UNIVERSITI TEKNOLOGI MARA

EVALUATING RELATIONSHIP BETWEEN EXPRESSION OF IRS-1 GENE AND INSULIN RESISTANCE IN THE BRAIN OF GESTATIONAL DIABETES MELLITUS RAT

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Dissertation submitted in partial fulfilment of the requirements for the Bachelor of Pharmacy (Hons)

Faculty of Pharmacy

July 2016

Acknowledgement

I would like to express my deepest appreciation to my supervisors Dr Cini Mathew John and Dr Fazlin Mohd Fauzi for all of their guidance and support while I was conducting this project. Thanks also to Dr Cini's master students Ms. Intan and Ms. Siti Hajar who has helped me a lot particularly in teaching me on how to use all the equipments and also to handle the rats.

Then, I would like to thank my parents because they constantly give me moral support whenever I'm down and in need of motivation. Without their help, I do not know whether I can cope with all the challenges and difficulties that I have experienced throughout conducting this project. Lastly thank you to my friend Nazatul Shuhadah who was there for me and keep me strong throughout this project and also lending me a helping hand whenever I need it.

TABLE OF CONTENTS

Abstract

This study was conducted to see the link between IRS-1 and insulin resistance in the brain of GDM rats. GDM seems to have similar pathophysiology with Type 2 Diabetes Mellitus (T2DM). Defect in pancreatic beta cell function contributes to GDM due to insulin resistance during the gestation period. IRS-1 is a protein that plays an important role in the insulin signaling pathway. Defect in IRS-1 function will affect the signaling pathway, which contributes to insulin resistant in GDM. The study was done on female Sprague-Dawley rats and the rats were fed with high-fat sucrose diet, impregnated and induced with Streptozotosin and Nicotinamide on gestational day 0 (D0). The rats were tested for glycemic parameter (glucose) and gene affecting insulin signaling (IRS-1). GDM group showed significantly higher blood glucose than control group. Besides, low levels of IRS-1 in GDM group than control group indicate possible defect of insulin signalling. Our results suggest that, the expression of IRS-1 is down-regulated in the GDM rat group compare to control rats group. However, statistical analysis showed that the expression of IRS-1 in the rat brain for both groups is statistically insignificance.

CHAPTER 1

Introduction

1.1 Background of Study

Glucose is the main source of the energy in the brain. Glucose is a polar molecule and it cannot diffuse into or out of the intact monolayer of the endothelial cells lining brain capillaries due to the tight junction of the blood-brain barrier (BBB). BBB blocks the solute in the cell from crossing into the brain extracellular space. Hence, in order to fulfil the glucose demand of the brain, the substrate is transported via a transporter protein (Shah et al., 2012).

IRS-1 protein plays an important role in the insulin-signaling pathway in the cells. Insulin signaling will begin on the surface of the cells where insulin binds to the receptor (transmembrane tyrosine kinase receptor) which causes the autophosphorylation and activation of the insulin receptor (IR). The activated receptor will induce the phosphorylation of several adopter molecules, including IRS proteins (Colomiere et al., 2010).

The phosphorylation of IRS-1 will lead to the recruitment of effectors such as phosphoinositide 3-kinase (PI3K). The activation of the PI3K will lead to the