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Controlled localized delivery of chlorhexidine for inhibition of plaque formation

D. S. JONES*, N. J. MEDLICOTT, M. J. RATHBONE, D. HOLBOROW AND I. G. TUCKER

School of Pharmacy, The Queen's University of Belfast, Medical Biology Centre, 97 Lisburn Road, Belfast, and School of Pharmacy, University of Otago, Dunedin, New Zealand

The treatment of periodontitis is mainly through the mechanical cleaning of the tooth surface, often in conjunction with antimicrobial agents. However, it has been shown that the control of supragingival plaque over the duration of healing of periodontal tissues, following intrapocket therapy, significantly reduces the recurrence of the disease. The clinical efficacy/acceptability of antimicrobial mouthwashes in this respect is poor. Previously, we reported the formulation and characterisation of polycaprolactone (PCL) films containing chlorhexidine, CHX (Medlicott et al. 1996), designed for application to the tooth surface for the control of supra-gingival plaque. This study reports the concentrations of CHX achieved at different times throughout the day following attachment of one such formulation to the teeth of human subjects.

The candidate formulation was composed of PCL (m.wt. 35000-45000) and contained 20% w/w chlorhexidine (particle size 63 - 125 μm). The film was manufactured by solvent evaporation as previously reported (Medlicott et al. 1996). Sections of the film (*circa* 9 mm^2) were weighed and then attached to the mesio-buccal and mesio-lingual areas of the lower left first molar tooth surface of five dentally healthy subjects using Scotchbond® adhesive. Subjects were requested to refrain from toothbrushing and the use of mouthwashes during the study. Saliva was collected on Periopaper® from six sites per subject, immediately prior to attachment of each film, then before breakfast (t_1), before lunch (t_2), after lunch (t_3) and late in the afternoon (t_4) for three days and before breakfast (t_1) on the fourth day. Quantification of the concentration of CHX in the collected saliva samples was performed by HPLC (Medlicott et al. 1994).

The % of the original drug load released from the films to the buccal and lingual sides of the lower left molar were 73 ± 5% and 51 ± 5%, respectively, these differences being significant at the 95% level. In addition, the surface of teeth adjacent to the attached films were visually free from plaque, whereas, accumulation of plaque had occurred on teeth distant from these sites. These anti-plaque effects may be accredited to localised super-minimum inhibitory concentrations of CHX. CHX concentrations adjacent to the film sections were significantly greater on the buccal than on the lingual sides of the tooth, indicating the possible effects of oral processes (e.g. mastication) on drug release and, also, lower CHX clearance from this site. In addition, the time of sampling significantly affected the CHX concentration at the sampling sites (two way ANOVA, $p<0.05$ denoting significance), reflecting the effects of variations in saliva flow rates on drug release.

Table 1. Mean (± sem) chlorhexidine concentrations (μg mL^{-1}) adjacent to buccal and lingual films

Day	Sampling Time	Buccal	Lingual
1	t_1	14.0 ± 3.0	3.0 ± 1.0
1	t_2	4.2 ± 0.8	2.7 ± 0.7
1	t_3	2.7 ± 1.5	0.6 ± 0.6
1	t_4	6.0 ± 2.0	3.0 ± 1.0
2	t_1	11.0 ± 5.0	2.0 ± 1.0
2	t_2	6.0 ± 2.0	1.0 ± 0.6
2	t_3	2.0 ± 1.0	0.3 ± 0.3
2	t_4	7.0 ± 2.0	5.0 ± 4.0
3	t_1	14.1 ± 5.2	2.1 ± 2.0
3	t_2	6.0 ± 3.1	1.0 ± 1.0
3	t_3	6.0 ± 4.0	0
3	t_4	8.1 ± 3.0	4.0 ± 4.0
4	t_1	18.0 ± 6.0	7.1 ± 3.0

In conclusion, the CHX-containing film exhibited antiplaque effects in areas adjacent to the site of application without interference with normal oral functions. This system may be useful for the reduction of re-infection of treated periodontal pockets.

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