AZITHROMYCIN SUPPRESSES P. GINGIVALIS LPS INDUCED PRO-INFLAMMATORY CYTOKINE AND CHEMOKINE PRODUCTION (IL-6, IL-8, MCP-1 & GRO) BY HUMAN GINGIVAL FIBROBLASTS IN VITRO

A thesis submitted to The University of Adelaide in partial fulfilment of the requirements of the Degree of Doctor of Clinical Dentistry (Periodontology)

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BDent, BSc (Biomedical Science) (Hons)
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Abstract

Azithromycin is a macrolide antibiotic that is well known for its antibacterial properties, as well as possessing potential anti-inflammatory and immune modulating effects. This antibiotic has therefore been widely used in medicine for treating conditions ranging from inflammatory pulmonary diseases to dermatologic skin conditions. It has also been shown to be an effective antibiotic against most common periodontal pathogens and is used as an adjunct to treat periodontitis, a condition with bacterial aetiology and an inflammatory pathogenesis. Furthermore, periodontal case studies report regeneration of alveolar bone accompanied by significant reductions in inflammation have been achieved with azithromycin. The mechanisms however, by which these are achieved in the periodontium are largely unknown. This study aimed to determine the potential anti-inflammatory effect of azithromycin on cytokine and chemokine production by healthy human gingival fibroblasts (HGFs) that were stimulated by *Porphyromonas gingivalis* lipopolysaccharide (*P. gingivalis* LPS). HGFs were isolated from healthy gingiva collected from three donors. The effects of azithromycin at concentrations ranging from 0.1 \( \mu \text{g/mL} \) to 10 \( \mu \text{g/mL} \) were tested. Cytokine and chemokine protein levels were assessed using the Luminex® multiplex immunoassay. *P. gingivalis* LPS induced cytokine/chemokine (IL-6, IL-8, MCP-1 and GRO) protein production in HGFs was suppressed by azithromycin at all concentrations tested, and in all three donors. Suppression by azithromycin of IL-6, IL-8, MCP-1 and GRO *P. gingivalis* LPS protein induction in HGF was statistically significant when all donor results were collated \((p<0.05)\). This study demonstrates that azithromycin suppresses *P. gingivalis* LPS induced cytokine/chemokine protein production in HGFs, which may explain some of the clinical benefits observed with the adjunctive use of azithromycin in the treatment of periodontitis.

Key words: azithromycin (AZM), periodontitis, human gingival fibroblasts (HGF’s), *Porphyromonas gingivalis* lipopolysaccharide (*P. gingivalis* LPS), cytokine, chemokine, interleukin-6 (IL-6), interleukin-8 (IL-8/CXCL-8), Monocyte chemoattractant protein 1 (MCP-1/CCL-2), growth-regulated oncogene (GRO).
**Declaration**

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Catherine Jane Doyle, and to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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