Research Article

Retention and characterisation of a sustained efficacy chlorohexidine-containing gel within a periodontal pocket model

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Abstract

Aims Periodontitis is a bacterially induced inflammation affecting the integrity of the connective tissues surrounding the tooth, impacting both oral function and aesthetics. Chlorhexidine (CHX) is a common biocide used widely in dentistry and medicine; however, current CHX-containing treatment aids for periodontitis are not well retained in the mouth due to rapid salivary clearance. The aim of this study was to investigate the suitability of a novel material, sustained efficacy CHX (SECHX), in a temperature-responsive gel, as a prospective aid for the management of periodontitis.

Methods Base gels were formulated using the thermosensitive hydrogel Poloxamer 407 (P407) at 30%, 40% and 50% (wt/vol.), and CHX tripolyphosphate (CHX-TPP; also known as SECHX) was added to the gel. SECHX gels were evaluated with respect to physical characteristics and their retention in an in vitro periodontal pocket model.

Results As the concentration of the P407 increased from 30–50%, the viscosity of the gel increased; however, viscosity decreased with the addition of CHX-TPP. The volume of gel retained over time in the periodontal pocket model decreased over time for both the control and CHX-containing gels. In comparison to the control gels, the CHX-containing gels were better retained over the same period of time. A substantial volume (34%) of the 50% p407 CHX-containing gel was retained after 7 days.

Conclusions Retention of the higher viscosity (50% P407) CHX-TPP containing gels may be beneficial in the management of periodontal disease, given their retention time.

Introduction

Periodontitis is an inflammatory disease affecting the integrity of the supporting tissues surrounding a tooth. It ranks as the sixth most prevalent health condition worldwide, with 45% of adults in the UK showing active or historical signs of the condition.[1] It is often life long and recurring, with detrimental effects on both oral function and aesthetics. Left untreated, it may result in tooth loss (see **Figure 1**).

Tissue destruction in periodontitis results from a combination of direct damage by pathogenic periodontal bacteria found in dental plaque, and the immunological and inflammatory host defence mechanisms against these bacteria and their antigenic by-products. Periodontitis has also been associated with systemic conditions, such as dementia, respiratory diseases, and with poor diabetic control, cardiovascular health and pregnancy outcomes.

Chlorhexidine (CHX) is a common biocide used widely in dentistry and medicine; however, current CHX-containing treatment aids for periodontitis are not well retained orally due to rapid salivary clearance.[3] Traditionally, slow release CHX preparations are used. These perform by releasing an initial high burst of CHX (front-loaded release), which is rapidly cleared, and a dwindling CHX concentration remains thereafter. There are two main problems with this mechanism: an initial high dose of CHX may increase the risk for adverse effects (contact rash, irritation, nausea) and the diminishing supply of CHX that follows may either be ineffective for antimicrobial function or may encourage microbial resistance. Sustained efficacy CHX (SECHX) may provide a good alternative to traditional CHX therapy. SECHX is unique in that it maintains a steady release of CHX, thus minimising the risk of these problems.[3]

The aim of this study was to investigate the suitability of a novel material,[4] SECHX in the form of a temperature-responsive gel (viscosity increases with temperature), as a prospective aid for the management of periodontitis. The developed gels were evaluated with respect to physical characteristics and their retention in an in vitro periodontal pocket model.

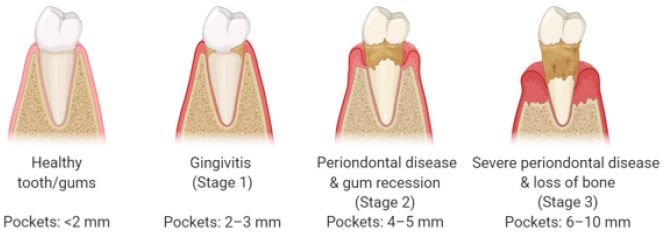

Figure 1. illustration of the progression of periodontal disease. Left to right: healthy gums, gingivitis, moderate periodontitis[2] and advances periodontitis. Created in BioRender.com.

Methods

A model was devised using artificial teeth surrounded by a root surface wax strip and set in silicone, simulating a periodontal pocket upon removal of the wax. Base gels were formulated using the thermosensitive hydrogel Poloxamer 407 (P407; Sigma-Aldrich Company, Dorset, UK) at 30%, 40% and 50% (wt/vol.) concentrations. CHX-containing gels were synthesised by addition of 1% (wt/wt) solid CHX tripolyphosphate (CHX-TPP; also known as SECHX; donated as a sample from Pertinax Pharma, Bristol, UK) to base gels.[4] Control samples contained no CHX-TPP.

Gels were characterised using rheometer oscillation and flow curve experiments, then imaged using differential interference contrast (DIC) microscopy. Retention of the gels in the simulated periodontal

pockets was assessed at days 1, 4 and 7 post-exposure to an artificial saliva bath at 37˚C.

Results

Physical property investigations using rheometry revealed shear modulus elastic component values (G') to be greater than shear modulus viscous component values (G"), confirming the CHX-loaded P407 product as a gel (data not shown). Additionally, rheometry testing indicated that as loading of the gels with CHX-TPP increased, viscosity decreased, whilst an increase in P407 volume resulted in increased viscosity (data not shown).

DIC microscopy demonstrated a grainy appearance of the CHX-containing gel (made with 50% P407) when compared with its control counterpart, indicating an even distribution of the CHX-TPP particles in the gel (see **Figure 2**).

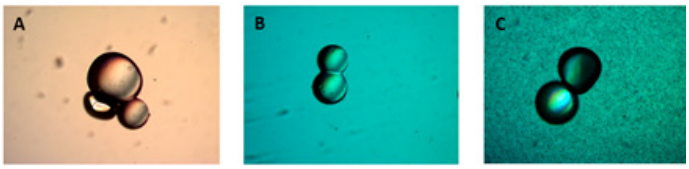

Figure 2. Verification of particle distribution in the gel preparations using DIC microscopy. Bright-field polarised DIC images at ×40 magnification with glass beads. **(a)** Clear control gel (P407 50% without CHX-TPP particles), **(b)** patent blue-dyed control gel (P407 50% without CHX-TPP particles) and **(c)** patent blue-dyed P407 gel (50%) with CHX-TPP particles.

When assessing gel retention in the in vitro periodontal pocket model, retention of both the control and the CHX-containing gels in the simulated periodontal pockets reduced over time. However, the CHX-containing gels were retained better than the controls at each time period. Gels with higher P407 concentration were better retained. A substantial volume (34%) of the CHX-containing gel made with 50% P407 was retained after 7 days (**Figure 3**)

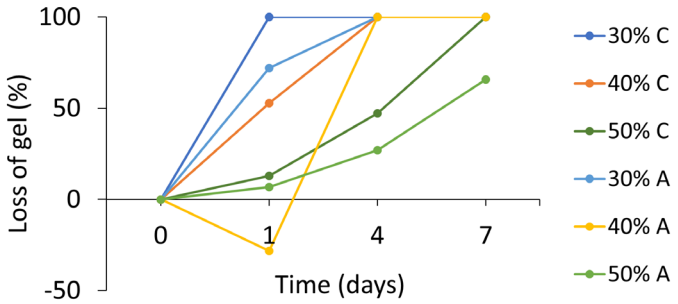

Figure 3. Per cent loss of CHX-TPP gel made with various concentrations of P407 (30%, 40% and 50%) versus respective control P407 gels. Control samples (C) did not include CHX-TPP particles. 'A' refers to samples containing CHX-TPP particles.

Discussion

This study aimed to investigate use of SECHX gel for the management of periodontitis. It was found that as loading of the gels with CHX-TPP increased, viscosity decreased, whilst an increase in P407 volume resulted in increased viscosity. The increase in viscosity with increased poloxamer concentration has also been found in other studies and is thought to be attributed to the closer packing of the lattice pattern within the material.[5]

DIC microscopy demonstrated an even distribution of the CHX-TPP particles in the gel. Clinically, this is important as it suggests a large surface area of the active ingredient (CHX-TPP), resulting in more exposure of the diseased area to this agent and, thus, greater efficiency of treatment.

The findings from the simulated periodontal pocket experiment indicated that an increase in viscosity owing to increased P407 concentration lead to increased retention. However, it was also shown that CHX-TPP containing gels were better retained than the controls at each time period, despite the rheometry findings indicating a reduction in viscosity following CHX-TPP addition to gels. This could potentially be due to a change in the physicochemical properties of the poloxamer gels following incorporation of a drug (in this case SECHX), as demonstrated by Inal and Yaper.[6]

Conclusions Retention of the higher viscosity (50% P407) CHX-TPP containing gels may be beneficial in the management of periodontal disease, given their retention time. Future considerations include testing CHX-TPP containing gels (using relevant control gels) in the presence of commonly found periodontal bacteria, to test their antimicrobial potential and the time period of any antimicrobial action.

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