CHAPTER I

INTRODUCTION

Principle, theory, rationale, and hypothesis

During orthodontic tooth movement, the forces, being applied to the tooth, are transferred to the attachment apparatus, including alveolar bone (ALV), periodontal ligament (PDL) and gingiva. Before the tooth begins to move, the primary responding tissues are PDL and ALV. The outcome of these responses is tissue remodeling by synthesis and degradation of the extracellular matrix (ECM) of the PDL and of the ALV. Such remodeling causes the release of some ECM components, such as collagen, osteocalcin (Griffiths *et al.*, 1998), osteonectin, and proteoglycans in sufficient quantities, which are diffused into gingival crevicular fluid (GCF).

In the past, many studies were conducted to determine the changes of proteoglycans and their constituent glycosaminoglycans (GAGs) in GCF. Proteoglycans are macromolecules that comprise of a core protein to which one or more GAGs chains are covalently attached. The predominant GAGs in human ALV are mainly chondroitin-4-sulfate (C-4-S) (Waddington *et al.*, 1989; Bartold, 1990), but C-6-S is also present in lower amount (Waddington and Embery, 1991). The predominant GAG in PDL is dermatan sulfate (DS) and the other GAGs include hyaluronan (HA), chondroitin sulfate (C-4-S, C-6-S) and keratan sulfate (KS) (Waddington, 2001). Although, C-6-S is a minor component in ALV and PDL, but the presence of C-6-S is associated with compressive force in orthodontic tooth movement (Kagayama *et al.*, 1996). Accordingly, the chondroitin sulfate levels in GCF reflect changes occurring in the deeper periodontal tissue (Last *et al.*, 1988; Waddington and Embery, 1991; Samuels *et al.*, 1993; Pender *et al.*, 1994; Waddington *et al.*, 1994; Baldwin *et al.*, 1999). This may suggest that C-6-S present in GCF be used as a marker for active ALV and PDL turnover, and that the detection of such a "biomarker" be useful in monitoring the deeper metabolic activities

of the periodontal tissue during orthodontic tooth movement. All previous studies pertaining to chondroitin sulfate in GCF during orthodontic tooth movement were a cross-sectional quantitative study (Last *et al.*, 1988; Samuels *et al.*, 1993; Pender *et al.*, 1994; Waddington *et al.*, 1994; Baldwin *et al.*, 1999). None of them was designed as a longitudinal study. Furthermore, the electrophoresis method was used to quantify the amount of chondroitin sulfate in GCF. However, this method is a lengthy procedure and requires a lot of sample manipulations. Consequently, the analysis of clinical samples by means of "a quickly chair-side method" is not possible. In recent years, a number of antibodies have been developed, which allow the development of an immunoassay towards the detection of GAGs in GCF. One of the widely-used methods in detecting molecules in fluid is "ELISA" (Enzyme-linked immunosorbent assay). By using monoclonal antibodies (mAb) as well as an ELISA technique, GAGs present in the samples in a trace amount can be detected. In collaboration with the Department of Biochemistry, Faculty of Medicine, Chiang Mai University, the newly synthesized monoclonal antibody WF6 against degenerative epitope of C-6-S (Peansukmanee *et al.*, 2003) was available for C-6-S detection in this study. Therefore, the present study was conducted to determine the longitudinal changes of C-6-S levels in human GCF during orthodontic canine movement.

The hypothesis of this study was that there was a specific pattern of C-6-S level changes in GCF during orthodontic tooth movement.

The objective of this study was to determine the longitudinal changes in the WF6 epitope levels of C-6-S in human GCF during orthodontic canine movement.

Anticipated benefits

This study may be useful for developing a non-invasive chair-side diagnostic test to assess the deeper metabolic changes in periodontal tissue during orthodontic treatment. The reason why the development of a diagnostic test is essential is because the accurate assessment for largely metabolic changes in deep tissues cannot be obtained from current clinical indices.