

**UNIVERSITI TEKNOLOGI MARA**

**FORMULATION AND EVALUATION  
OF THREE DIMENSIONAL  
BIOADHESIVE HYDROGEL FOR THE  
TREATMENT OF PERIODONTAL  
DISEASE**

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## ABSTRACT

Periodontal diseases remain highly prevalent, and negatively affect the quality of life of young and adult populations. This local inflammatory disease causes loss of the supporting tissues of the teeth. Failure of treatment and therapeutic interventions to relieve the disease could eventually result in the loss of teeth. The aim of the current study was to investigate a three dimensional (3D) titrated extract of *Centella asiatica* (TECA) hydrogel new formulation produced to assist in the alleviation of these conditions. TECA hydrogel was synthesised to have macroporocities which provided the gel scaffold architecture that mimic extracellular tissue matrix and facilitates cell migration, fluid movement and drug delivery. The formulated polymer hydrogel was evaluated for its mechanical properties which included hardness, adhesiveness, compressibility, cohesiveness and syringeability using profile texture analyser. Furthermore, the hydrogel was tested for its flowability and consistency by rotational rheometer; and active ingredient release by Franz diffusion test. It was also tested for its efficacy in modulating cellular senescence by using the senescence marker SA- $\beta$ -gal stain; in modulating the induction of secretory associated heterochromatic foci (SAHF) in the cells by TNF- $\alpha$  and detection by using DAPI stain; in the formation of newly synthesised DNA using EdU stain; in accelerating cell migration during *in vitro* wound healing by utilizing the scratch wound assay; in reducing telomere length shortening or DNA damage response by Southern Blotting technique; in stimulating cell viability or proliferation, as well as in reducing the oxidation-induced cell proliferation suppression as assessed by MTT assay. The study indicated that gel formulations with high concentrations of polymers could have better characteristic features in terms of mechanical properties which facilitate the application and adhesion of hydrogel in the wet oral environment and prolong the releasing time of the active agent. The optimal formulation with 4% w/w HPMC and 5% w/w pectin was used in the culture analysis. The optimal TECA concentration was found to be 20  $\mu$ g/ml. The study revealed that the 3D TECA hydrogel was effective in reducing cellular senescence and chromatin condensation. It was also found that the hydrogel was beneficial in stimulating DNA synthesis and preserve telomere length during inflammation. Three dimensional TECA hydrogel treated samples showed higher migration rates than the controls. The smart hydrogel was also effective in reducing the cellular oxidative damage and in promoting cell proliferation. Together with the above mentioned effect of TECA hydrogel, and its 3D macro-porous structure, this hydrogel could become a promising and feasible candidate to be used as an adjunct for the treatment of periodontal problems and diseases. The results of the study imply that induction of cellular senescence does not need the “aging factor” as a prerequisite. In addition, upon inducing inflammation, periodontal ligament cells exhibited senescence marker, and signs of chromatin condensation (SAHF), which are behavioural criteria of cancer cells. Hence, the study suggests that inflamed periodontal cells are swiftly degraded as an evolutionary way to escape the carcinogenesis pathway which could generate them to multiply and metastasize as cancer cells. The degradation of the chronically inflamed periodontium results in noticeable alteration in the periodontal architecture.

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# CHAPTER ONE

## INTRODUCTION

### 1.1 BACKGROUND

Oral diseases remain highly prevalent globally, affecting 3.9 billion people (Richards 2013). Severe periodontitis is the 6th most prevalent condition affecting 11.2% of individuals worldwide. Oral conditions combined accounted for 15 million DALYs\* globally (1.9% of all YLDs\*\* and 0.6% of all DALYs), implying an average health loss of 224 years per 100,000 people. DALYs due to oral conditions increased 20.8% between 1990 and 2010, mainly due to population growth and aged population increase (Marcenes et al., 2013). While DALYs due to severe periodontitis and untreated caries increased, those due to severe tooth loss decreased (Kassebaum et al., 2014)

All over the world, periodontal disease remains highly prevalent and is negatively affecting the quality of life (QoL) of the middle-aged and older populations (Preshaw et al., 2012). Periodontitis is directly associated with lower levels of education and higher levels of poverty (socio-economic), both of which influence the use of dental services by adults (Borrell, Burt, & Taylor, 2005, 2008, Borrell & Talih, 2012; Thornton-Evans et al., 2013). Educational attainment, demographics and socio-economic factors might mediate significant differences in the prevalence of periodontal disease between different racial/ethnic populations. Smoking and some chronic diseases such as diabetes are important modifiable risk factors for periodontitis (Genco & Borgnakke, 2013).

Due to the previous mentioned factors, the probability of periodontal structure break down is expected to persist at least for the next few decades, hence the efforts to find a solution to alleviate pain and preserve the periodontium and subsequently the teeth is desired.

\* \*\* (Disability-adjusted life-years (DALYs) and years lived with disability (YLDs) metrics were used to quantify the disease burden).