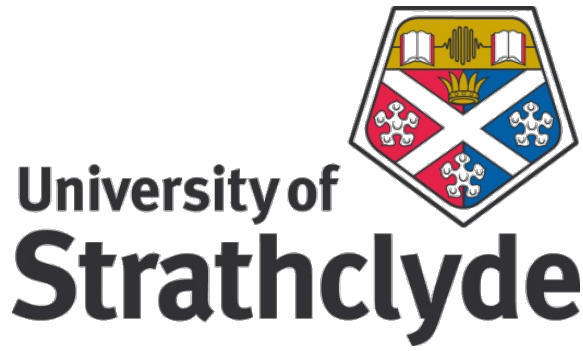

Strathclyde Institute of Pharmacy and Biomedical Sciences

Amorphous calcium phosphate nanocomplexes in dental film formulations

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Copyright statement

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Abstract

The present thesis concerns the exploration of novel amorphous calcium phosphate nanocomplexes stabilised by food grade additives. The concept is to generate a formulation to prevent dental caries through enamel remineralisation, supplementing the calcium and phosphate concentrations by delivery from an adhesive dental film dosage form.

A formulation containing calcium chloride, dibasic sodium phosphate and stabiliser in hydrochloric acid solution at a pH of 5 was complexed by pH adjustment to 7 in the presence of fractioned hydrolysed casein or negatively charged peptides. This allowed the formation of stabilised amorphous calcium phosphate nanocomplexes. An alternative method in which carboxymethyl cellulose with short chain length with measured molecular weight and degree of substitution, produced by acid hydrolysis, was similarly able to stabilise the amorphous calcium phosphate nanocomplex. The prepared amorphous calcium phosphate nanocomplexes were suitable for formulation into dental film dosage forms.

The prepared nanocomplexes were formulated into dental films based on hydroxy propyl methyl cellulose (HPMC) of various grades which formed hydrogels with good adhesive properties. The physical properties of the prepared films were characterised by texture analysis, tensile strength and structure and the calcium release was measured using film strips in a specially designed dissolution cell. The formulated dental films containing a mixture of 2% w/v E10M and 1% w/v F4M hydroxy propyl methylcellulose, loaded with 2 % w/v 4 hours acidic hydrolysed carboxy methylcellulose and hydrolysed casein, had a suitable release of calcium. The release pattern of the calcium was characterised using different diffusion/erosion models and was best described by a Higuchi modes with Fickian, non-Fickian and super case II transport kinetics depending on the type of ACP and the grade of HPMC used.

The effect of a biofilm generated on the tooth surface to make the substrate more hydrophobic was examined. The adhesion of 15% (w/v) HPMC-E10M hydrogel to enamel slabs was studied, and was found to be highly variable. The effect of ACP on the culture of the biofilm using confocal laser scanning microscopy was investigated and a substantial inhibitory effect was obtained with 8% w/v ACP.

The remineralisation effect of preparations containing 2% w/v NGP-ACP, HC-ACP and acid hydrolysed CMC-ACP loaded into films formulated with a mixture of 2% w/v E10M and 1%

w/v F4M hydroxy propyl methylcellulose was investigated. The method employed used scanning electron probe microanalysis to determine the elemental deposition of the calcium and phosphorous up to a depth of 400μm in enamel samples. Both 2% w/v 4h ahCMC-ACP and 2% w/v HC-ACP containing dental films showed an uptake of calcium and phosphate with uniform and constant deposition of the elements in depth of 400μm into the enamel samples.