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**Influence of Periodontal Therapy on the
Expression of the Receptor of Advanced Glycation
End-Products (RAGE) in Gingival Tissues of
Patients with Type 2 Diabetes Mellitus**

Thesis

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To the soul of my Mother,

My great Father,



My supporting husband,

And my lovely daughter.

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List of abbreviations

Aa: Actinomyces actinomycetemcomitans

AGEs: Advanced glycation end-products

Bf: Bacteroides forsythus

CAL: Clinical attachment level

CRP: C-reactive protein

EGF: Epidermal growth factor

EN-RAGE: Extracellular newly identified RAGE binding proteins

FPG: Fasting plasma glucose

GCF: Gingival crevicular fluid

GI: Gingival index

H₂S: Hydrogen sulphide

HbA_{1c}: Glycated hemoglobin

HMGB1: Amphoterin

IgA: Immunoglobulin A

IgG: Immunoglobulin G

IL-1 β : Interleukine-1 β

IL-6: Interleukine-6

Kd: Kilodalton

LDL: Low density lipoprotein

LPS: Lipopolysaccharide

Mac-1: Macrophage-1 (β 2 integrin)

MMPs: Matrix metalloproteases

MPs: Mononuclear phagocytes

mRNA: Messenger RNA

NF- κ B: Nuclear factor kappa- light-chain-enhancer of activated B cells)

NH₃: Ammonia

PD: Probing depth

Pg: Porphyromonas gingivalis

PGE₂: Prostaglandin E₂

Pi: Prevotella intermedia

PMN: Polymorphonuclear leukocytes

PPG: Post prandial glucose

RAGE: Cell surface receptor for advanced glycation end-products

ROS: Reactive oxygen species

RT-PCR: Reverse transcriptase polymerase chain reaction

sRAGE: Soluble receptor for advanced glycation end-products

SRP: Scaling and root planing

TNF- α : Tumor necrosis factor- α

Type II *fimA* gene: The major fimbriin gene in Pg

VCAM-1: Vascular cell adhesion molecule-1

VEGF: Vascular endothelial growth factor

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INTRODUCTION

Diabetes mellitus is a highly prevalent metabolic disorder, with 150 million cases estimated worldwide; it constitutes a global public health burden. The primary feature of this disorder is hyperglycemia. Sustained hyperglycemia has been shown to affect almost all tissues in the body and is associated with significant complications of multiple organ systems **(Marshall and Flyvbjerg, 2006)**.

Diabetes mellitus develops from either a deficiency in insulin production or an impaired utilization of insulin. Based upon these 2 conditions, diabetes mellitus can be divided into 2 main types: Type 1 (formerly insulin-dependent diabetes mellitus) and Type 2 (formerly non-insulin dependent diabetes) **(Mealy, 2000)**.

Hyperglycemia dramatically alters the function of multiple cell types and their extra cellular matrix. This results in structural and functional changes in the affected tissue **(Nishimura et al. 2000)**.

It is well established that exposure of the body's proteins and lipids to reducing sugars leads to a series of complex molecular re-arrangements, and the irreversible advanced glycation end-products (AGEs) are formed **(Lalla et al. 2000)**.

AGEs are biologically active and may initiate a range of cellular responses including stimulation of monocyte chemotaxis, osteoclast-induced bone resorption, proliferation of vascular smooth muscle cells, aggregation of platelets, and stimulation of secretion of inflammatory cytokines,