UNIVERSITI TEKNOLOGI MARA

THE EFFECT OF *Azadirachta excelsa* (SENTANG) ETHANOLIC EXTRACT ON BIOCHEMICALS PARAMETERS IN SERUM, PANCREAS, KIDNEYS AND BONE AND TISSUE HISTOMORPHOMETRIC ANALYSIS OF STREPTOZOTOCIN-INDUCED DIABETIC RATS

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PhD

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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 Graduates, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Hyperglycemia causes tissue damages by inducing oxidative stress. Plant flavonoids have recently emerged as popular therapeutic drugs, against oxidative damage associated with diabetes. *Azadirachta excelsa* has been shown in animal models to significantly decrease fasting blood glucose as well as improves antioxidant activities. The roles of *A. excelsa* in alleviating hyperglycemia and hyperglycemic aggravated tissue damage in diabetic-induced rats were investigated in this study. The objective of this study was of two-folds: 1) To determine antidiabetic properties of the *A. excelsa* extract, 2) To evaluate the effects of *A. excelsa* extract on hormonal serum contents and selected organs in terms of their biochemical, histology and histomorphometrical changes in diabetic induced rats. Intraperitoneal (IP) injection of STZ (60 mg/kg body weight) was used for induction of diabetes. Four groups of male Sprague-Dawley rats consisted of normal control (NC), diabetic control (DC) and two diabetic treated groups were included. The both of the control groups were given saline and the diabetic treated groups were given 1000 mg/kg bwt metformin (DMET) and 250 mg/kg bwt *A. excelsa* (DAE), respectively. The treatments were administered through oral-gavage for eight weeks. The intraperitoneal glucose tolerance test (IPGTT) and intraperitoneal insulin tolerance test (IPITT) were conducted to examine glucose and insulin tolerance, respectively. Serum insulin, amylin and osteocalcin as well as quantification measurement of oxidant and antioxidant levels were evaluated in the three selected organs (pancreas, kidney and bone). The fatty acid composition in tissues was determined by Gas Chromatography (GC) method. The histology and histomorphometrical of the pancreas, kidney and bone tissues were analyzed using hematoxylin-eosin (H&E) staining. The bone was scanned *ex-vivo* using micro-computed tomography (micro-CT) to measure the trabecular bone microarchitecture and other morphometric parameters. The study showed a significant increase in insulin and a decrease in amylin secretion, following *A. excelsa* treatment. An increase in serum osteocalcin implied that *A. excelsa* enhances osteoblast differentiation and bone development. Both IPGTT and IPITT indicated that *A. excelsa* extract improved glucose and insulin tolerance among the diabetic rats. In addition, the plant extract influenced pancreas β-cell replenishment, improved kidney and bone morphology along with increased in antioxidant enzymes and reduced the oxidative stress level in the tissues involved. The degrees of antioxidant enzymes, malondialdehyde (MDA) and kidney function markers were reinstated to nearly normal especially in uric acid level with *A. excelsa* treatment. The trabecular morphometric assessment also showed improvement in trabecular bone. This study highlighted the enhancements of the pancreas, kidney and bone functions supported by interrelated with hormonal profiles of their tissues which stand as the novelty of the research. In conclusion, administration of *A. excelsa* extract appears to provide better effects to the pancreas, kidney and bone of STZ-induced diabetic rats. These findings suggest that *A. excelsa* extract could a possible substitute of metformin in managing diabetes complications.

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