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THE ROLE OF OXIDATIVE STRESS AND THE EFFECT OF ANTIOXIDANT (VITAMIN E & MELATONIN) IN THE DEVELOPMENT OF HYPERTENSION IN SPONTANEOUSLY HYPERTENSIVE RATS

PENYELIDIK

PROFESSOR DR. K.N.S. SIRAJUDEEN

PENYELIDIK BERSAMA

PROFESSOR HARBINDAR JEET SINGH

2012

RESEARCH TITLE : **The role of oxidative stress and the effect of antioxidant (Vitamin E & Melatonin) in the development of hypertension in spontaneously hypertensive rats**
Tajuk Penyelidikan

PROJECT LEADER : **Assoc. Prof.Dr.K.N.S.Sirajudeen**
Ketua Projek

PROJECT MEMBERS (including GRA) : 1. **Professor Harbindar Jeet Singh**
2.
Ahli Projek

PROJECT ACHIEVEMENT *(Prestasi Projek)*

ACHIEVEMENT PERCENTAGE			
Project progress according to milestones achieved up to this period	**0 - 50%**	**51 - 75%**	**76 - 100%**
Percentage			100%

RESEARCH FINDINGS		
Number of articles/ manuscripts/ books	**Indexed Journal**	***Non-Indexed Journal***
	1 (under review)	
Paper presentations	**International**	***National***
	2	4
Others (Please specify)		

HUMAN CAPITAL DEVELOPMENT

Human Capital	Number	
	On-going	Graduated
PhD Student		
Masters Student	1	
Undergraduate Students		
Temporary Research Officer		
Temporary Research Assistant		
Total	1	

Others (Please specify):
Mr. Arunkumar A/L Sundaram Pillay **(M.Sc)*** on the project entitled " Antioxidant status and the effect of tocotrienol rich fraction (TRF) supplementation on the antioxidant enzymes and development of hypertension in spontaneously hypertensive rats (SHR)".
(*Thesis submitted in December 2009 & waiting for viva)

EXPENDITURE (Perbelanjaan)

C

Budget Approved *(Peruntukan diluluskan)* : **RM 159,000.00**
Amount Spent *(Jumlah Perbelanjaan)* : **RM 158,970.46 (including Pending Q form bill)**

Balance *(Baki)* : **RM 29.54**
Percentage of Amount Spent : 99. 98 %
(Peratusan Belanja)

ADDITIONAL RESEARCH ACTIVITIES THAT CONTRIBUTE TOWARDS DEVELOPING SOFT AND HARD SKILLS
(Aktiviti Penyelidikan Sampingan yang Menyumbang Kepada Pembentukan Kemahiran Insani)

D

International

Activity	Date (Month, Year)	Organizer
(e.g : Course/ Seminar/ Symposium/ Conference/ Workshop/ Site Visit) - **2** **Details In the Appendix**		

National

Activity	Date (Month, Year)	Organizer
(e.g : Course/ Seminar/ Symposium/ Conference/ Workshop/ Site Visit) - **4** **Details In the Appendix**		

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

E —

RECOMMENDATION (Cadangan Penambahbaikan)

F

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

Hypertension has been increasingly linked with oxidative stress but its precise relationship remains unclear, particularly at the onset of hypertension in SHR. To examine the link between oxidative stress and hypertension, this study determined the levels of markers of oxidative stress, activities of antioxidant enzymes and mRNA expressions of primary antioxidant enzymes in the kidneys of spontaneously hypertensive rats (SHR) and Wistar-Kyoto rats (WKY) from the age of 4 weeks (prehypertensive) to 16 weeks (established hypertension in SHR). In addition, it also examined the effects of Vitamin E-Tocotrienol Rich Fraction (TRF-SHR), and melatonin (Mel-SHR) supplementation on these parameters from the prehypertensive age in SHR. After the measurement of systolic blood pressure (SBP) rats, aged 4-16 weeks, were sacrificed and the kidneys were collected and used for the estimation of oxidative stress markers. Systolic blood pressure was significantly higher from the age of 6 weeks in SHR. When compared with age matched WKY rats, renal Catalase (CAT) activity and mRNA levels were significantly higher and glutathione peroxidase (GPx) activity and mRNA levels were significantly lower in SHR from the age of 4 weeks onwards, and no differences were observed in other parameters studied. The reason for these is unclear and since they become evident before the actual rise in blood pressure it might be inferred that these alterations in some way (possibly with increased substrate availability) contribute to the development and maintenance of hypertension in SHR. Although TRF has been known for its antioxidant properties, compared with age matched non-supplemented SHR, SBP was only significantly lower at 6 weeks, but higher at 12 & 16 weeks in TRF-SHR and this despite decreases in the levels of Malnodialdehyde (MDA) and increased Total Antioxidant Status (TAS). Melatonin supplementation delayed the rate of rise in blood pressure in SHR, but the systolic pressure continued to be significantly higher in Mel-SHR when compared to normotensive rats. The effect of melatonin in increasing GPx and Glutathione-S-Transferase (GST) activities, and their relation in high blood pressure amelioration in SHR needs to be further investigated. Perhaps with the application of GPx or GST knock out normontensive mice or infusion of GPx or GST substances in hypertensive rats might better provide information.

Date : 16th March 2010
Tarikh

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

H

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.....

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Name:
Nama:

Signature:
Tandatangan:

Date:
Tarikh:

UNIVERSITI SAINS MALAYSIA
JABATAN BENDAHARI
KUMPULAN WANG PENYELIDIKAN FUNDAMENTAL
PENYATA PERBELANJAAN SEHINGGA 28 FEBRUARI 2010

Jumlah Geran	RM159,000.00	Ketua Projek	DR K.N.S. SIRAJUDEEN
Peruntukan 2006 (Tahun 1)	RM8,300.00	Tajuk Projek	THE ROLE OF OXIDATIVE STRESS AND THE EFFECT OF ANTIOXIDANT (VITAMIN E & MELATONIN IN THE DEVELOPMENT OF HYPERTENSION IN SPONTANEOUSLY HYPERTENSIVE RATS
Peruntukan 2007 (Tahun 2)	RM77,450.00	Tempoh	39 BULAN (NOV 2006 - 31 JAN 2010)
Peruntukan 2008 (Tahun 3)	RM52,550.00	No. Akaun	203/PPSP/6170021
Peruntukan 2009 (Tahun 4)	RM20,700.00		

Kwgan	Akaun	PTJ	Projek	Peruntukan Projek	Perbelanjaan Terkumpul sehingga Tahun lalu	Peruntukan Semasa	Tanggungan Semasa	Bayaran Tahun Semasa	Belanja Tahun Semasa	Baki Projek
203	11000	PPSP	6170021	21,000.00	23,338.50	(2,338.50)	-		-	(2,338.50)
203	14000	PPSP	6170021	-	-	-	-	-	-	-
203	15000	PPSP	6170021	-	-	-	-	-	-	-
203	21000	PPSP	6170021	4,000.00	5,580.78	(1,580.78)	-	2,520.88	2,520.88	(4,101.66)
203	22000	PPSP	6170021	-	-	-	-	-	-	-
203	23000	PPSP	6170021	500.00	-	500.00	-	-	-	500.00
203	25000	PPSP	6170021	-	-	-	-	-	-	-
203	26000	PPSP	6170021	-	-	-		-	-	-
203	27000	PPSP	6170021	131,500.00	113,182.30	18,317.70	4,336.00	5,576.00	9,912.00	8,405.70
203	28000	PPSP	6170021	-	-	-	-	-	-	-
203	29000	PPSP	6170021	2,000.00	3,680.00	(1,680.00)	-		-	(1,680.00)
203	35000	PPSP	6170021	-	-	-	-	-	-	-
				159,000.00	145,781.58	13,218.42	4,336.00	8,096.88	12,432.88	785.54

APPENDIX

International

Activity	Date (Month, Year)	Organizer
1. 4th International qPCR Symposium Industrial Exhibition and Application Workshops, Germany.	9-13th March 2009	Technical University Munchen, Freising-Weihenstephan, Germany
2. International Conference on Advances in Free radicals, Natural products, antioxidants and radioprotection in Health & 9th Annual Meeting of the Society of Free radical Research, India" at Hyderabad, India	11 -13th Jan 2010	Nizam's Institute of Medical sciences, Hyderabad, Davis Heart& Lung Research Institute, Ohio Sta

National

Activity	Date (Month, Year)	Organizer
1. 22nd Malaysian Society of Pharmacology & Physiology Scientific Meeting 2008".	5-6th April 2008	University Malaya, Kualalumpur
2. 13th national conference on Medical sciences	22nd-23rd May 2008	PPSP, Health Campus,USM
3. 7th Asian-Pacific Congress of Hypertension, Kualalumpur	19th-22nd Feb 2009 .	Malaysian Society of Hypertension
4. Glutathione Peroxidase Activity, Protein Abundance and mRNA Expression in the Kidney of Spontaneously Hypertensive Rats and Normotensive Wistar Kyoto Rats Ranging in Age from 4-16 Weeks. Symposium of USM Fellowship Holders 2009.	14-15th Nov 2009	USM, Penang, Malaysia

Conference presentations:

1. Age-related changes in antioxidant enzyme status in the kidneys of spontaneously hypertensive rats and normotensive rats. Arunkumar S, Lee Siew Keah, KNS Sirajudeen, HJ Singh. Presented in **22nd Malaysian Society for physiology and Pharmacology (MSPP) Meeting,** Universiti Malaya, Malaysia, 2008

2. Age-related changes in superoxide dismutase in the kidney of spontaneously hypertensive rats and normotensive rats. Arunkumar S, Lee SK, Sirajudeen KNS, Singh HJ. Presented in **13th National Conference on Medical Sciences,** USM, Malaysia, 2008.

3. Effect of Melatonin supplementation on blood pressure and renal oxidant/antioxidant status in spontaneously hypertensive rats. Lee Siew Keah, Arun Kumar, Rahimah Zakaria, KNS Sirajudeen, HJ Singh. **"7th Asian-Pacific congress of Hypertension 2009"** at Kualalumpur convention centre, Malaysia on 19th-22nd February 2009. p48

4. Comparison of AOE activities and expression levels in the kidney during the development of hypertension in SHR. Arunkumar, S, Lee, SK , Sirajudeen, KNS ,Singh, HJ. **"4th International qPCR Symposium & Industrial Exhibition & Application Workshop"** ,in Technical University of Munich, Physiology-Weihenstephan, Germany on 9 - 13th March 2009.

5. SK Lee, Arunkumar Sundaram, **KNS Sirajudeen,** HJ Singh.Glutathione Peroxidase Activity, Protein Abundance and mRNA Expression in the Kidney of Spontaneously Hypertensive Rats and Normotensive Wistar Kyoto Rats Ranging in Age from 4-16 Weeks. Symposium of USM Fellowship Holders 2009, USM, Penang, Malaysia 14-15 Nov 2009.

6. Siraludeen KNS, Arunkumar S, Lee SK, Singh HJ Oxidative stress markers and the effect of tocotrienol rich fraction supplementation in spontanesouly hypertensive rats as an **invited lecture** in **"International Conference on Advances in Free radicals, Natural products, antioxidants and radio protection in Health & 9th Annual Meeting of the Society of Free radical Research, India"** held on 11th -13th January 2010 at Hyderabad, India

Publication (International):

Lee SK , Arunkumar Sundaram , **KNS Sirajudeen** , HJ Singh Glutathione system in Young Spontaneously Hypertensive Rats (2010). **Journal of Physiology and Biochemistry** (Under review)

Journal of and

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Action	Manuscript Number	Title	Initial Date Submitted	Status Date	Current Status
Action Links	JPBY38	Glutathione system in Young Spontaneously Hypertensive Rats	09 Feb 2010	20 Feb 2010	Under review

Page: 1 of 1 (1 total submissions) Display 10 results per page.

<< Author Main Menu

Editorial Manager(tm) for Journal of Physiology and Biochemistry
Manuscript Draft

Manuscript Number: JPBY38

Title: Glutathione system in Young Spontaneously Hypertensive Rats

Short Title: Glutathione system in Young Spontaneously Hypertensive Rats

Article Type: Original Research

Section/Category: Cardiovascular Physiology - M.Pilar Lostao

Keywords: Glutathione; glutathione peroxidase; hypertension; SHR

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Corresponding Author's Institution:

First Author: Lee SK

Order of Authors: Lee SK; S Arunkumar; K.N.S. Sirajudeen, Ph.D; HJ Singh, Ph.D

Abstract: The glutathione (GSH) system plays a vital role in preventing oxidative stress, and an imbalance of oxidant/antioxidant system has been linked to the pathogenesis of hypertension. The aim of this study was to investigate the status of the GSH system in the kidney of spontaneously hypertensive rats (SHR). Components of the GSH system, including glutathione peroxidase (GPx), glutathione reductase (GR), glutathione-S-transferase (GST) and total GSH content, were measured in the kidneys of 4, 6, 8, 12 and 16 weeks old SHR and WKY rats. Systolic blood pressure of SHR was significantly higher from the age of 6 weeks onwards compared to age-matched WKY rats. GPx activity in the SHR was significantly lower from the age of 8 weeks onwards when compared to that in age-matched WKY rats. No significant differences were evident in the GPx-1 protein abundance and its relative mRNA levels, GR, GST activity and total GSH content between SHR and age-matched WKY rats. The lower GPx activity suggests of an impairment of the GSH system in the SHR, which might be due to an abnormality in its protein rather than non-availability of a cofactor. Its role in the development of hypertension in SHR however remains unclear.

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