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Evaluating Immunopathological Effects of *Nigella Sativa* Oil and its Major Component, Thymoquinone in a Streptozotocin-Induced Type1 Diabetes Rat Model

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of UniversitiTeknologi MARA. It is original and is the result of my own, unless otherwise indicated or acknowledge as referenced work. This thesis has not been submitted to any other academic or non-academic institution or non-academic institution for any other 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.
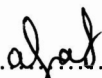
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ABSTRACT

Type 1 diabetes mellitus (T1DM) is considered as an autoimmune disease. It is characterised by the presence of antibody (humoral) and T-cell (cellular) responses to islet proteins (antigens). *Nigella sativa* oil and its major component thymoquinone (TQ) have been documented to have hypoglycemic properties in both type 1 and type 2 diabetes, but to the best of our knowledge the effect of this plant on the immunopathology of IDDM has never been examined.The objectives of this study were to determine the potential immunomodulatory effect of administration of *Nigella sativa* oil and it major compound thymoquinone (TQ) in the disease process of IDDM by assessing the levels of anti- islet cell antibodies, pan T- lymphocytes marker (CD90), pan B-lymphocytes markers (CD19), and pan innate cells marker (CD11b).Method: Type 1 diabetic state was induced to overnight fasted animals by intraperitoneal injection with a single dose of STZ (65 mg/kg body weight). Six equal sized groups of male Sprague-Dawley rats received or not different doses of *N. sativa* oil and TQ. Blood glucose was tested every morning through 30 days of the experimental period. After completion of the 4 weeks experimental protocols, blood samples were collected from overnight fasted rats by the cardiac puncture under anesthesia. Serum was assayed for autoimmune anti- Islet cell antibodies (ICA), pan T- lymphocytes marker (CD90), pan B-lymphocytes marker (CD19), and pan innate cells marker (CD11b) in addition to serum insulin using enzyme-linked immunosorbent assay (ELISA) . The animals were dissected after sacrificed and the pancreas was taken for histology. This organ was placed in 10% formalin for fixation. Results: T1DM causesincreased the levels of serum glucose, levels of T, B lymphocytes markers, innate cells marker, and ICA and decreased serum insulin level, meanwhile treatment of diabetic rats with *N. sativa* oil and TQ significantly decrease the levels of all immunological (p< 0.05) beside it significantly resulted in elevation of serum insulin level (p< 0.05). The study also emphasized that, *N. sativa* oil and TQ are effective against STZ diabetes as its administration ameliorated most of the pathological changes.Conclusions: These experimental results indicate the immunomodulatory effect of *N.sativa* against autoimmune reactions occurs in T1DM. This data provide new strategies for using this plant to be recommended in the clinical management, control, and prevention of T1DM. Moreover, *N. sativa* oil and TQ may be suggested to be used in the management of other autoimmune diseases.

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CHAPTER ONE

INTRODUCTION

1.1   GENERAL INTRODUCTION

Diabetes mellitus (DM) is commonly considered as a metabolic disease of the endocrine system, resulting from either insufficient production or insufficient action of insulin (American Diabetes Association, 2010). The DM has a tremendous impact not only on health of individuals but also on health care around the world. It encompasses a family of disorders of carbohydrate metabolism disease that are characterized by hyperglycaemia and the development of long-term macro vascular, microvascular, neuropathic and retinopathy complications (Ganesan et al., 2011). Diabetes mellitus and its complications are one of the common causes of death in the developing countries. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in the year 2000 and 4.4% in the year 2030 (Sarah et al., 2004). From the World Health Organization (WHO) reports, about 10% of people are suffering from type1 diabetes whilst 90% of people are type 2 sufferers. The summary of estimated numbers of people with diabetes in the different regions for the year 2000 and 2030 is shown in Table 1.1.