Design of Chlorhexidine Loaded Periochip

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Abstract

Periodontitis is a dental disease, resulting from bacteriological infections which destroys the attachment apparatus of teeth leading to formation of the periodontal pocket. The periodontal chip is a pharmaceutical composition which is applied to a periodontal pocket for the purpose of treating periodontal diseases. This study was performed to develop a biodegradable periodontal chip containing chlorhexidine and to evaluate its effectiveness for managing chronic periodontitis.Chlorhexidine is a broad-spectrum biocide effective against Gram-positive bacteria, Gram-negative bacteria and fungi. Chitosan, a partially deacetylated chitin, which is a biologically safe biopolymer, prolongs the adhesion time and drug release from periochips. Chitosan also has a broad antimicrobial spectrum. The main objective of this study was to design a formulation containing chitosan for local delivery of Chlorhexidine to the oral cavity for managing chronic periodontitis. Various formulations were prepared at various concentrations of chitosan 1%, 2%, 3% and 4% and evaluation studies were performed. Periochip properties like thickness, weight uniformity, folding endurance, tensile strength of all the formulations are within the acceptable range. All the prepared formulations provide an acceptable pH range that is compatible with normal buccal mucosa. The drug content of each formulation was evaluated and was found to be uniform ranging from 94.5% to 99%. The in-vitro dissolution comparison was made. The formulations with higher percentage of chitosan (CPC 4) shows slower drug release than other formulations. On the basis of in vitro characterization it was concluded that chlorhexidine could be incorporated in a slow release chitosan chip for the treatment of periodontitis. Further, detailed investigation is required to establish in-vivo efficiency of these periochip.

Key Words: Chlorhexidine, Periochip, Biodegradable

1. INTRODUCTION

Periodontitis is an inflammation of the periodontium that extends beyond the gingiva and destructs the connective tissue to which teeth attach. Bacteria associated with dental plaque have been widely accepted as the cause of inflammatory periodontal diseases Chlorhexidine is a bis-bisguanide widely used to treat skin and mucosa infections, shown to possess a broad-spectrum of topical anti-microbial activity. It is used for plaque control and for the treatment of gingival inflammation [1].

The periodontal chip is a pharmaceutical composition which is applied to a periodontal pocket for the purpose of treating periodontal diseases [2].Periodontal chip is a unique biodegradable chip, which contains medicament shown to be an effective and safe adjunctive treatment for reduction of pocket depth in patients with adult periodontitis [3].In the present study our objective was to formulate intrapocket dental films, which could be easily placed into the periodontal pocket, and be capable of delivering therapeutic concentrations of Chlorhexidinefor prolonged period of time.

2. EXPERIMENTAL METHODS

2.1 Preparation of periodontal chips

Accurately weighed quantities (Table 1) of polymer (Chitosan) were dissolved in required quantity of solvent (Acetic acid) in which drug (Chlorhexidine) and plasticizer (PEG 200) were added.The solution was mixed with magnetic stirrer to get homogeneous consistency. Mercuric substrate method was used to cast the periodontal films [3,4].

Table 1.Formulation of chlorhexidine loaded periochip

Formulation code	Drug in each periochip	Chitosan	PEG 200
CPC1	2mg	1%	40%ofchitosan
CPC2	2mg	2%	40% of chitosan
CPC3	2mg	3%	40% of chitosan
CPC4	2mg	4%	40% of chitosan

2.2 Evaluation parameters

a. Thickness of the film

The thickness of patches was measured at three different places using a micrometer and average values were calculated.

b. Uniformity of weight of the films

Film (size of 10x5 mm^2) is taken from different areas of film. Then the weight variation of each film can be calculated.

c. Surface pH

Periodontal films are left to swell for 1 hour on the surface of 2% (w/v) agar gel. The surface pH can be measured by means of pH paper placed on the surface of the swollen film [3].

d. Folding endurance

Folding endurance was determined by repeatedly folding one film at the same place till it broke. The number of times the film could be folded at the same

place without breaking/cracking gave the value of folding endurance [4].

e. Tensile strength of the films

In order to determine the tensile strength, the polymeric patch was pulled by means of a pulley system; weights were gradually added to the pan to increase the pulling force till the patch was broken. The tensile strength was calculated to all formulations and expressed in N/mm^2 [5].

f. Drug content uniformity of films

Film (size of 10x5 mm^2) is taken from different areas of the film and placed into a 25 ml volumetric flask, in to which 25 ml of artificial saliva was added and kept aside till the film is completely dissolved. Sample was withdrawn and absorbance was measured. The polymeric solution without drug served as blank.

g. In vitro drug release

Static dissolution methods were used to study the drug release from the periodontal chip. Films of known weight and dimensions (size of 10×5 mm^2) are placed separately into small test tubes containing 2 ml of simulated saliva. The test tubes were sealed with aluminum foil and kept at 37°C for 24 hours. The medium is drained off and replaced with fresh 2 ml of the simulated saliva after 24 hours. The concentration of drug in the medium is measured. The procedure can be repeated for 10 days [6].

h. In vitro antibacterial activity

Sterilized nutrient agar medium was prepared by autoclaving under aseptic condition and transfer the medium to sterile Petri plates. After solidification of nutrient agar medium, made a lawn with 0.1 ml microorganism i.e. S. aureus and E. coli in separate Petri plates, over that the films were placed and incubate for 48 hrs at 37° C. Measure the zone of inhibition using "Hi Antibiotic Zone Scale". Same procedure is followed by replacing the films over the next plates and measures the zone of inhibition [7,8].

3. RESULTS AND DISCUSSIONS

The film thickness of each formulation was measured and uniformity was observed in the range 0.075 to 0.315 mm.Theweight uniformity was satisfactory for all the formulations.The average weights of formulated patches range from 5.8 – 10.7mg. The foldingendurance was measured manually, byfolding the filmrepeatedly at a point till they were broken. The maximum averagefolding was found to be the highest for formulation CPC1 whilethe lowest for CPC4. The folding endurance values were foundto be optimum. The patches exhibited good physical andmechanical properties.The surface pH of the films was and attempts were made to keep the surface pH as close as to salivary pH. The pH values of all theformulations were within the range of salivary pH. Nosignificant difference was observed in surface pH fordifferent formulations.Drug content in all formulationswas found to be uniform ranging from 94.5% to 99%. Thisindicates that the drug was dispersed uniformly throughoutthe patches.Static dissolution methods were used to study the drug release from the periodontal chip. The percentage drug release is shown in the Fig. 1. CPC 1 was found to release drug upto 72% and CPC4 shows 56% at the end of 48 hrs. All the formulation shows a prolong release of drug which aids in treatment. After 24hours of incubation, the diameter of zone of inhibition was observed. It shows better antibacterial activity over S. aureus and E. coli microorganisms.

Table 2.Periochip properties - thickness, weight uniformity, folding endurance, tensile strength, drug content

Formulation	Thickness in mm	Wt uniformity in mg
CPC1	0.075	5.8
CPC2	0.15	9.5
CPC3	0.225	8.5
CPC4	0.315	

Table 2. Periochip properties - folding endurance, tensile strength, drug content

Formulation	Folding endurance	Tensile strength in N/mm^2	Drug content in %
CPC1	-	6.29	98
CPC2	271	2.99	96.5
CPC3	228	2.74	99
CPC4	117	1.52	94.5

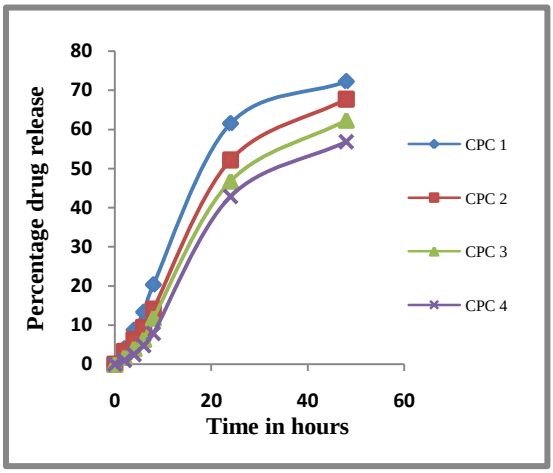

Fig. 1 Comparison of In-vitro drug release pattern of Periochip formulations (CPC1 – CPC4)

4. CONCLUSIONS

In the present study we attempted to load chlorhexidine in the polymeric material for use in periodontal infections and characterize the prepared films. After evaluating these for various parameters we concluded that it is an excellent system for drug delivery. The films were smooth, homogenous, non-sticky and flexible. The films were capable of inhibiting the growth of S. aureus and E. coli strains commonly found in periodontal disease. Films were developed to a satisfactory level in terms of drug content, drug release, mechanical properties and microbiological evaluation. On the basis of in vitro characterization it was concluded that chlorhexidine could be incorporated in a slow release chitosan chip for the treatment of periodontitis. Further, detailed investigation is required to establish in-vivo efficiency of these periochip.

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