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PREFACE

This thesis reports on research work related to the investigation of enamel wear prevention using a new remineralizing agent CPP-ACP (casein phosphopeptide – amorphous calcium phosphate nanocomplexes) that was carried out during my PhD candidature at the School of Dentistry, The University of Adelaide, from March 2005 until February 2009. Aspects of this research were conducted in collaboration with Prof David Bartlett from King’s College London, and with Dr Andrew Lewis and Prof Roger Smart from The University of South Australia.

This thesis is structured in a combined conventional/publication format and consists of nine chapters. A review of the literature, leading to the overall aims and hypotheses, is presented in Chapter 1, and the overall materials and methods are discussed in Chapter 2. Specific details relating to materials and methods for aspects of research have been discussed in Chapters 3, 4, 5 and 6. The overall findings of this project, along with its significance and limitations, are discussed in Chapter 7, and a list of references is presented in Chapter 8. The Appendices are included in Chapter 9.

Chapters 3, 4, 5 and 6 are written as manuscripts that have been accepted by, or are intended for submission to international journals. The Appendices (Chapter 9) comprise research publications related to the PhD project as well as other academic activities performed during the candidature. For example, paper 1 under Chapter 9, Section 1.1.1 (Arch Oral Biol 53: 1011-1016) presents findings related to the work that was completed during the early phase of the PhD. While not specifically involving work presented in this thesis, this paper provides basic information about the role of third body components in lubricating the wear interface and forms the basis of the research protocol used in the PhD project.

Chapter 3 represents a paper related to the effect of CPP-ACP on preventing enamel wear under conditions simulating attrition and erosion, and this paper has been accepted for publication in
the Archives of Oral Biology (Paper 2, Chapter 9, Section 1.1.1). Chapter 4 represents a manuscript on the effect of CPP-ACP on reducing erosive enamel wear involving toothbrush abrasion. This chapter forms part of a Journal of Dentistry paper relating to the investigation of CPP-ACP on both enamel and dentine wear (Paper 3, Chapter 9, Section 1.1.1). As this thesis focuses on enamel wear prevention, findings on dentine wear prevention have not been included in this chapter. Chapter 5 relates to the effect of CPP-ACP in reducing enamel erosion, and this paper will be submitted for publication after further experiments involving fluoride have been conducted (Paper 1, Chapter 9, Section 1.1.2). Chapter 6 covers preliminary findings on the spectral analysis of the enamel surface after treatment with CPP-ACP, and it will be submitted for publication after experiments on a larger sample have been conducted (Paper 2, Chapter 9, Section 1.1.2).

A section on overall acknowledgements is included on pages xiv and xv of this thesis. Specific acknowledgements are also provided at the end of each chapter to conform with the format of manuscripts, and to highlight the contribution of different individuals, funding bodies and research centers relating to each manuscript.
ABSTRACT

There is an increasing awareness in clinical dentistry of the need to better understand the aetiology and management of tooth wear, as increasing numbers of elderly patients are retaining their natural teeth to a stage when they present with extensive wear. In addition, more younger patients are presenting with wear of both primary and permanent teeth. In order to comply with the philosophy of minimal intervention dentistry, clinical management of tooth wear should focus on early detection and prevention before a restorative approach is considered.

Fluoride is a commonly used agent in the management of tooth wear, with previous studies showing that it can protect teeth against erosion (at around pH 2.0 and 3.0) and toothbrush abrasion in an acidic environment (at around pH 3.0). However, it does not reduce attritional wear between opposing tooth specimens. Nightguards are commonly used to prevent attritional wear but there is still a need to improve preventive strategies to manage the risk of erosive tooth wear.

Previous in vitro studies have shown that a remineralizing agent in the form of CPP-ACP (casein phosphopeptide – amorphous calcium phosphate) can reduce erosion of both enamel and dentine by white wine. A recent study has also highlighted the potential lubricating and remineralizing properties of a CPP-ACP containing paste (Tooth Mousse®, G C Asia Pty Ltd) in reducing dentine wear in both an acidic environment (pH 3.0) and a near neutral environment (pH 6.1). In this context, it is desirable to investigate the effect of CPP-ACP on enamel wear under conditions simulating various clinical situations and to better understand the nature of third-body components at the wear interface.

The aims of the present study were: (i) to determine the effect of CPP-ACP on enamel wear under conditions simulating three clinical situations: heavy attrition with gastric regurgitation (at pH 1.2); toothbrush abrasion after an erosive episode (at pH 3.2); and erosion from gastric
regurgitation (at pH 1.2), and (ii) to clarify its mode of action by characterizing the enamel surface treated with CPP-ACP. Electro-mechanical tooth wear machines were used to simulate attrition and toothbrush abrasion in combination with erosion, but no machine was used in experiments investigation erosion alone. The effect of paste containing CPP-ACP in reducing erosive tooth wear was also compared with that without CPP-ACP. Enamel surfaces with and without treatment with CPP-ACP were then characterized by using Time of Flight – Secondary Ion Mass Spectrometry (ToF-SIMS).

CPP-ACP was found to reduce enamel wear under conditions simulating heavy attrition combined with gastric regurgitation, and toothbrush abrasion after an erosive episode. However, it did not protect enamel from erosion under conditions simulating gastric regurgitation alone, indicating that its lubricating effect was more pronounced than its remineralizing effect. Silicone and ethyl siloxane were present in trace amounts on the enamel surface treated with Tooth Mousse®, thus they were found to be included in its formulation. These findings imply that CPP-ACP nanocomplexes and silicon can act as third body components to lubricate the wear interface.

The findings presented in this thesis have implications for clinical management of tooth wear and may lead to new strategies of tooth wear prevention. Although some caution is needed in extrapolating these findings to the in vivo situation, it should be noted that in vitro studies provide valuable insights into separate components of the tooth wear process that are often difficult to distinguish in clinical situations. Overall, this thesis provides new information about the role of CPP-ACP in reducing erosive enamel wear and provides a basis for future experimental and clinical studies focussing on tooth wear prevention.
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 <Sarbin Ranjitkar> 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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*Figure 2.4 (page 40) of this thesis was obtained from this web-site: Physical Electronics. Online access: http://www.phi.com/techniques/tof-sims.html (accessed on 23 June, 2009).
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I would like to give sincere thanks to my supervisors, Prof Lindsay C Richards, Dr John A Kaidonis and Prof Grant C Townsend, for all their advice and guidance over the years. They have greatly influenced my personal and professional development. I would also like to thank our collaborators from the King’s College London, including Prof David W Bartlett for organizing my visit and Dr Jose M Rodriguez for advice and technical assistance. I extend my gratitude to Prof Tim Watson for providing access to the laboratory facility in London. I also had the privilege of collaborating with Dr Andrew Lewis and Prof Roger Smart from the University of South Australia on work related to mass spectrometry, enabling me to develop a holistic approach to the investigation of tooth wear. My thanks also goes to Dr John Denman from the University of South Australia for providing me with a schematic diagram of the ToF-SIMS equipment, and to both Drs Lewis and Denman for providing me with background information on this equipment.

The support of the National Health and Medical Council of Australia (NHMRC) in the form on a dental postgraduate research award is gratefully acknowledged. This project was also supported by research grants from the Australian Dental Research Foundation Inc, G C Asia Pty Ltd and Dentsply Pty Ltd. Furthermore, travel to the King’s College London was supported by an NHMRC Travelling Award, Research Abroad Scholarship and Faculty of Health Sciences Fellowship. My trips to attend the 84th and 86th General Sessions of the IADR were supported by a G C Travelling Award and a Wrigley’s Postgraduate Travel Award.

I would like to thank Ms Nancy Briggs and Dr Toby Hughes for their assistance with statistical analysis, G C Asia Pty Ltd for providing Tooth Mousse® samples, and the 3M ESPE Corporation for donating impression materials. Technical assistance provided by staff from the University of Adelaide (Dr My Anh Vu, Mr Victor Marino, Ms Archana Paneru, Mr Nabaraj Dahal and Dr Chin Nguyen), Adelaide Microscopy, the University of South Australia (Mr Mani
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