UNIVERSITI TEKNOLOGI MARA

Evaluating Immune Responses of Nicotinamide Supplementation on Muscle Wasting in Type II Diabetic Rats

MUHAMMAD HAKIM BIN MAHMUD

Dissertation submitted in partial fulfillment of the requirement for the degree of

Bachelor of Pharmacy (Hons)

Faculty of Pharmacy

JUNE 2014

ACKNOWLEDGEMENT

All the praise to Almighty god, ALLAH S.W.T as final year project can be done successfully in given time. I would to convey my greatest gratitude to ALLAH.S.W.T the one who has given me health, strength, ability, time and ideas to complete this study. My heartfelt thank goes to my supervisor, Mdm Cini Mathew John for her fully encouragement and dedication. Her valuable ideas, suggestion, comments and advices also help throughout the process in completing this study.

I would like to express my special thanks to my parents Mahmud bin Mat Zin and , and my friend Muhammad Ridzuan Ramli for encouraging and inspiring me. Special thanks is also given to postgraduate students in antioxidant lab and tissue culture lab of Faculty Pharmacy who are give me a hand while doing lab work and sharing knowledge.

TABLE OF CONTENT

ABSTRACT

Diabetes Mellitus has many complications such as neuropathy and muscle wasting. Muscle wasting is thought associated with activation of the ubiquitin-proteasome proteolytic (UPP) pathway and presence of proinfammatory cytokines in muscle. From the previous study nicotinamide supplementation had been proved in lessen muscle wasting. So we hypothesized that nicotinamide helps in reducing musle wasting. We evaluate the association of proinflammatory cytokine such as interleukin-4, tumor necrosis alpha and interferon gamma and antioxidant agent which is glutathione with muscle wasting in STZ+NA induced diabetic rats after injecting nicotinamide of different dose (NA 50mg, NA 100mg, NA 200mg). After 4 weeks, concentration interferon gamma and tumor necrosis factor alpha showed decreasing in STZ+NA induced diabetic rats while interleukin-4 had no result. Nicotinamide also improves oxidative stress as glutathione level is decrease after forth weeks which indicate there is no or less oxidative stress presence in the STZ+NA induced diabetic rats.

CHAPTER 1: INTRODUCTION

Diabetes or diabetes mellitus (DM) is a condition in which the body cannot use glucose normally. It is also a group of diseases characterized by high levels of blood glucose resulting from defects in producing insulin by the pancreatic beta cells or insulin resistance or both. DM is a chronic and non-communicable disease that has reached epidemic proportion and becomes disabled and killers (Ding, Teng, & Koh, 2006). The prevalence of new cases of diabetes mellitus has kept rising over time due to growth in population, aging, urbanization, obesity and sedentary lifestyle (Wild, Roglic, Green, Sicree, & King, 2004). The research that published in 2010 with the title of Prevalence of Diabetes in the Malaysian National Health Morbidity Survey III 2006 has shown that the prevalence of diabetes mellitus is 11.9% among Malaysian (Letchuman et al., 2010).

DM is classified in three types. Type 1, or insulin-dependent diabetes, which is an autoimmune disease that involves in the destruction of insulin-producing -cells in the islets of the pancreas (Bresson & von Herrath, 2009). Type 1 DM is the most severe and needs insulin injection for the entire lives in order for the person with type 1 DM to survive (Lernmark, 1999). Type 2 diabetes is the condition in which the blood glucose level is high due to metabolic disorder whereby the insulin resistance leads to beta cells dysfunction (Srinivasan, Viswanad, Asrat, Kaul, & Ramarao, 2005). Gestational