

UNIVERSITI TEKNOLOGI MARA

**EFFECTS OF NARINGENIN ON
CARDIOVASCULAR CHANGES IN
PROLONGED HYPERGLYCAEMIA
IN FRUCTOSE-STREPTOZOTOCIN
INDUCED DIABETIC RAT MODEL**

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MSc

May 2020

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.

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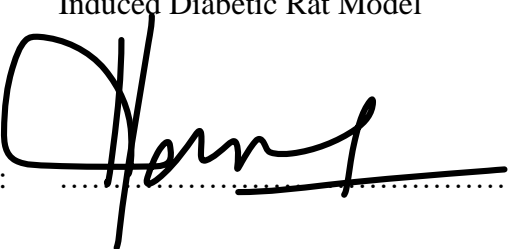
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ABSTRACT

Diabetes mellitus (DM) is a metabolic disease that has become a global burden. Its complications secondary to uncontrolled hyperglycaemia cause significant increase in the morbidity and mortality rate. Numerous natural products have been studied to combat the disease. Naringenin, obtained from citrus-based fruits has shown potential effects as an anti-diabetic, anti-oxidant, anti-atherosclerotic and anti-fibrotic properties when introduced at the beginning of the diabetic disease. However, the effects of naringenin as cardiovascularprotective agent in tissue exposed to prolonged hyperglycaemia has not been documented extensively. Thus, this study was aimed to determine the effect of naringenin on cardiovascular changes after prolonged exposure of the cardiac and aortic tissue to hyperglycaemia in a diabetic rat model. Thirty (30) adult male Sprague-Dawley rats were used in this study. Diabetic groups were induced with fructose and streptozotocin. After 4 weeks of induction, the rats were randomly divided into 5 groups each consisting of 6 animals: control, control treated with naringenin, non-treated DM, DM treated with naringenin and metformin-treated DM. Treatment with naringenin (50 mg/kg) and metformin were continued for 5 weeks. At the end of the experiment, the data on the weight, RBG, blood pressure and fasting serum lipid profile were analysed. The biochemical analysis on malondialdehyde and nitric oxide levels in the aortic tissue as well as total antioxidant and hydroxyproline levels in the cardiac tissue were evaluated. The morphological changes in the cardiac and aortic tissue present in the experimental rats were examined under light microscopy using H&E, Alcian blue and Sirius red staining besides TEM. Results showed that consumption of naringenin after prolonged hyperglycaemia (4 weeks) did not significantly improved the blood sugar, fasting serum lipid and blood pressure. However, naringenin had shown to improve malondialdehyde and total antioxidant level in the aortic and cardiac tissue respectively. No significant changes were observed on the nitric oxide level of the aorta and hydroxyproline level in the heart. Histological analysis using light and transmission electron microscopy (TEM) showed that naringenin ameliorated the changes in diabetic heart and aorta by reducing the cardiac atrophy and thickness of tunica intima and media in the diabetic aorta in the experimental animals. TEM findings showed less injury on the endothelial lining of the diabetic aorta and reduced morphological deterioration in the mitochondria of the diabetic cardiomyocytes. These findings suggest that introduction of naringenin after prolonged exposure to hyperglycaemia improved the cardiovascular changes caused by diabetes partly by reducing the oxidative stress in the diabetic aorta and heart.

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