UNIVERSITI TEKNOLOGI MARA

THE INFLUENCE OF TOCOTRIENOL ON THE DEVELOPMENT OF PREIMPLANTATION EMBRYOS AND PREGNANCY OUTCOME IN CORTICOSTERONE-TREATED MICE

NASIBAH AZME

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

Faculty of Medicine

December 2013

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 result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institutions or non-academic institution for any other degree of 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	: Nasibah Bt Azme
Student ID No.	: 2008426986
Programme	: Master of Science (MD 780)
Faculty	: Faculty of Medicine
Tittle	: The Influence of Tocotrienol on the Development of Preimplantation Embryos and Pregnancy Outcome in Corticosterone-Treated Mice
Signature of Student	: _____
Date	: December 2013

ABSTRACT

Tocotrienol (TCT), a component of vitamin E is a powerful antioxidant whereas corticosterone (CORT), a known prooxidant has been shown to impair the development of embryo and pregnancy outcome. This study aims to determine the effect of TCT supplementation on the quality and *in vitro* development of embryos and the pregnancy outcome in CORT-treated mice. In embryonic experiment, 5- to 6 weeks old female mice were divided into four groups of eight animals. They received CORT (10 mg/kg) intraperitoneal (ip) concurrently with TCT at the dose of 30, 60 and 90 mg/kg orally and the control group had 0.1 ml corn oil (ip) and orally for seven consecutive days. On Day 7, after superovulation and mating, animals were euthanized and embryos were flushed out from the fallopian tubes. The morphology and *in vitro* development of embryos were recorded. In pregnancy outcome experiment, 7- to 8 weeks old female mice were divided into similar groups and treatment for the first seven days of pregnancy were conducted as above with using TCT at 60, 90 and 120 mg/kg. On Day 7 of pregnancy, laparotomy was done to determine the number of implantation sites; to observe any resorption signs while litter sizes were measured at birth. It was found that TCT (90 mg/kg) improved the quality of embryo whereas TCT (60 mg/kg) increased the number of embryos that reached hatched blastocyst stage in CORT-treated groups. In addition to that, TCT (60 mg/kg) increased the implantation sites, whereas TCT (120 mg/kg) decreased the resorption percentage and increased the level of progesterone hormone towards control in CORT-treated pregnant mice. Tocotrienol supplementation in our study is able to reverse the CORT-induced adverse impact on all reproductive outcomes as mentioned above. The effect of TCT alludes further exploration to ascertain their mechanism.

ACKNOWLEDGMENTS

Alhamdulillah, praise be to Allah that this thesis finally sees its completion. With His Blessings, I have been able to experience lots of difficulties and new things during this degree of Master programme.

I would like to extend my sincere gratitude and deepest appreciation to a number of people, without them this thesis would not be possible. Particularly, to my supervisor, Associate Prof. Dr. Nuraliza Abdul Satar, for her invaluable guidance, support and encouragement throughout this research and preparation of thesis. My sincere thanks also dedicated to the members of my supervisory committee, Prof Dr. Mohd Hamim Rajikin and Associate Prof. Dr. Nor Ashikin Mohamed Noor Khan for their professional assistance, useful suggestions and extensive discussion throughout this research process. My thanks to Prof. Dr. Harbindar Jeet Singh, Coordinator of Physiology discipline and all lecturer in the discipline for their support and guidance.

I am also indebted to Mdm. Fara Fariza Jahar and staff of Tissue Culture Laboratory, Faculty of Dentistry, UiTM Shah Alam for helping and assisting me during embryonic culture work at the Faculty of Dentistry, UiTM. For one and half year duration doing culture work there, they have helped me a lot by giving technical and workplace support. My special thanks to staff of Animal House, Faculty of Pharmacy. UiTM Shah Alam. Thank you to staff of LACU, IMMB and CPDRL, Faculty of Medicine, UiTM Sg. Buloh for their help and for the usage of equipment in those labs.

My heartiest gratitude and special thanks also goes to my husband, Muhammad Jauhar Azmi and my son, Ziyad Faris for always there for me through thick and thin. Million thank for the endless love and encouragement. My special appreciation to my beloved parents, Ir. Azme Idris and and my entire siblings for their endless prayers, support, encouragement and sacrifice.

Finally, my appreciation goes to Faculty of Medicine, UiTM and Jabatan Pembangunan Sumber Manusia (JPbSM), UiTM for scholarship and financial support throughout this study.

TABLE OF CONTENTS