UNIVERSITI TEKNOLOGI MARA

AMELIORATIVE EFFECT OF GLUTATHIONE ADMINISTRATION ON TESTICULAR AND SPERM PARAMETERS IN STZ-INDUCED DIABETIC MICE

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of the requirements for the degree of
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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 Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Diabetes mellitus (DM) is known to cause reproductive impairment. In men, it has been linked to altered sperm quality and testicular damage. Oxidative stress (OS) plays a pivotal role in the development of DM complications. Glutathione (GSH) is a part of a non-enzymatic antioxidant defence system that protects lipid, protein and nucleic acid from oxidative damage. However, the protective effects of exogenous GSH on the male reproductive system have not been comprehensively examined. This study determined the impact of GSH administration in ameliorating the adverse effect of DM on testicular and sperm parameters in C57BL/6NTac STZ-induced diabetic mice. The mice were divided into four groups; non-diabetic control group (Group C), diabetic control group (Group D), GSH-treated non-diabetic group (Group GSH) and GSH-treated diabetic group (Group DGSH15). Administration of GSH at a dose of 15 mg/kg body weight was given for 6 consecutive weeks to Groups GSH and DGSH15 mice. Diabetic mice showed significant impairment in testicular and sperm parameters compared to non-diabetic mice. The administration of GSH at 15 mg/kg body weight improved testicular and sperm parameters in diabetic mice. Histological examination of testes also showed a significant difference in the diameter of seminiferous tubules, epithelial height, and diameter of the lumen in GSH-treated group, compared to diabetic control. The apoptotic index calculated using the fluorescent TUNEL assay was lower in GSH-treated compared to diabetic control group, showing the ability of GSH to improve diabetes-related reproductive impairment. Malondialdehyde (MDA) and 8-hydroxy-2'-deoxyguanosine (8-OHdG) were significantly lower in the GSH-treated group than in the diabetic control group. The expression of 17 different genes were examined using RT-qPCR. The antioxidative actions of GSH were seen in GSH-treated mice, supported by the upregulations of *Bcl-2*, *Sod1*, *Gpx1*, *Mfn1*, *Ndufs1*, *Ndufs2* and *Uqcrfs1*. Five Caspase pathway genes were further examined using ELISA for protein expression. The Bax/Bcl-2 ratio was found to be lower in the GSH-treated group, indicating reduced OS with GSH intervention. In conclusion, GSH at 15 mg/kg body weight was adequate to reverse the effect of DM on sperm quality and testicular damage in C57BL/6NTac mice. The determination of the effective dose of GSH in this study is expected to provide a baseline for further exploration into the mechanisms underlying the possible protective effects of GSH and its development for clinical application.

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