

AZITHROMYCIN SUPPRESSES HUMAN OSTEOCLAST FORMATION AND ACTIVITY *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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Abstract

Azithromycin is an antibiotic with anti-inflammatory properties used as an adjunct in the treatment of periodontitis, a common inflammatory mediated condition featuring pathologic alveolar bone resorption. The aim of this study was to determine the effect of azithromycin on human osteoclast formation and resorptive activity *in vitro*. Osteoclasts were generated from peripheral blood mononuclear cells stimulated with macrophage colony stimulating factor (M-CSF) and receptor activator of nuclear factor kappa B (RANK) ligand. The effects of azithromycin at concentrations ranging from 0.5 µg/mL to 40 µg/mL were tested. Osteoclast formation and activity, acidification, actin ring formation and expression of mRNA and protein encoding for key osteoclast genes were assessed. The results demonstrated that azithromycin reduced osteoclast resorptive activity at all concentrations tested with osteoclast formation being significantly reduced at the higher concentrations (20µg/mL and 40µg/mL). mRNA and protein expression of the key osteoclast transcription factor Nuclear Factor of Activated T cells (NFATc1) was significantly reduced by azithromycin at later stages of osteoclast development (day 17). Azithromycin also reduced tumour necrosis factor receptor associated factor-6 (TRAF6) mRNA expression at day 14, and cathepsin K mRNA expression at day 14 and 17. Integrin β3 and MMP-9 mRNA expression was reduced by azithromycin at day 17 in osteoclasts cultured on dentine. The osteoclast proton pump did not appear to be affected by azithromycin, however formation of the actin ring cytoskeleton was inhibited. This study demonstrates that azithromycin inhibits human osteoclast function *in vitro*, which may account for at least some of the beneficial clinical effects observed with azithromycin treatment in periodontitis.

Declaration

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 Siobhan Catherine Gannon 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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Statement of Authorship

NOTE: The Statement of authorship appears in the print copy of the thesis held in the University of Adelaide Library.

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