International Journal of Pharmaceutical Development & Technology

e ISSN - 2248 - 910X

www.ijpdt.com

Print ISSN - 2248 - 9096

FORMULATION AND EVALUATION OF DENTAL FILM FOR PERIODONTITIS

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ABSTRACT

The study was to formulate and evaluate chitosan film containing tobramycin which will give local action for the treatment of periodontitis. Chitosan film containing tobramycin was prepared by solvent casting method. IR studies were done to determine the compatibility of drug with the polymer. Minimum inhibitory concentration of tobramycin was done by cup-plate method. The films were evaluated for their physicochemical properties like weight variation, thickness, drug content uniformity, folding endurance, % moisture loss, tensile strength and stability. Drug content uniformity was performed on *Staphylococcus aureus*. Scanning electron microscope (SEM) studies were done to determine the surface characteristics of the film.IR studies revealed that there is compatibility of drug with the polymer. Minimum inhibitory concentration of tobramycin was found to be 1 µg/ml. The physiochemical properties of the film showed good results.

Keywords: Chitosan, Dental film, Periodontitis, Tobramycin.

INTRODUCTION

Periodontitis is an inflammatory response in which the structural support to the tooth is destroyed. The disease results in resorption of the alveolar bone, detachment of the periodontal ligament supporting the tooth and formation of periodontal pocket [1].

Dental diseases are recognized as a major public health problem throughout the world. WHO reported that 10 – 15% of the world populations suffer from severe periodontitis. Prevalence of more than 20 % was seen in the populations of Bangladesh, Canada, Germany, India, Belarus and Chile. In India, the prevalence of severe periodontitis is in the range of 19- 32% [2].

Local delivery leads to higher concentration of the drug at the intended site of action using a lower dose with an associated reduction in side effects. To overcome these challenges, the film can be a better option for sustained release of drug for local action [3].

Films are matrix delivery systems in which the drug is distributed throughout the polymer and drug release occurs by diffusion and/or matrix dissolution or erosion. The size and shape of the film can be controlled according to the dimensions of the pocket where the film is to be inserted and should be easily placed with minimal pain to the patient. A periodontal film should be non toxic, non interfering and should have sufficient adhesiveness. Both degradable and non - bio degradable films have been developed. The films that release drug by diffusion alone are prepared using water insoluble or non-degradable polymers whereas those that release drug by diffusion and matrix erosion use soluble or biodegradable polymers in the matrix [4].

Chitosan is a natural polymer. A major advantage of natural polymers is that they do not affect periodontal tissue regeneration. Chitosan is a hydrophilic biopolymer obtained by alkaline deacetylation of chitin, a major component of arthropod shells, and possesses favorable properties such as nontoxicity, biocompatibility, bioadhesivity and biodegradability [5].

MATERIALS AND METHODS

MATERIALS

Tobramycin was obtained as gift sample from Teva API India Limited, Gajraula, UP. *Staphylococcus aureus* ATCC No. 29737 was procured from National Chemical Laboratories, Pune. Chitosan obtained from Research-Lab Fine Chem Pvt. Ltd., Mumbai., India. Mueller Hinton agar, Muller Hinton broth was obtained from Difco Laboratories, Detroit, Mich. Other materials used in the study were of analytical grade.

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METHODOLOGY

Drug-polymer compatibility study

The drug with excipient like tobramycin and chitosan in ratio 1:1 were stored for 4 weeks. Then the mixture of tobramycin & chitosan were evaluated by IR spectra by FTIR spectrometer.

Minimum inhibitory concentration

MIC was determined by Cup-plate method [6,7]

Preparation of tobramycin-loaded chitosan film

Chitosan was soaked in 100 ml aqueous acetic acid solution (1% v/v) for 24 hour to get a clear solution, which was later filtered through a muslin cloth to remove undissolved polymer (chitin). PEG 400 was added as a plasticizer. Tobramycin (based on the weight of chitosan) was incorporated in 100 ml of chitosan solution and vortexed for 15 min. The viscous dispersion was kept aside for 30 min for complete expulsion of air bubbles. Films were cast by pouring the drug-polymer solution into the center of glass moulds and allowed to dry at room temperature. The dried films were cut into strips of (5 × 5 mm), wrapped in aluminum foil and stored in desiccators at room temperature [5].

Evaluation of the film

Thickness of the films

Thickness of the film was measured using screw gauge at different areas of the film and the average was calculated [8].

Uniformity of weight of the films

Film (size of 5x5 mm) was taken from different areas of film. The weight variation of each film was calculated [9].

Folding endurance

The folding endurance of the films was determined by repeatedly folding the film at the same place till it broke or folded, which is considered satisfactory to reveal good film properties. This test was carried out on all the films [9].

Drug content uniformity of films

Content uniformity was determined by measuring the zone of inhibition by anti-microbial method. The films of the same size (5×5 mm) were place on the agar medium and the zones of inhibition were measured.

Moisture loss

The films of different concentrations were weighed accurately and then they are kept in desiccators for 3 days and then reweighed and by using the formula % moisture loss was calculated [9].

[(initial wt – final wt)/initial wt] ×100

Tensile strength of the film

Tensile strength was evaluated using a tensile strength tester (Brookfield Engineering Labs, Inc.) with a 5 g load cell. Films of the required dimension and free from air bubbles or physical imperfections were held between two clamps. During measurement, the top clamp, at a rate of 0.5 mm/s, was pulled, and the force was measured when the film broke. Only results from film samples that broke between the clamps were used [5].

Scanning electron microscopy

The morphology and surface topography of the films were examined by SEM (Nova Nanosem 450). Spherical samples (5 mm^2) were mounted on the SEM sample stab using a double-sided sticking tape. The samples were coated with chromium (200 A^0) under reduced pressure (0.001 torr) for 2 min using an ion sputtering device. The chromium-coated samples were observed under the SEM and photomicrographs of suitable magnifications were obtained [5].

Stability studies

The films were wrapped individually in aluminium foil and butter paper and placed in Petri dishes. These containers were stored at ambient humidity conditions in a refrigerator at 4-8ºC and in an oven at 45 ± 2ºC for 3 months. The samples were analyzed for its physiochemical properties.

RESULTS AND DISCUSSION

A) FTIR study

The IR spectra of drug excipients mixtures showed the presence of characteristic drug peaks thus indicating no evidence of interaction between the drug and excipients used in the study.

From Fig 1& Fig 2 study, the characteristic peak of drug such as The FTIR analysis of pure Tobramycin gave strong absorption bands around 3363 cm^{-1}, 2921 cm^{-1} attributed to the stretching of amine and hydroxyl groups, and the stretching of aliphatic CH respectively. Other peaks at 1601.12 cm^{-1}, 1470.67 cm^{-1}, 1381.04 cm^{-1} respectively attributed to the bending of NH group, CH_2 scissoring, OH bending and finally 1033.95 cm^{-1} corresponding to C-O & C-N.

Minimum inhibitory concentration

The Minimum inhibitory concentration of Tobramycin was found to be 1 µg/ml [7].

Optimization of film

Optimization of film was done by kill kinetics method. Kill kinetics curves are pharmacodynamic examples of bactericidal activity expressed as rate of killing by a fixed concentration of antimicrobial. Time-kill kinetics gives a good overview of how fast an antimicrobial can kill

certain bacteria and prevent their regrowth. These parameters are important for the assessment of the efficacy of bactericidal drugs [10,11].

1.5% chitosan concentration with PEG 400 (0.5%) as a plasticizer was optimized for the preparation of film by kill kinetics.

Physicochemical properties of chitosan film

a) Thickness

It was confirmed that the film prepared was of uniform thickness. The thickness of the film was 0.09 ± 0.01 mm (Table 1).

b) % Weight variation

The weight variation indicated that different weights were relatively similar of the film form different areas of film and was found to be 2.1 ± 0.06 mg (Table 1).

c) Folding endurance

Folding endurance results of dental film was found to be 257 ± 0.1 indicating that the film would not break and would maintain their integrity with the periodontal pocket (Table 1).

d) Moisture Loss (%)

The moisture content of the film was found to be 5.1 ± 0.25. The results revealed that the moisture absorption and moisture content was found to increase with increasing concentration of hydrophilic plasticizer (PEG 400). The moisture content in the formulations helps them to remain stable and from being a completely dried and brittle film (Table 1).

e) Tensile strength

The tensile strength was found to be 3.16±0.1 kg/cm^2 which show that the film showed good tensile strength indication the film wound not break and will remain intact in the periodontal pocket (Table 1).

f) Drug content uniformity

Table 2 indicates that the film from the left, middle and right position of the film prepared with the concentration 1%-5% having mean range from 1.2-2.5 and SD in the range from 0.05-0.1. This indicated that the drug is uniformly distributed throughout the film signifying appropriation method of preparation of film.

Scanning electron microscopy

Figure 3, Scanning electron microscopy showed that the surface of chitosan film was smooth suggesting that the drug was dissolved in the polymer solution prior to film formation.

Stability studies

From table 3, the physicochemical parameter of the optimized formulation was not significantly changed on storage in case of chitosan film. The result indicates that the chitosan film formulation was stable on the required storage condition.

Fig 1. FTIR spectra of Drug (Tobramycin)

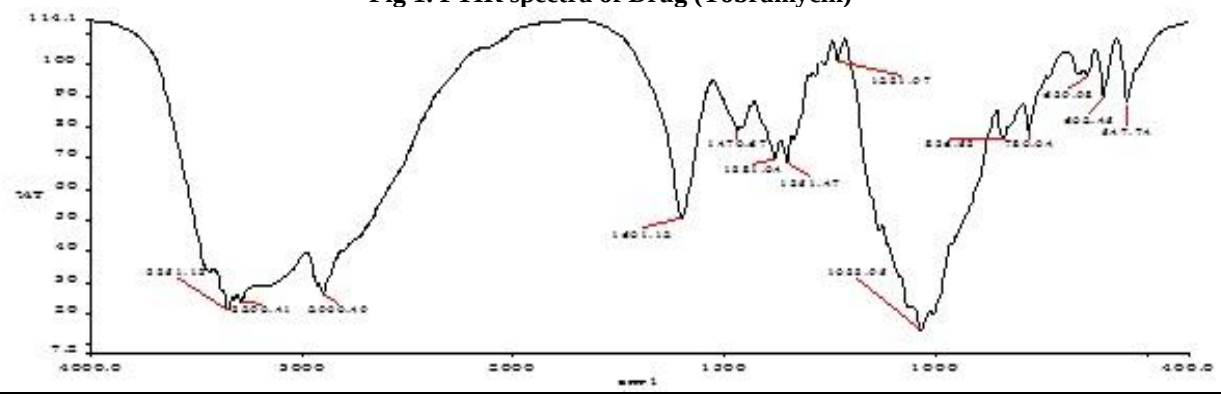

Fig 2. FTIR spectra of Drug + Chitosan

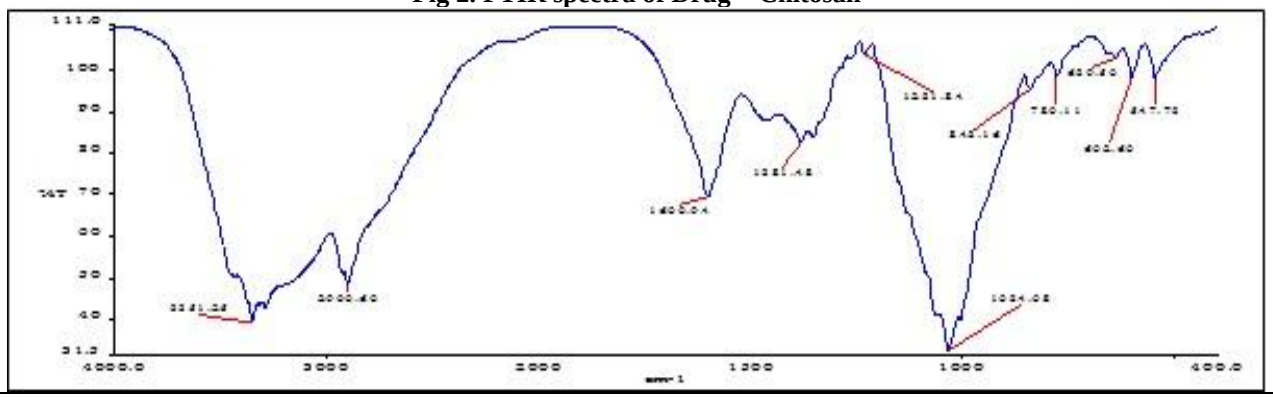

Fig 3. Scanning electron microscopy

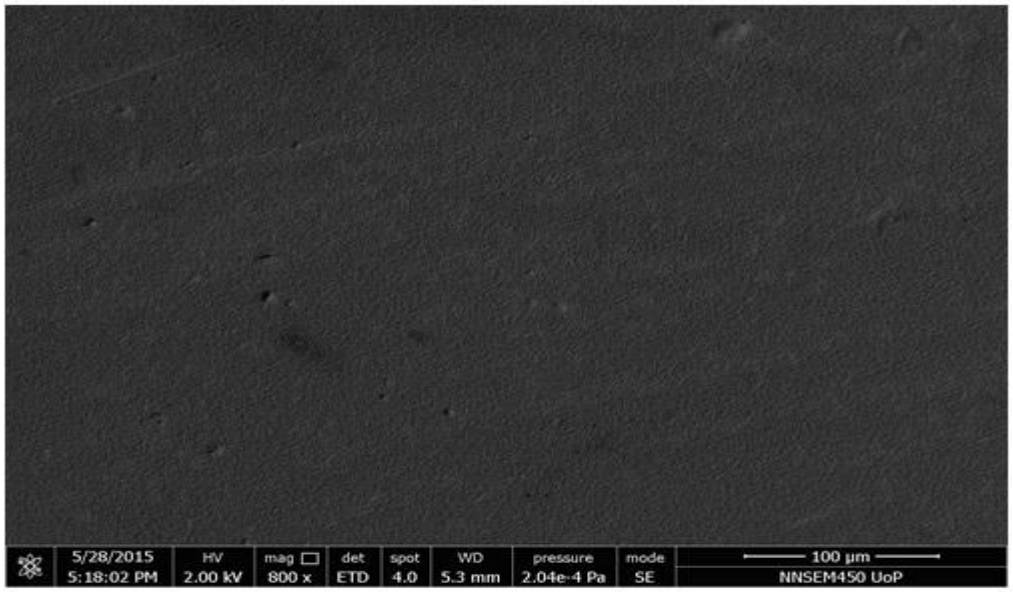

Table 1. Physicochemical properties of chitosan film

Film type	Thickness (mm)	Weight Uniformity (mg)	Folding endurance	Moisture Loss (%)	Tensile strength (kg/cm^2)
1.5 % Chitosan film	0.09 ± 0.01	2.1 ± 0.06	257 ± 0.1	5.1 ± 0.25	3.16 ± 0.1

Table 2. Drug content uniformity of chitosan film

Drug concentration of drug in film	Left		Middle		Right	
	Mean	SD	Mean	SD	Mean	SD
1%	1.3	0.1	1.4	0.1	1.2	0.1
2%	1.5	0.05	1.6	0.1	1.6	0.15
3%	1.73	0.11	1.9	0.05	1.6	0.05
4%	1.96	0.05	2.2	0.05	2	0.05
5%	2.3	0.05	2.5	0.1	2.3	0.1

Table 3. Physicochemical properties of chitosan film (Stability studies)

Film type	Thickness (mm)	Weight Uniformity (mg)	Folding endurance	Moisture Loss (%)	Tensile strength (kg/cm^2)
1.5 % Chitosan Film	0.09 ± 0.01	2.3 ± 0.05	245 ± 0.1	5.1 ± 0.15	3.45 ± 0.1

CONCLUSION

In case of periodontitis as higher concentration of drug can be released at the intended site, dental film can be a better option for sustained release of drug for local drug delivery along with fewer side effects. The drug-loaded chitosan films showed good tensile strength and also satisfactory physicochemical characteristics. Also from the stability studies it can be observed that the film is stable on its required storage conditions.

ACKNOWLEDGEMENT

The authors would like to thank to Teva API India Limited, Gajraula, UP for providing Tobramycin as a gift sample and also to AISSMS College of Pharmacy, Pune for providing required facilities for research work.

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