

UNIVERSITI TEKNOLOGI MARA

**THE ROLE OF GLUCAGON-LIKE
PEPTIDE-1 (GLP-1) ON ADIPOSE
CELLS IN TYPE-2 DIABETES
MELLITUS (T2DM)**

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ABSTRACT

Glucagon-like peptide 1 (GLP-1) is a member of incretin group hormone. It is produced by the L-cells of the intestines, serving as a postprandial communication messenger between the gut and other organs. It has numerous physiological roles, such as improving glucose-stimulated insulin secretion, enhancement of pancreatic β -cell proliferation, inhibition of glucagon release and promotion of satiety. GLP-1 has attracted an immense interest in research due to its antidiabetic effects for the treatment of patients with Type-2 Diabetes Mellitus (T2DM). However, the direct effects of GLP-1 on adipocytes are poorly characterized. In this study, an *in vitro* model of a dexamethasone-induced T2DM 3T3-L1 mouse adipose cells was chosen to demonstrate the metabolic effects of GLP-1 treatment and its actions on the cell's gene expression. Four parameters were measured to observe the changes in the cells; (i) glucose uptake, (ii) glycerol release in cellular adipolysis, (iii) glycogen synthesis, and (iv) gene expressions of adipokines and glucose transporters through real-time PCR. Results showed that successful adipocyte differentiation was obtained from the methylisobutylxanthine, dexamethasone and insulin (MDI) mix resulted in the presence of lipid droplets as observed with oil red O staining. GLP-1 has stimulated the glucose uptake by 3T3-L1 adipocyte cells and its utilization for lipid synthesis was enhanced. It also appears that GLP-1 preferentially inhibited lipid degradation and encouraged glycogen synthesis. From the findings, GLP-1 has demonstrated ameliorative effects on the metabolic process that involves glucose and lipid in the cells, as well as on the secretion of adipokines and glucose transporters by the 3T3-L1 cells. Thus, GLP-1 may have a potential role as an antidiabetic therapy in the treatment of T2DM.

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CHAPTER ONE

INTRODUCTION

1.1 Problem Statement

Type-2 Diabetes Mellitus (T2DM) has been thought in terms of defect in insulin biosynthesis, secretion and action. Now it has been identified that abnormalities in Glucagon-like Peptide-1 (GLP-1) and Gastric Inhibitory Peptide hormones contribute to hyperglycaemia which eventually leads to T2DM. GLP-1 is involved in insulin biosynthesis, beta-cell proliferation, inhibition of glucagon secretion and inhibition of food intake, which eventually helps in lowering the blood glucose level.

Present literatures Kim *et al.*, 2014; Lotfy *et al.*, 2014; and Mondragon *et al.*, 2014 reported an extensive research about GLP-1 effects on pancreatic physiology but poor evidence on adipocytes although there is much expression of GLP-1 receptors on them (Liu *et al.*, 2014; Pyke *et al.*, 2014). The role of GLP-1 in glucose metabolism too, is still under intensive investigation (Gastaldelli *et al.*, 2017). Research on the ameliorative effects of T2DM on adipocytes could be beneficial and may provide new insights on the disease pathophysiology, for example, concerning secretion of adipokines by adipocytes during adipolysis inhibition (Morigny *et al.*, 2016). Hence, the idea of this work is to investigate the effects of GLP-1 on normal and *in vitro* model of T2DM-induced adipose cells.

1.2 Background of Study

Diabetes mellitus (DM) is a metabolic disease, characterized by hyperglycaemia as a result of defects in insulin metabolism. DM can be categorised into two; Type-1 Diabetes Mellitus (T1DM) and Type-2 Diabetes Mellitus (T2DM). In T1DM, or also known as insulin-dependent diabetes, the cause is in the absolute deficiency of insulin secretion with an autoimmune pathologic process in the pancreatic islet cells. Meanwhile in T2DM, or non-insulin dependent diabetes, a combination of resistance to insulin action and inadequate compensatory insulin secretory response are the causes of the disorder.