge DPPH radicals as potent as BHT (Butylatedhydroxytoluene) but lesser than ascorbic acid. It also inhibited the growth of HepG₂ cells dose dependently with an IC₅₀ of 2 mg/ml which is higher than the IC₅₀ for ginger oleoresin (0.5 mg/ml).

Conclusion: Water extract of ginger displays high antioxidant activity and inhibits the growth of liver cancer cells (HepG₂).

INTERACTIONS OF PHYTOCHEMICALS COMBINATIONS INHIBIT GROWTH OF 1321N1, SW1783 AND LN18 GLIOMA CANCER CELLS

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Introduction: Phytochemicals is suggested to play a crucial role in modulating various cellular signaling events in cancer cells. In this report, we investigated the interaction in cell culture of five individual phytochemical compounds through the use of an isobologram.

Methods: The compounds, tocotrienol rich fraction (TRF), gamma-tocotrienol (GTT), 6-gingerol (GING), epigallocatechin gallate (EGCG), asiaticoside (AC), hydroxychavicol (HC) were tested for cytotoxicity on glioma cell lines 1321N1 (Grade II), SW1783 (Grade III) and LN18 (Grade IV) in culture by [3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxy-phenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt] MTS assay. With the exception of AC, nine combinations of compounds were tested and the interactions of each combination were evaluated by using the combination index (CI).

Results: The cytotoxicity of combined compounds varies between different grades of glioma cancer cells. In 1321N1 cells, the combination of GING + GTT and GTT + HC exhibited a strong synergistic effect with CI=0.60 and CI=0.55 respectively. The combination of EGCG + HC (CI=0.54) and GTT + HC (CI=0.51) gave the highest synergistic interaction in SW1783 cells. While in LN18 cells, strong synergism interaction were observed in EGCG + GING, EGCG + HC and EGCG + GTT combinations with CI value ranging from 0.43-0.58. Overall, combination between GTT and HC seemed to be most effective throughout grade II, grade III and grade IV cell lines, where the interaction were shown to be strong synergism for 1321N1 (CI=0.55), SW1783 (CI=0.51) and synergism for LN18 (CI=0.73). Interestingly, combination of TRF and EGCG produced an antagonistic interaction (CI>1.0) in glioma cell lines.

Conclusion: Our current data suggests that the combination between EGCG, GTT and HC has potential as preventive/therapeutic compounds for grade II, III and IV glioma cancer.

PENGEKSPRESAN SMA, CD10 DAN SMMHC PADA TUMOR PAYUDARA EPITELIUM DAN FIBROEPITELIUM MENGGUNAKAN TEKNIK TISU MIKROARAY

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Pengenalan: Aktin otot licin (*smooth muscle actin*, SMA) merupakan penanda molekul yang digunakan di kebanyakan makmal diagnosis bagi mengesan komponen mioepitelium. Kajian ini dijalankan untuk mengesan pengekspresan SMA, CD10 dan rantai berat miosin otot licin (*smooth muscle myosin heavy chain*, SMMHC) pada komponen mioepitelium, epitelium dan stroma bagi tumor payudara epitelium dan fibroepitelium serta menentukan hubungan ekspresi penanda-penanda molekul ini dengan data patologi klinikal.

Kaedah: Pewarnaan imunohistokimia dijalankan ke atas blok tisu mikroarray (TMA) yang terdiri daripada 16 kes payudara benigna, 69 karsinoma invasif, 110 fibroadenoma dan 78 tumor filodes menggunakan penanda molekul SMA, CD10 dan SMMHC.

Hasil Kajian: SMA menunjukkan sensitiviti paling tinggi dalam mengesan sel mioepitelium berbanding CD10 dan SMMHC (97.9% vs 86.5% vs 78.9%). Nilai spesifisiti, prediktif positif dan negatif bagi SMA masing-masing adalah 92.2%, 92.6% dan 97.8%. manakala bagi CD10 dan SMMHC adalah 87.3% vs 100%, 87.2% vs 100% dan 86.6% vs 82.6%. Kesemua tumor payudara invasif tidak menunjukkan pewarnaan pada sel mioepitelium. Sebanyak 3/65 (4.6%) kes menunjukkan pewarnaan SMA positif pada sel epitelium dan mempunyai hubungan signifikan dengan tumor Gred 3 ($p=0.016$) dan ER negatif ($p=0.003$). Positiviti SMA pada sel stroma juga menunjukkan hubungan signifikan dengan tumor Gred 3 ($p=0.022$) dan ER negatif ($p=0.004$). Manakala positiviti CD10 pada sel stroma meningkat dengan peningkatan peringkat tumor invasif ($p<0.001$). Pengekspresan SMA, CD10 dan SMMHC pada sel stroma juga meningkat dengan malignansi tumor filodes, tetapi tidak signifikan.

Kesimpulan: SMA, CD10 dan SMMHC didapati mengesan sel mioepitelium dengan baik di mana SMA menunjukkan sensitiviti paling tinggi dan SMMHC lebih spesifik. Penanda-penanda molekul ini juga berguna bagi tumor filodes kerana pengekspresannya di sel stroma meningkat dengan malignansi tumor filodes.

MENGENALPASTI HUBUNGAN RESEPTOR ANDROGEN DAN KARSINOMA PAYUDARA MELALUI KAEDAH MIKROARAY

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Pengenalan: Peranan penentuan reseptor estrogen dan progesteron dalam pengurusan kanser payudara telah biasa kedengaran dan digunakan tetapi kepentingan ekspresi reseptor androgen masih baru diperkenalkan. Tujuan kajian ini dijalankan adalah untuk melihat hubungan pengekspresan reseptor androgen dengan faktor klinikal patologi serta menentukan hubungan ekspresinya dengan reseptor estrogen dan progesteron dengan menggunakan kaedah tisu mikroarray.

Metodologi Kajian: Sebanyak 82 sampel payudara yang terdiri dari 62 karsinoma duktal invasif (*Invasive Ductal Carcinoma*, IDC) dan 20 kes tisu payudara benigna dari tahun 2007 hingga 2010 diperolehi daripada Jabatan Patologi, PPUKM. Konstruksi tisu mikroarray (TMA) ke atas sampel kajian dilakukan dengan menggunakan MTABooster (Alphelys Plaisir, Perancis) dengan diameter 0.6mm. Blok TMA seterusnya dipotong dan pewarnaan imunohistokimia dilakukan. Reseptor androgen diinterpretasikan sebagai positif apabila $\geq 10\%$ sel nukleus menunjukkan pewarnaan perang.

Hasil Kajian: Kajian ini mendapati ekspresi reseptor androgen sebanyak 41.9% (26/62) bagi kes IDC menunjukkan pewarnaan positif berbanding 65% (13/20) bagi kes benigna. Namun tiada hubungan

signifikan didapati di antara ekspresi reseptor androgen dengan faktor klinikal patologi termasuk umur pesakit, pengkelasan gred histologi dan status nodus limfa.

Kesimpulan: Reseptor androgen boleh menjadi penanda molekul berguna pada diagnosis sampel kanser payudara. Walau bagaimanapun kajian lanjutan perlu untuk menyokong hasil kajian ini.

EFFECTS OF GST ACTIVITIES AND GSH LEVELS BY PTEROSTILBENE AS A CHEMOPREVENTIVE AGENT ON HT-29 COLON CANCER CELL LINE

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Introduction: Drug metabolizing enzymes are present in most epithelial of human gastrointestinal tract to protect against xenobiotics. Pterostilbene, an analogue of resveratrol, has been demonstrated the anticancer, antioxidant, anti-inflammatory activity and other potential health benefits. This study was conducted to investigate the potential of pterostilbene as a chemopreventive agent using HT-29 colon cancer lines as a model to study the modulation of GST activities and GSH levels.

Methods: Firstly, we investigated the optimum dose for treatment of pterostilbene on HT-29 cell line using MTT assay. Then, the effects of pterostilbene (12.5, 25.0 and 50.0 μ M) towards GST activity and GSH level were determined using GST and Ellman assays respectively.

Results: Pterostilbene (0 -100 μ M) showed no reduction of the viable cell to 50%. We also revealed that 50.0 μ M of pterostilbene was suitable as the highest concentration of treatment because it retained approximately 80% of cell viability. Treatment of pterostilbene increased GST activities significantly ($p < 0.05$) compared to negative control at 12.5, 25.0 and 50.0 μ M that were reported as 4034.24 ± 183.55 , 4170.59 ± 145.25 and 4169.63 ± 154.07 nmol/min/mg protein respectively. In addition, treatment of 25 μ M pterostilbene increased the GSH level significantly ($p < 0.01$) compared to negative control with value of 74.23 ± 4.60 nmol/mg protein.

Discussion: Induction of phase 2 enzymes such as glutathione s-transferase (GST) and its thiol conjugate, glutathione (GSH), enhances detoxification of carcinogens, thus carcinogenesis can be prevented.

Conclusion: Pterostilbene can be developed as a potential chemopreventive agent by its modulation of drug metabolizing enzymes.

TOCOTRIENOL RICH FRACTION (TRF) SUPPRESSED THE FORMATION OF ABERRANT CRYPT FOCI (ACF) IN AZOXYMETHANE (AOM) INDUCED COLON CANCER F344 RATS

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Introduction: Colon cancer is the second most common cancer in Malaysia. Aberrant Crypt Foci (ACF) is believed to be the earliest identifiable morphological changes that occur in the colonic mucosa of human during the progression of colon carcinogenesis. ACF is also seen in colon carcinogenesis induced by Azoxymethane (AOM) in rats. Many dietary agents rich in polyphenols have been shown to have chemopreventive effect against cancer. The aim of this study is to determine the chemopreventive effect of Tocotrienol Rich Fraction (TRF) in reducing the number of ACF in rats.

Methods: 72 Male F344 rats were divided into 4 groups: 2 control groups: rats administered with Olive Oil and TRF, and 2 treatment groups: AOM induced colon cancer group + Olive Oil and AOM + TRF. The rats were treated for 2 months (Phase 1) and 6 months (Phase 2). At week 8 and 24, all rats were sacrificed. The colon was longitudinally opened and flushed with normal saline and fixed in formalin for 24 hours. The quantification of ACF was done by staining colonic mucosa of rats with 0.02% methylene blue and viewed under the microscope.

Results: AOM groups showed increased number of ACF in both Phase 1 and Phase 2 groups. Treatment of TRF reduced the number of ACF significantly in Phase 2 ($P < 0.05$) group but not in Phase 1 group.

Conclusion: TRF has a huge potential as chemopreventive agents in inhibiting the formation of ACF at the early stage of colon carcinogenesis.

CONSTRUCTION OF A 3-DIMENSIONAL HUMAN SKIN EQUIVALENT FOR CHEMICAL TESTING

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Introduction: Recently the use of animals for chemical or cosmetic products safety testing has come under scrutiny. Hence, human skin equivalent has become increasingly important as an alternative to replace animal testing. In our study, we aimed to produce a 3 dimensional human skin equivalent for chemical or cosmetic testing.

Methods: We fabricated a PLGA scaffold to mix with human plasma, collagen solution and thrombin seeded with foreskin keratinocytes and fibroblasts to construct the skin equivalent. Various fibroblasts seeding density were tested in order to produce a mature skin equivalent. Culture duration of skin equivalent was evaluated. Histological evaluation (hematoxylin and eosin staining) was carried out to examine the structure of the skin equivalent.

Results: We found that two weeks cultured skin equivalent was able to form dermis and stratified epidermis with keratin layer. Keratin layer is required to provide protection towards skin and it is needed to make the skin equivalent suitable for testing. Both 100,000 and 200,000 fibroblasts seeding density were able to produce a skin equivalent with mature keratin layer.

Conclusion: Two weeks human skin equivalent cultured at air-liquid interface with 100,000 or 200,000 fibroblasts incorporated with keratinocytes, PLGA, collagen and thrombin was able to form a mature skin equivalent.

IN VIVO IMAGING WITH MICROCOMPUTED TOMOGRAPHY USING GOLD NANOPARTICLES FOR MESENCHYMAL STEM CELLS TRACKING IN A RAT MODEL

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Introduction: Mesenchymal stem cells (MSC) have been widely investigated for cellular therapies including tissue repair and tissue regeneration. In vivo imaging is important in understanding the role and mechanism of MSC in tissue repair and regeneration throughout the process. In this study, we want to assess the efficiency of MSC labelling with gold nanoparticles and to track the labelled cells following subretinal injection in a rat model without rat sacrifice.

Method: The cultured cells and the gold nanoparticles are prepared separately and incubated together for 22 hours. The cells are then assessed; in particular for cellular viability and cell uptake with phase contrast microscopy and live/dead staining. The cells are then injected subretinally into the eyes of a rat model and microlocalised using a microcomputed tomography (microCT) at day 1, 14 and 30. Histology is then analysed using a transmission electron microscopy (TEM) to confirm the subretinal location.

Results: The uptake for the gold nanoparticles by the cell is good and the cell proliferation is not affected by the loading with gold nanoparticles. The percentage of viability of cells after loading is

89.80%-95.04%. MicroCT showed C-shaped hyperdensity area at the site of injection of gold loaded MSC and TEM confirmed the subretinal location of cell.

Conclusion: Gold nanoparticles can be used to label and track MSC after subretinal injection and can be traced in vivo with microCT over time without sacrificing the rats.

EFFECTS OF AQUEOUS EXTRACT OF *Carica papaya* LINN. LEAVES ON PLATELETS OF SPRAGUE DAWLEY RATS

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Introduction: Papaya (*Carica papaya* Linn.) leaves are known worldwide for its nutritional and medicinal values. The potential of papaya leaves formulation in palm oil to treat dengue haemorrhagic fever has led our study to investigate the effects of aqueous extract of *Carica papaya* leaves (CPL) on platelet count, bleeding time, plasma thrombopoietin level and platelet morphology.

Method: A total of 24 male Sprague Dawley rats were divided into four groups of: normal saline control, positive thrombopoietin (TPO) control, CPL 100 mg/kg and CPL 300 mg/kg. CPL supplement and normal saline were given by oral gavages while TPO was injected intraperitoneally for 10 days. Blood was collected for platelet count, plasma thrombopoietin level measurements and platelet morphology. Tail bleeding time was determined before the rats were sacrificed.

Results: There were significant ($p < 0.05$) increase in mean platelet counts on day 4 and 10 after treatment with CPL 100 mg/kg and on every two days with CPL 300 mg/kg and TPO treatment compared to baseline mean platelet counts. On the other hands, rats fed with CPL 100 mg/kg and CPL 300 mg/kg extracts also showed a significant ($p < 0.05$) reduction in tail bleeding time. The platelet morphology of all groups was similar to each other and to negative control but there were some **rouleaux formation** and acanthocytes with TPO and CPL treatment.

Discussion: Results suggest the beneficial effect of the CPL extract in preventing excessive bleeding in animals.

Conclusion: CPL extracts have potential to stimulate platelets production and functions.

PROLONGED CONSUMPTION OF REPEATEDLY HEATED SOY OIL CAUSES BLOOD PRESSURE ELEVATION WITH INCREASED INFLAMMATION IN RATS

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Introduction: Repeated heating of cooking oil promotes lipid peroxidation that might induce inflammation, causing an increased risk of hypertension. This study aimed to investigate the role of inflammation in the blood pressure raising effect of repeatedly heated soy oil in rats.

Methods: Male Sprague-Dawley rats were divided into four groups: control, fresh soy oil (FSO), five-time-heated soy oil (5HSO), and ten-time-heated soy oil (10HSO). Feeding duration was six months. Blood pressure was measured at the beginning and monthly using tail-cuff method. Plasma prostacyclin (PGI₂) and thromboxane A₂ (TXA₂) were measured prior to treatment and at the end of the study. After six months, the rats were sacrificed and the aortas were dissected for immunohistochemical analyses on vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1).

Results: Blood pressure was increased significantly in 5HSO and 10HSO groups. FSO maintained blood pressure throughout the study. Plasma TXA₂/PGI₂ ratio was increased significantly in the 5HSO and 10HSO groups compared to the control and FSO groups. Endothelial VCAM-1 and ICAM-1

expressions were significantly increased in 5HSO and 10HSO groups. FSO group showed no significant difference in the prostanoids ratio and adhesion molecules expressions compared to the control.

Conclusion: Prolonged consumption of repeatedly heated soy oil increases blood pressure, which may be due to the increased inflammatory responses, leading to disturbance in the prostanoids productions.

THE EFFECT OF COMBINATION STUDIES BETWEEN STILBENOID FROM *Shorea gibbosa* AND VANCOMYCIN AGAINST METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)

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Introduction: The aim of this study is to determine the combination effects of stilbenoids from *Shorea gibbosa* with vancomycin against methicillin-resistant *Staphylococcus aureus* (MRSA).

Methods: A total of nine pure compounds, 5 stilbenoid dimers ; ϵ -viniferin, ampelopsin A, balanocarpol, laevifonol and diptoinonesin G and 4 stilbenoid trimers; α -viniferin, johorenol A, ampelopsin E and vaticanol G were evaluated for their antibacterial activities against ATCC 33591 and HUKM clinical isolate. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) for each active compound were determined using serial microdilution and plate-streak technique. Combination effects of stilbenoids with vancomycin against MRSA were evaluated using checkerboard assay to determine their fractional inhibitory concentration (FIC) index values.

Results: The MIC value of α -viniferin on both MRSA strains was 0.1 mg/ml whereas that of johorenol A on ATCC 33591 and HUKM strain was 0.1 mg/ml and 0.2 mg/ml, respectively. The MIC values of ampelopsin E and vaticanol G were higher than 0.4 mg/ml. Out of five stilbenoid dimers, only ϵ -viniferin was capable of inhibiting the growth of both MRSA strains at MIC 0.4 mg/ml. The MBC value of ϵ -viniferin, α -viniferin and johorenol A showed bacteriostatic action against MRSA. The FIC index value of ϵ -viniferin and α -viniferin in combination with vancomycin showed additive effect ($0.5 < \text{FIC} \leq 2.0$) against both MRSA strains. Johorenol A-vancomycin combination against HUKM strain was also additive but it showed synergistic interaction with vancomycin against ATCC 33591 ($\text{FIC} < 0.5$).

Conclusion: Stilbenoid compounds from *Shorea gibbosa* has anti-MRSA activity and huge potential as an alternative phytotherapy in combating MRSA infection.

OPTIMIZATION OF PROTEIN FROM METHICILLIN-RESISTANT *Staphylococcus aureus* (MRSA) AFTER TREATMENT WITH QUERCUS INFECTORIA FOR 2-D GEL ELECTROPHORESIS

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Introduction: The widespread outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) has been an important clinical and epidemiological problem in hospital environments. The emergence of vancomycin-intermediate *S. aureus* and, more recently, vancomycin-resistant *S. aureus* is of further concern.

Objective: The objective of this study is to determine the optimum concentration of sample protein from MRSA after treatment with acetone extract of *Quercus infectoria*. *Q. infectoria* is an oak tree of the family Fagaceae in which its twigs develop galls ('biji manjakani') resulting from the deposition of eggs by *Cynips gallae tinctoriae* wasp.

Methods: Comparison of the protein expression profile (PEP) between the treated MRSA and untreated strain as control was obtained using 2-dimensional gel electrophoresis. The minimum inhibitory concentration (MIC) value of acetone extract of galls from *Q. infectoria* against two strains of MRSA; ATCC 33591 and PPUKM clinical isolate was determined by broth microdilution method.

Results & Discussion: MIC values of acetone extracts against both strains of MRSA were 0.3125 mg/ml compared to 0.00195 mg/ml to that of vancomycin. The optimum concentration of MRSA protein that produced the best resolution was 100 µg. Manifold technique was observed to produce a better resolution gel and greater number of spot compared with the strip holder technique. This study showed that there were 7 protein spots that represented the increased in the protein expression of more than 2-fold in the MRSA treated with acetone extract of galls *Q. infectoria* compare to the untreated group.

Conclusion: This preliminary study on the PEP of *Q. infectoria* gal extract-treated MRSA may provide an insight of its antimicrobial mechanism which could lead to the development of a new effective regimen for the treatment of MRSA infections.

INVESTIGATION OF THE HEAVY METAL CONTENT AND PRESENCE OF BACTERIA IN HERBAL SLIMMING PRODUCT

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Introduction: The increase rate in obesity/overweight, the phenomenon of fat phobia as well as the increased practice of herbal medicine particularly in Malaysia have lead to the emergence of herbal slimming products. However, numerous of bacteria and heavy metal contaminations are often found in herbal products due to the irregular handling practices.

Methods: Ten different brands of products (labeled as A-J) were investigated. Determination of seven heavy metals content (As, Cd, Pb, Co, Cr, Cu and Zn) was analyzed by Inductively Coupled Plasma-Mass Spectrometry (ICP-MS). Determination of bacteria presence was carried out by counting the total aerobic count, while the identification of bacterial isolates by the macroscopic and microscopic observation, biochemical tests and the use of commercial kits (Mircrogen GN-ID A + B and API 20 E).

Results: All heavy metal contents in the analyzed samples were under the standard limitation by Drug Control Authority (DCA) and Health Canada. However, sample A contained the highest total daily intake of heavy metals. Order of total aerobic count was sample H> G> A> B> C> F> E, I and J, whereas G and H were exceeded the standard total aerobic count by DCA. A total of nine isolates of *Bacillus* sp. and ten isolates of Gram-negative bacteria were found. Among them, those food poisoning causing bacteria, such as *Bacillus cereus* and *Pseudomonas aeruginosa* were found in samples C and F respectively.

Conclusion: The heavy metal contents in ten herbal slimming products were below the standard limitations and seven of them were contaminated by the bacteria.

IN VITRO ACTIVITY OF TIGECYCLINE AND IMPENEM/TIGECYCLINE COMBINATION AGAINST CARBAPENEM-RESISTANT *Acinetobacterbaumanii*

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Introduction: *A. baumannii* is an opportunistic bacterium causing widespread nosocomial infection, and tends to be multi-resistant towards majority antibiotics. Tigecycline has a wide-range spectrum action of activity and is very active in vitro towards variety of resistant pathogens, including *A. baumannii*. The aim of this study was to evaluate the interaction effect of Imipenem/Tigecycline combination against four Carbapenem-resistant *A. baumannii* (CRAB) strains.

Methods: Minimal Inhibitory Concentration (MIC) for both antibiotics was determined using E-strip method. Checkerboard technique was employed using 96-well microtiter plate for determination of interaction effect between Imipenem and Tigecycline and to obtain Fractional Inhibitory Concentration (FIC) index value. Time kill (TK) study was performed to identify (if any) the presence of synergistic effects within the duration of 24 hours. Confirmation for the presence of carbapenemases genes was evaluated using PCR method.

Results: Results showed that the Imipenem MIC values were 32 µg/ml for all *A. baumannii* strains tested. However, the combination of Imipenem and Tigecycline demonstrated additive effect (FIC > 0.5-4) for all the strains and synergistic activity (decrement of > 2 log₁₀ CFU/ml) towards strains AC 34/07 (2.70 log₁₀ CFU/ml) and AC 32/06 (2.12, 3.58, 2.49 log₁₀ CFU/ml). Presence of *oxa-51* gene possibly indicates the mechanism of resistance exerted by CRAB isolates towards Imipenem.

Conclusion: The use of Imipenem with Tigecycline in combination has a better activity and capable of controlling CRAB infections. This interaction effect showed potential and importance in the development or modification of antimicrobial agent for application in the treatment of CRAB infection.

Keywords: CRAB; Tigecycline; Imipenem

GELAM HONEY INHIBITS THE EXPRESSION OF PRO-INFLAMMATORY MEDIATORS iNOS, COX-2, TNF-α AND IL-6 IN CARRAGEENAN-INDUCED ACUTE PAW EDEMA IN RATS

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Introduction: Natural honey is well known for its therapeutic values and has been used in traditional medicine of different cultures throughout the world. The aim of this study was to investigate the anti-inflammatory effect of Malaysian Gelam honey in inflammation induced rats.

Methods: Paw edema was induced by subplantar injection of 1% carrageenan into the rat right hind paw. Rats were treated with NSAID Indomethacin (10mg/kg, p.o.) and Gelam honey at different doses (1 and 2 g/kg, p.o.) for two time points, 1 and 7 days. Paw tissues were collected to analyze the gene and protein expressions of inflammatory mediators such as: TNF-α, IL-6, iNOS and COX-2, using real time- PCR and Western Blot analysis.

Results: The results showed that Gelam honey was able to suppress the gene and protein expressions of iNOS, COX-2, TNF-α and IL-6 in inflamed rats paw tissues. Oral pre-treatment of Gelam honey at 2g/kg body weight in both time points (1 and 7days) showed significantly decreased expression of pro-inflammatory mediators which was almost similar to the effect of anti-inflammatory drug Indomethacin (NSAID).

Conclusion: Our results suggest that Gelam honey has anti-inflammatory effects by inhibiting the gene and protein expressions of inflammatory mediators. Gelam Honey is potentially useful for treating inflammatory conditions.

SEKALUNG PENGHARGAAN

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- Pengarah Institut Perubatan Molekul (UMBI)
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