UNIVERSITI TEKNOLOGI MARA

EFFECT OF EXERCISE ON TRB3 AND GLUT4 EXPRESSION FOLLOWING GLUCOSE LOADING IN CHRONIC LEPTIN TREATED RAT

SITI NURR ATIKA BINTI MOHD SANIF

Thesis submitted in fulfillment
of the requirements for the degree of
Master of Science

Faculty of Medicine

January 2016

CONFIRMATION BY PANEL OF EXAMINERS

I certify that a Panel of Examiners has met on 26th October 2015 to conduct the final examination of Siti Nurr Atika Binti Mohd Sanif on her Master of Science thesis entitled "Effect of exercise on TRB3 and GLUT4 expression following glucose loading in chronic leptin treated rat" in accordance with Universiti Teknologi MARA Act 1976 (Akta 173). The Panel of Examiners recommends that the student be awarded the relevant degree. The Panel of Examiners was as follows:

Mohd Hamim Rajikin, PhD
Professor
Faculty of Medicine, Physiology
Universiti Teknologi MARA
(Chairman)

Damayanthi Durairajanayagam, PhD
Senior Lecturer
Faculty of Medicine, Physiology
Universiti Teknologi MARA
(Internal Examiner)

Roland Gamini Sirisinghe, PhD
Professor
School of Medicine
Taylor's University
(External Examiner)

Siti Norashikin Mohd Tambeh
Lecturer
Faculty of Medicine, Physiology
Universiti Teknologi MARA
(Minute Taker)

SITI HALIJJAH BINTI SHARIFF, PhD
Associate Professor
Dean
Institute of Graduate Studies
Universiti Teknologi MARA
Date: 20 January 2016

AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student	:	Siti Nurr Atika Binti Mohd Sanif
Student I.D. No.	:	2011635786
Program	:	Master of Science (Sport Biochemistry)
Faculty	:	Medicine
Thesis Title	:	Effect of Exercise on TRB3 and GLUT4 Expression Following Glucose Loading in Chronic Leptin Treated Rat
Signature of Student	:	.....
Date	:	January 2016

ABSTRACT

Leptin affects insulin secretion and action through either a central or peripheral mechanism. It increases glucose metabolism and energy expenditure. Though overweight and obese individuals have been reported to have high circulating leptin level, these effects of leptin are not evident. Exercise, on the other hand, has been found to increase glucose uptake in these individuals. This study examined the effect of chronic leptin treatment and exercise on glucose homeostasis in Sprague-Dawley rats. Eight-week old rats were treated with either intraperitoneal injection of normal saline (Control; n=8), or leptin (60 μg/kg body weight/day; Leptin; n=8), or leptin and exercise (60 μg/kg body weight/day plus running on a treadmill every other day for 30 minutes at a speed of 30 m/min with 10° inclination; Leptin-exercise; n=8) or exercise only (running every other day for 30 minutes at a speed of 30 m/min with 10° inclination on a treadmill; Exercise; n=8) for six weeks. Following six weeks of treatment, glucose challenge was performed by intravenous infusion of 100 mg/ml of glucose for 5 minutes. Skeletal muscle tissues were collected at 0, 15, and 30 minutes respectively during the protocol for blood glucose, serum glucose, insulin, TRB3, GLUT4 protein and mRNA expression determination. Liver was harvested for TRB3 and GLUT2 protein and mRNA determination. Data were analyzed using One Way ANOVA with post-hoc analysis, and expressed as mean ± standard error of mean (SEM). Glucose clearance was delayed in the leptin group. This delay in glucose clearance might be associated with the significantly lower GLUT2 mRNA expression in the liver of leptin-treated rats. Leptin treatment also significantly reduced TRB3 mRNA levels in both muscle and liver tissues. More importantly, exercise reversed the leptin effects by promoting glucose clearance despite a significantly lower insulin peak, indicating a significant increase in insulin sensitivity. Exercise also significantly reduced TRB3 mRNA expression levels and increased GLUT4 mRNA levels in the muscle. In conclusion, six weeks of daily leptin administration resulted in delayed glucose clearance but concurrent exercise however prevented these effects of leptin by promoting glucose clearance and increasing insulin sensitivity.

(344 words)

ACKNOWLEDGEMENT

Alhamdulillah. I wish to thank Allah for giving me the opportunity to embark on my Masters program and for completing this long and challenging journey successfully. My gratitude and thanks to my supervisor Professor Harbindar Jeet Singh, and co-supervisors, Associate Professor Dr. Justin Vijay Gnanou and Dr. Brinnell Annette Caszo. Thank you for the support, patience and ideas in assisting me with this project. I also would like to express my gratitude to the staff of the Institute of Molecular Medicine Biotechnology for providing the facilities, knowledge and assistance.

My appreciation goes to Laboratories Animal Care and Use (LACU) of Faculty of Medicine, Universiti Teknologi MARA that provided the facilities and assistance during sampling. Special thank to my colleagues and friends for helping me with this project.

Finally, this thesis is dedicated to my loving husband and both my parents and in laws as well as my siblings for their continuous support and love. This piece of victory is dedicated to all of you.