CHAPTER 5

Periodontal Mucoadhesive Strips

5.1 INTRODUCTION

A far more widely used intra pocket periodontal delivery device has been the strip or film form. Strips are matrix delivery systems in which drugs are distributed throughout the polymer and release occurs by drug diffusion and/ or matrix dissolution or erosion. This dosage form has several advantageous physical properties for intra pocket use (Soskolne and Freidman 1996). Based on the type of drug release and to be remained submerged without any noticeable interference to the patient's oral hygiene habits, strips can be classified into degradable (release of drug by both diffusion and matrix erosion or dissolution and use water soluble polymers) (Noguchi et al, 1984; Higashi et al, 1990) or biodegradable polymers in the matrix (Baker et al, 1988; Larsen 1990; Collins et al, 1989; Minabe et al, 1989; Addy et al, 1984) and non-degradable (release of drug by diffusion and use water insoluble non-degradable polymers) (Goodson et al, 1983; Addy et al, 1982) forms.

However, mucoadhesive periodontal strips are preferred in terms of flexibility and comfort. In addition, they can circumvent the relatively short residence time of oral gels on the mucosa, which are easily washed and removed by saliva. Moreover periodontal strips are also suitable for protecting wound surfaces, thus reducing pain and increasing the treatment effectiveness (Peh and Wong, 1999). These systems could be effectively used in the treatment of periodontal diseases by periodontal route as it would increase the residence time in the periodontal cavity associated with increased drug absorption to periodontal cavity for minocycline hydrochloride and clindamycin phosphate. The local transfer of minocycline hydrochloride and clindamycin phosphate to target site will not only result in rapid onset of action but also increases the residence time of the formulation in the periodontal cavity and so will result in highly effective antimicrobial therapy.

In the past no attempt has been ever done to deliver minocycline hydrochloride/ clindamycin phosphate in a biodegradable strip dosage form to the periodontal cavity. This chapter deals with development of effective periodontal delivery system containing minocycline hydrochloride/ clindamycin phosphate using biodegradable polymer hydroxy propyl methyl cellulose and polyvinyl alcohol. The formulations were evaluated for various physicochemical and mechanical properties such as mass uniformity and strip thickness, drug

content uniformity, moisture absorption, surface pH, folding endurance, tensile strength, elastic modulus, elongation at break, strain, swelling index, residence time, mucoadhesion force, etc. The periodontal strips were also evaluated for in vitro diffusion through membrane and in vitro permeation across sheep buccal mucosa.

5.2 EXPERIMENTAL

5.2.1 Preparation of periodontal mucoadhesive strips containing minocycline hydrochloride/ clindamycin phosphate

The plain placebo strips were first prepared by coating technique (Cui et. al, 2004), using 5.0, 7.5, 10.0% w/v PVA and 1.0, 1.25, 1.50 % w/v HPMC. In all cases, 2.5% (w/v) propylene glycol was added as plasticizer. PVA and HPMC polymer was dissolved in warm water at 40 to 50^0C, and then propylene glycol was added under stirring after cooling and the final volume was adjusted with distilled water. The viscosity of the prepared gels was measured. The gels were left overnight at room temperature till clear, bubble-free gels were obtained. The gels were coated on a 30 mm polyester strip and allowed to dry in an oven maintained at 40^0C till it dried completely.

The drug loaded periodontal mucoadhesive strips were prepared following the similar manner. The drug solution was added to the polymer solution containing propylene glycol with continuous stirring. After formation of a clear gel the volume was adjusted with distilled water. The dried periodontal strips were visually observed for any imperfections or air bubbles. The drug coated periodontal strips were cut into strips of $1cm^2$ diameter, so that each strip contains 2 mg of the drug. The samples were packed in aluminum foil and stored in glass container maintained at room temperature and 58% relative humidity (Peh and Wong, 1999). This condition maintained the integrity and the elasticity of the periodontal strips. To improve the elasticity, film forming property and mucoadhesive property of the periodontal strips, carbopol 934P was added. Carbopol 934P was first dissolved in a small volume of distilled water, and then added to the polymeric solution and the periodontal strips were prepared as described above.

5.3 CHARACTÉRISATION OF FORMULATION

5.3.1 Mass uniformity and strip thickness

Assessment of mass uniformity was done in 10 different randomly selected periodontal mucoadhesive strips from each batch and thickness of the periodontal strips was measured at 10 different randomly selected spots of different periodontal strips using a micrometer (Digimatic micrometer, Mitutoyo, Tokyo, Japan) from each batch. The mean and standard deviations were calculated.

5.3.2 Drug content uniformity

The drug content uniformity of drug loaded periodontal mucoadhesive strips were determined by weighing 5 periodontal strips (1cm^2) and allowed to dissolve in 25 ml isotonic phosphate buffer, pH 6.75 (PBS) for 4h. After suitable dilution the resultant solution was filtered and analyzed spectrophotometrically for minocycline hydrochloride/ clindamycin phosphate content.

5.3.3 Moisture absorption

A modification of the ASTM test No-D570-59T was used for testing of moisture absorption/ loss of water from periodontal strips (1.8 × 1.8 cm), which was determined as reported by Kanig and Goodman in 1962.

5.3.4 Surface pH

Mucoadhesive periodontal strips (1 cm^2) were allowed to swell in for 2 h on the surface of an agar plate, prepared by dissolving 2% (w/v) agar in warm isotonic phosphate buffer of pH 6.75 under stirring and then pouring the solution into the petridish till gelling at room temperature (Parodi et al,1996). The surface pH was measured by means of pH indicator paper. After 90 s the color developed was compared with the standard color scale. The mean of the six readings was recorded.

5.3.5 Viscosity

Aqueous solutions containing both polymer and plasticizer were prepared in the same concentration as that of the drug loaded mucoadhesive periodontal strips. A model LVDV-II

Brookfield viscometer attached to a helipath spindle no. 4 was used to measure the viscosity at 20 rpm at room temperature. The recorded values were the mean of three determinations.

5.3.6 Folding endurance test

The folding endurance of the drug loaded mucoadhesive periodontal strips was determined by repeatedly folding one strip at the same place till it broke or folded up to 300 times at the same place without breaking gave the value of the folding endurance (Khanna et al, 1997).

5.3.7 Measurement of Mechanical Properties

Mechanical properties of the drug loaded mucoadhesive periodontal strips were evaluated using universal testing machine (UTM) equipped with a 10 kg load cell (LF Plus, Lloyd Instruments, UK). Periodontal strips prepared in dimension of 100×50 mm were free from air bubbles or any physical imperfections. The mucoadhesive strips were held between two clamps positioned at a distance of 5 cm. A piece of paper was attached on the surface of the clamp via a double-sided tape to prevent the drug loaded mucoadhesive periodontal strip from being cut by the groove of the clamp. During measurement, the periodontal strips were pulled by the top clamp at a rate of 1.00 mm/s to a distance of 10 cm before returning to the starting point. The force and elongation were measured when the periodontal strip broke. Results from periodontal strip samples, which broke at and not between the clamps were not included in calculation. Measurements were run in triplicates for each strip. The following equations were used to calculate the mechanical properties of the strip;

$$\text{Tensile strength } (kgmm^{-2}) = \frac{\text{Force at break (kg)}}{\text{Initial cross sectional area of the sample } (mm^2)}$$

$$\text{Elastic Modulus } (kgmm^{-2}) = \frac{\text{Force at corresponding strain (kg)}}{\text{Cross-sectional area } (mm^2)} \times \frac{1}{\text{Corresponding strain}}$$

$$\text{Elongation at break } (\%\ mm^{-2}) = \frac{\text{Increase in length (mm)}}{\text{Original length (mm)}} \times \frac{100}{\text{Cross-Sectional area } (mm^2)}$$

$$\text{Strain} = \frac{\text{Tensile strength}}{\text{Elastic modulus}}$$

5.3.8 Swelling index

The swelling studies of mucoadhesive periodontal strips were conducted using two media, namely, distilled water and PBS pH 6.75. Each periodontal strip sample (surface area 5 cm^2) was weighed and placed in a pre-weighed stainless steel wire mesh with sieve opening of approximately 500 μm. The mesh containing the periodontal strip samples was then submerged into 25 ml medium contained in a glass container. Increase in weight of the periodontal strip was determined at preset time intervals until a constant weight was observed. Each measurement was repeated for six times. The degree of swelling was calculated using equation given by Peh and Wong in 1999;

Degree of swelling = $(W_t - W_0) / W_0$

Where, W_t is the weight of periodontal strip at time t

W_0 is the weight of periodontal strip at time zero.

5.3.9 Residence time

The in vitro residence time was determined using a modified USP disintegration apparatus, (Nakamura et al, 1996). The disintegration medium was composed of 800 ml PBS of pH 6.75 maintained at 37±1^{0}C. A segment of sheep cheek mucosa, 3 cm long was glued to the surface of the glass slab, vertically attached to the apparatus. The mucoadhesive part of the drug loaded periodontal strip was hydrated using 50 micro liters of PBS pH 6.75 and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to move up and down so that the periodontal strip was completely immersed in the buffer solution at the lowest point and move till the highest point. The time necessary for complete detachment of the periodontal strip from the mucosal surface was recorded.

5.3.10 Mucoadhesion force

The tensile strength required to detach the drug loaded mucoadhesive periodontal strips from the mucosal surface was applied as a measure of the bioadhesive performance. The apparatus was locally assembled and was a modification of the apparatus previously applied by Parodi (Parodi et al, 1996) using sheep cheek mucosa membrane. The device was mainly composed of a two arm balance. The left arm of the balance was replaced by a small platinum lamina

vertically suspended through a wire. At the same side, a movable platform was maintained in the bottom in order to fix the model mucosal membrane. For determination of the mucoadhesion force, the drug loaded mucoadhesive periodontal strip was fixed to the platinum lamina using cyanoacrylate adhesives. A piece of sheep cheek mucosa, 3 cm long, was also glued to the platform. The exposed periodontal strip surface was moistened with 50 micro liter of PBS, and left for 30 s for initial hydration and swelling. The platform was then raised upward until the hydrated periodontal strip was brought into contact with the mucosal surface. A preload of 20 g was placed over the platinum lamina for 3 min as initial pressure. On the right pan, a constant weight of 1 g was added at 2 min intervals. The total weight required for complete detachment of the periodontal strip was recorded and the mucoadhesion force was calculated per unit area of the strip as follows;

$$F = (W_w \times g)/ A$$

Where, F is the mucoadhesion force (kg m^{-1} s^{-2}), W_w is the mass applied (g), g is the acceleration due to gravity (cm s^{-2}), A is the surface area of the drug loaded periodontal strip (cm^2). The adhesion force data reported represents the mean of six determinations.

5.3.11 In vitro release study

The drug loaded mucoadhesive periodontal strips were evaluated for drug release using Franz-diffusion cells. Cellophane sheets treated with 5% w/v of glycerin (Viegas et al, 1988; Anders et al, 1989) were mounted between the donor and receptor compartment clamped together. The receptor compartment was filled with phosphate buffer, pH 6.75 and the hydrodynamic in the receptor compartment was maintained by stirring with a magnetic bead at 100 rpm. The cell temperature was maintained at 37±1°C through a circulating water bath. At predetermined time interval, samples were withdrawn and an equal volume of pre-warmed buffer was replaced. The samples were analyzed after appropriate dilution for minocycline hydrochloride/ clindamycin phosphate content.

5.3.12 In vitro Permeation studies

In vitro permeation studies of various drug loaded mucoadhesive periodontal strips were done as described by many research groups (Caschel et al, 2000; Pisal et al, 2004). Cheek mucosal tissues were carefully removed from the oral mucosal cavity of sheep obtained from

the local slaughter house. Fresh sheep cheek mucosal membrane was fixed onto the Franz-diffusion cell. The 1cm^2 of periodontal strip was placed on to the mucosa previously fixed in between the donor and the receptor compartment of Franz-diffusion cell. The receptor compartment contained phosphate buffer, pH 6.75. The temperature of the elution medium was thermostatically controlled at 37±1^{0}C by a surrounding water jacket and the medium was stirred with a bar magnet at 100 rpm, using a magnetic stirrer. Aliquots withdrawn at predetermined intervals over 8 h. were spectroscopically estimated to quantitate the amount of minocycline hydrochloride/ clindamycin phosphate content.

5.3.13 Data Analysis of Permeation studies

The steady state permeation flux was determined from the slope of the linear portion of the cumulative amount permeated (Q) versus time (t) plot. The lag time (t_L) was determined by extrapolating the linear portion of Q versus t curve to the abscissa. The partition coefficient of minocycline hydrochloride/ clindamycin phosphate was calculated as described by equation (Saket et al, 1984);

$$\text{Partition coefficient} = \frac{Cs - Ceg}{Ceg} \times \frac{1000}{We}$$

Where, Cs, Ceg and We are the initial concentration of minocycline hydrochloride/ clindamycin phosphate in phosphate buffer solution (mg.ml^{-1}), equilibrium concentration (mg.ml^{-1}) and weight (mg) of mucous membrane respectively. The dry weight of the mucous membrane was considered for calculating the partition coefficient.

The permeability coefficient (P) was calculated using the relation derived from fick's first law of diffusion (Aslani and Kennedy, 1996);

$$P = \frac{J.h}{C}$$

Where J is the steady state permeation flux, c is the initial concentration and h is the thickness of the mucous membrane.

Diffusion coefficient was calculated using the relation derived from fick's second law of diffusion (Pefile et al,, 1998);

$$D = \frac{h^2}{6L}$$

Where h is the thickness of the mucous membrane and L is the lag time.

5.3.14 FTIR studies

FTIR spectral measurements of drug loaded periodontal mucoadhesive strips were performed using a Shimadzu FTIR spectrometer. Periodontal strips were grounded with KBR and FTIR spectra were taken in the range 4500-500cm^{-1}.

5.3.15 Stability study

The optimized batch was subjected to stability studies. Formulation was stored in pouches at room temperature for six months. The change in percentage entrapment efficiency and particle size was determined after 180 days.

5.4 RESULTS AND DISCUSSION

5.4.1 Preparation of plain HPMC and PVA strips

Periodontal mucoadhesive strips are prepared by coating technique. The formation of plain placebo strips involves the following processes: the formation of polymer solution, coating of the polymer solution in the polyester film, followed by drying of the coated film. Finally placebo HPMC/ PVA strips were cut into 1cm^2. Effect of polymer concentration on the placebo strip formation was investigated. Effect of carbopol 934P on the formation of strips and their mucoadhesive property were investigated.

5.4.1.1 Effect of polymer concentration on the strip formation

Biodegradable polymer hydroxy propyl methyl cellulose and polyvinyl alcohols were tried for the preparation of the periodontal strips. For optimization of the polymer concentration for the formation of the periodontal strips different concentrations of hydroxy propyl methyl cellulose (0.75 % w/v, 1.0 % w/v, 1.25 % w/v, 1.5 % w/v) and polyvinyl alcohol (2.5 %w/v, 5.0 % w/v, 7.5 % w/v, and 10.0 % w/v) were investigated. Periodontal strips formulated using 0.75 % w/v of hydroxy propyl methyl cellulose was found to be very thin. Similarly the periodontal strips formulated using 2.5 % w/v of polyvinyl alcohol does not form strips properly. Therefore 1.0 % w/v, 1.25 % w/v, 1.5 % w/v of hydroxy propyl methyl cellulose and 5.0 % w/v, 7.5 % w/v, and 10.0 % w/v polyvinyl alcohol were selected as the optimized polymer concentration for the preliminary investigation.

5.4.1.2 Effect of plasticizer concentration on the periodontal strip formation

Periodontal strips should possess the suitable flexibility as hard and rigid strips are difficult to be placed in the periodontal cavity. Hence, to improve the strip softening and flexibility, propylene glycol was incorporated in the formulation as a plasticizer. Effect of propylene glycol on the strip forming property was investigated. Three different concentrations (2.5 % w/v, 5.0 % w/v and 7.5 % w/v) of propylene glycol were investigated. From the visual observation it was found that the formulations prepared using 2.5 % w/v was found to be brittle in nature and very much hard to remove from the polyester films. Formulations prepared with 5.0 % w/v propylene glycol formed good strips with easy removal from the polyester films. Similarly the formulations prepared with 7.5 % w/v propylene glycol formed oily strips, which showed that the polymer to plasticizer concentration is high. The results of the folding endurance shown in the table no 5.01 conformed the visual observations. Formulations prepared using 2.5% w/v propylene glycol showed a very little resistance to the folding stress, which again conformed that the strips to be rigid in nature. Formulations containing 5.0 % w/v propylene glycol showed a folding endurance between 120 -180 for PVA containing periodontal strips and 107 - 155 for HPMC periodontal strips.

There was not much difference in the folding endurance in formulations prepared using 7.5% w/v propylene glycol in comparison to 5.0 % w/v propylene glycol containing periodontal strips. However, the oily nature of the periodontal strips containing 7.5% w/v propylene glycol after drying resulted in discarding of the formulation. Hence, 5.0% w/v propylene glycol was optimized as the concentration to be used in all the formulations.

Table no: 5.01: Composition and effect of concentration of polymer and plasticizer on the strip formation

Composition / Characteristics	Batch code					
	SF1	SF2	SF3	SF4	SF5	SF6
PVA (%,w/v)	5.00	7.50	10.00	-	-	-
HPMC (%,w/v)	-	-	-	1.00	1.25	1.50
Propylene glycol (% w/v)	2.50	2.50	2.50	2.50	2.50	2.50
Folding endurance	5.00±1.0	7.00±1.0	10.00±2.0	3.00±1.0	6.00±1.0	8.00±1.0
Visual observation	Brittle strips were formed					

Composition / Characteristics	Batch code					
	SF7	SF8	SF9	SF10	SF11	SF12
PVA (%,w/v)	5.00	7.50	10.00	-	-	-
HPMC (%,w/v)	-	-	-	1.00	1.25	1.50
Propylene glycol (% w/v)	5.00	5.00	5.00	5.00	5.00	5.00
Folding endurance	120 ±5.0	150 ±7.0	180 ±10.0	107 ±6.0	125 ±7.0	155 ±9.0
Visual observation	Good strips were formed					
Composition / Characteristics	Batch code					
	SF13	SF14	SF15	SF16	SF17	SF18
PVA (%,w/v)	5.00	7.50	10.00	-	-	-
HPMC (%,w/v)	-	-	-	1.00	1.25	1.50
Propylene glycol (% w/v)	7.50	7.50	7.50	7.50	7.50	7.50
Folding endurance	135 ±7.0	165 ±9.0	190±9.0	115±5.0	135±8.0	170±6.0
Visual observation	Oily strips were formed					

5.4.1.3 Effect of mucoadhesive polymer concentration on the strip formation

To improve the mucoadhesive property of the periodontal strips, carbopol 934P (possessing mucoadhesive property) was incorporated in the strip formulation. Effect of different concentrations of the carbopol 934P (0.25 % w/v, 0.50 % w/v and 0.75 % w/v) on the periodontal strips was investigated. Formulations prepared with 0.75 % carbopol 934P does not form the strip as it holds the moisture within it for a longer period of time due to the high concentration of carbopol 934P. Formulations prepared with 0.25 % w/v carbopol 934P along with 5.00 % w/v PVA and 1.0 % HPMC formed a soft film. Similar results were observed in the formulations prepared using 0.5 % w/v carbopol 934P along with 5.0 % w/v, 7.5 % w/v PVA and 1.0 % w/v, 1.25 % w/v HPMC periodontal strips. From the results of folding endurance as shown in the table no 5.02 it was found that incorporation of the carbopol 934P softened the film leading to an increase in folding endurance. The texture property confirmed the formation of soft strips due to the retention of the moisture in the strip, because of the holding of the moisture by the polymer used in the strips. Therefore, the formulations SF20, SF21, SF23, SF24, SF27 and SF30 were optimized for further study.

5.4.2 Mass uniformity and strip thickness

Mass uniformity and the strip thickness confirm the uniformity of the coating for the preparation of the periodontal strips. Mass uniformity was done in 10 different randomly selected periodontal strips from each batch and weighed. Thickness of the periodontal strips was measured at 10 different randomly selected spots of different periodontal strips from each batch by using a micrometer.

From the results of the periodontal strip formulations given in the table no 5.03, 5.04 and 5.05, it was concluded that the mass of the periodontal strips varied from 228.33 mg to 522.33 mg for the plain periodontal strips, while for minocycline hydrochloride loaded periodontal strips variation was from 230.33 mg to 526.33 mg. Similarly the mass of clindamycin phosphate loaded periodontal strips ranged from 231.66 mg to 525.50 mg. All the periodontal strips showed uniform mass content, which conformed to the uniformity of the periodontal strips. The thickness of the periodontal strips depends on the mass content parameter of the periodontal strips.

Table no: 5.02: Composition and effect of mucoadhesive polymer on the periodontal strip formation

Composition / Characteristics	Batch code					
	SF19	SF20	SF21	SF22	SF23	SF24
PVA (%,w/v)	5.00	7.50	10.00	-	-	-
HPMC (%,w/v)	-	-	-	1.00	1.25	1.50
Carbopol 934P (%,w/v)	0.25	0.25	0.25	0.25	0.25	0.25
Propylene glycol (% w/v)	5.00	5.00	5.00	5.00	5.00	5.00
Folding endurance	135.50 ± 7.0	175.50 ± 5.0	210.00 ±7.5	120.50 ± 5.0	150.00 ± 6.5	190.50 ± 8.5
Visual observation	Soft strips	Good strips	Good strips	Soft strips	Good strips	Good strips
Composition / Characteristics	Batch code					
	SF25	SF26	SF27	SF28	SF29	SF30
PVA (%,w/v)	5.00	7.50	10.00	-	-	-
HPMC (%,w/v)	-	-	-	1.00	1.25	1.50
Carbopol 934P (%,w/v)	0.50	0.50	0.50	0.50	0.50	0.50
Propylene glycol (% w/v)	5.00	5.00	5.00	5.00	5.00	5.00
Folding endurance	145.50 ± 8.0	210.50 ± 6.0	255.50 ± 5.50	135.00 ± 5.0	185.50 ± 7.0	220.00 ±7.5
Visual observation	Soft strips	Soft strips	Good strips	Soft strips	Soft strips	Good strips

Composition / Characteristics	Batch code					
	SF31	SF32	SF33	SF34	SF35	SF36
PVA (%,w/v)	5.00	7.50	10.00	-	-	-
HPMC (%,w/v)	-	-	-	1.00	1.25	1.50
Carbopol 934P (%,w/v)	0.75	0.75	0.75	0.75	0.75	0.75
Propylene glycol (% w/v)	5.00	5.00	5.00	5.00	5.00	5.00
Folding endurance	-	-	-	-	-	-
Visual observation	No strips formed					

The thickness of the plain periodontal strips varied from 1.13 mm to 5.77 mm, while minocycline hydrochloride/ clindamycin phosphate loaded periodontal strips varied from 1.27 mm to 5.81mm and 1.25 mm to 5.82 mm respectively. The thickness added the conformation of the periodontal strip uniformity throughout the geometry of the strips.

5.4.3 Drug content uniformity

Drug content uniformity of drug loaded mucoadhesive periodontal strips were determined by weighing 5 periodontal strips (1 cm^2) and allowed to dissolve in 25 ml isotonic phosphate buffer, pH 6.75 (PBS) for 4h. After suitable dilution the resultant solution was filtered and analyzed spectrophotometrically for drug (minocycline hydrochloride/ clindamycin phosphate) content. The drug content of the minocycline hydrochloride loaded periodontal strips varied from 100.07 to 101.91 %, while for clindamycin phosphate content varied from 101.47 to 103.40 %. From the results it was concluded that the drug distribution is uniform throughout the periodontal strips.

5.4.4 Moisture absorption

All the optimized mucoadhesive periodontal strip formulations (1.8 × 1.8 cm) were subjected for testing of moisture absorption/ loss of water by using a modified ASTM test No-D570-59T, as determined previously by Kanig and Goodman in 1962. For determination of the moisture absorption, plain and drug loaded periodontal strips were subjected to exposure to the controlled relative humidity environment for 7 days and weight gain by the periodontal strips was determined at 1 day and 7 day. The periodontal strips were also observed visually for any physical changes. From the results as shown in table no 5.06, 5.07 and 5.08 it is

evident that all the periodontal strips gained moisture when exposed to humidity. The periodontal strips prepared with PVA gained less amount of moisture compared to the HPMC containing periodontal strips. Moisture gain in plain PVA periodontal strips varied from 1.78 to 3.48% after 24h exposure, while for HPMC plain periodontal strips variation was from 2.53 to 4.46 %. On 7^{th} day the moisture gained was about 6.10 to 11.54% for plain periodontal strips. The drug loaded mucoadhesive periodontal strips gained more moisture compared to the plain periodontal strips which may be due to holding of the moisture by the salt of the minocycline hydrochloride/ clindamycin phosphate. After 7 days, the minocycline hydrochloride loaded periodontal strips gained 6.48 to 10.05 % for PVA strips while HPMC strips gained 7.26 to 11.94%. For clindamycin phosphate loaded mucoadhesive periodontal PVA strips variation was from 6.82 to 10.29% and for HPMC periodontal strips it is from 7.46 to 12.42%. From the visual observation it was conformed that there was absence of any color change in any of the periodontal strips.

From the results of the folding endurance it was found that the periodontal strips were shown higher value of folding endurance indicating the softening of the periodontal strip. Therefore storage of the periodontal strips should be done in a controlled environment to avoid the moisture gain.

5.4.5 Surface pH

All the optimized drug loaded mucoadhesive periodontal strips (1 cm^2) were allowed to swell in for 2h on the surface of an agar plate, prepared as described by Parodi et al,. The surface pH was measured by means of a pH indicator paper. After 90 s the color developed was compared with the standard color scale and the mean of the six readings was recorded. From the results given in the table no 5.03, 5.04 and 5.05 it was concluded that the plain periodontal strips showed pH varying from 5.23 to 5.73, while the minocycline hydrochloride/ clindamycin phosphate loaded periodontal strips varied from 5.36 to 5.83 and 5.43 to 5.90 respectively. There was not much difference in pH observed between the plain and drug loaded periodontal strips and found to be within the mucosal pH, hence possibility of mucosal irritations is not expected.

5.4.6 Viscosity

Aqueous solutions containing both polymer and plasticizer were prepared in the same concentration as that of the optimized drug loaded mucoadhesive periodontal strips. A model LVDV-II Brookfield viscometer attached to a helipath spindle no. 4 was used to measure the viscosity at 20 rpm at room temperature. The recorded values were the mean of three determinations. It was found that the 10.00 % w/v PVA solutions showed less viscosity compared to the 1.50 % w/v HPMC solutions. Addition of the mucoadhesive polymer, carbopol 934P, to the formulations increases the viscosity of the formulations. By controlling the viscosity of the formulations, the release characteristics of the periodontal strips can be controlled.

5.4.7 Folding endurance test

The folding endurance of the drug loaded mucoadhesive periodontal strips was determined by repeatedly folding one strip at the same place till it broke or folded up to 300 times at the same place without breaking gave the value of the folding endurance (Khanna et al,1997). The results recorded are the mean of three observations, from which the nature of the periodontal strips can be concluded. All the drug loaded mucoadhesive periodontal strips showed the folding endurance between 162 to 267 times, which concluded that all the periodontal strip formulations are soft in nature. Addition of the mucoadhesive polymer carbopol 934P increases the folding endurance of the periodontal strips, which indicates the increase in the flexibility of the strips.

Table no: 5.03: Composition and characteristics of plain periodontal strips

Composition / Characteristics	Batch code					
	SF20	SF21	SF23	SF24	SF27	SF30
PVA (%,w/v)	7.50	10.00	-	-	10.00	-
HPMC (%,w/v)	-	-	1.25	1.50	-	1.50
Carbopol 934P (% w/v)	0.25	0.25	0.25	0.25	0.50	0.50
Propylene glycol (% w/v)	5.00	5.00	5.00	5.00	5.00	5.00
Strip mass (mg)	337.33 ± 3.51	507.00 ± 4.58	228.33 ± 2.51	253.66 ± 4.50	522.33 ± 2.08	261.66± 1.52
Strip thickness (mm)	3.72 ± 0.07	5.62 ± 0.10	1.13 ± 0.03	1.29 ± 0.04	5.77 ± 0.02	1.34 ± 0.02
Surface pH	5.23 ± 0.15	5.56 ± 0.20	5.63 ± 0.20	5.73 ± 0.15	5.63 ± 0.30	5.53 ± 0.23
Folding endurance	175.50 ± 5.0	210.00 ± 7.5	150.00 ± 6.5	190.50 ± 8.5	255.50 ± 5.50	220.00 ± 7.5
Viscosity (mPa s)	10.25	12.85	18.62	22.14	15.24	28.35

Table no: 5.04: Composition and characteristics of minocycline hydrochloride loaded mucoadhesive periodontal strips

Composition / Characteristics	Batch code					
	MSF20	MSF21	MSF23	MSF24	MSF27	MSF30
PVA (%,w/v)	7.50	10.00	-	-	10.00	-
HPMC (%,w/v)	-	-	1.25	1.50	-	1.50
Carbopol 934P (% w/v)	0.25	0.25	0.25	0.25	0.50	0.50
Propylene glycol (% w/v)	5.00	5.00	5.00	5.00	5.00	5.00
Minocycline hydrochloride	2.00	2.00	2.00	2.00	2.00	2.00
Strip mass (mg)	340.66 ± 1.52	509.66± 2.51	230.33 ± 1.58	255.66 ± 3.21	526.33 ± 1.25	267.93± 2.27
Strip thickness (mm)	4.04 ± 0.07	5.73 ± 0.08	1.27 ± 0.04	1.43 ± 0.05	5.81 ± 0.02	1.53 ± 0.03
Drug content uniformity (%)	101.91 ± 1.03	101.16 ± 1.71	101.78 ± 2.00	100.34 ± 2.61	100.07 ± 2.46	100.54 ± 1.96
Surface pH	5.36 ± 0.11	5.63 ± 0.25	5.73 ± 0.15	5.83 ± 0.25	5.66 ± 0.40	5.46 ± 0.20
Folding endurance	183.00 ± 3.60	224.66 ± 4.50	164.00 ± 3.60	197.66 ± 3.05	265.33± 5.50	235.66 ± 6.65
Viscosity (mPa s)	10.85	13.15	19.41	23.18	16.04	29.24

Table no: 5.05: Composition and characteristics of clindamycin phosphate loaded mucoadhesive periodontal strips

Composition / Characteristics	Batch code					
	CSF20	CSF21	CSF23	CSF24	CSF27	CSF30
PVA (%,w/v)	7.50	10.00	-	-	10.00	-
HPMC (%,w/v)	-	-	1.25	1.50	-	1.50
Carbopol 934P (% w/v)	0.25	0.25	0.25	0.25	0.50	0.50
Propylene glycol (% w/v)	5.00	5.00	5.00	5.00	5.00	5.00
Clindamycin phosphate	2.00	2.00	2.00	2.00	2.00	2.00
Strip mass (mg)	241.33 ± 1.04	510.00± 2.64	231.66 ± 2.51	265.66 ± 3.21	525.50 ± 2.00	264.06± 3.64
Strip thickness (mm)	3.99 ± 0.04	5.71 ± 0.09	1.25 ± 0.03	1.41 ± 0.05	5.82 ± 0.04	1.54 ± 0.02
Drug content uniformity (%)	103.20 ± 3.00	103.40 ± 2.14	101.47 ± 2.69	102.44 ± 2.61	102.69 ± 1.83	103.27 ± 1.72
Surface pH	5.43 ± 0.15	5.76 ± 0.20	5.83 ± 0.25	5.90 ± 0.17	5.70 ± 0.53	5.53 ± 0.23
Folding endurance	184.33 ± 4.16	222.66 ± 1.53	162.66 ± 1.53	195.00 ± 2.65	267.00 ± 2.00	238.66 ± 3.51
Viscosity (mPa s)	10.98	13.41	19.21	23.05	16.18	29.49

5.4.8 Measurement of Mechanical Properties

Mechanical properties of the drug loaded mucoadhesive periodontal strips were evaluated using universal testing machine (UTM) equipped with a 10 kg load cell (LF Plus, Lloyd Instruments, UK). Periodontal strips prepared in dimension of 100×50 mm were checked and confirmed to be free from air bubbles or any physical imperfections. Individually the plain periodontal strips and the drug loaded mucoadhesive periodontal strips were tested for their elongation at break, tensile strength, elastic modulus and strain. The results were recorded as the mean of three observations.

The tensile strength testing gives an estimate of the strength and elasticity of the periodontal strip, shown by the parameters like; tensile strength (TS), elastic modulus (EM) and elongation at break (EB). A soft and weak polymer is characterized by a low TS, EM and EB, where as a hard and brittle polymer by a moderate TS, high EM and low EB and a soft and tough polymer by high EB, and a hard and tough polymer is characterized by a high TS, EM and EB (Aulton et. al, 1981). Strain, an indicator of the overall mechanical quality of the

periodontal strips (Rowe, 1983), if high, indicates that the periodontal strip to be strong and elastic. Hence, it is suggested that a suitable periodontal strip should have a relatively high TS, EB and strain but a low EM. Table no 5.06 depicts various mechanical and biological properties of various plain PVA and HPMC periodontal strips. Table no 5.07 and 5.08 depict mechanical and biological properties of drug loaded mucoadhesive PVA and HPMC periodontal strips. Addition of carbopol 934P to PVA or HPMC causes a decrease in tensile strength of the plain periodontal strips evidenced by reduction of EM but increases both EB and strain significantly. This indicates a strong, more elastic, flexible and soft periodontal strip.

5.4.9 Swelling index

The swelling index of mucoadhesive periodontal strip formulations were conducted using two media, namely, distilled water and PBS pH 6.75. The increase in weight of the periodontal strips was recorded at preset time intervals until a constant weight was observed. Each measurement was repeated for six times and the mean of the readings were recorded.
Figure 5.01 depicts the degree of swelling of various placebo periodontal strips in PBS pH 6.75 and figure 5.02 indicates the degree of swelling in distilled water. The periodontal strips prepared with 10.00 % w/v PVA along with 0.5 % w/v carbopol 934P (SF27) showed maximum swelling of 65.7% in PBS pH 6.75, followed by 1.5 % w/v HPMC along with 0.5% w/v carbopol 934P (SF30) periodontal strips. The least swelling was found in 1.25 % HPMC containing 0.25 % w/v carbopol 934P (SF23) periodontal strips. The swelling of the plain periodontal strips in distilled water shows less swelling compared to PBS pH 6.75, but all the periodontal strips followed the similar pattern as that of the PBS pH 6.75. Figure 5.03 and 5.05 depict the degree of swelling of various minocycline hydrochloride/ clindamycin phosphate containing periodontal strips in PBS pH 6.75. Comparing the swelling character of plain periodontal strip with those of the minocycline hydrochloride/ clindamycin phosphate loaded periodontal strips in PBS pH 6.75; it was evident that the addition of the drug increased swelling of the periodontal strips. Alteration in (PBS pH 6.75) distribution within such systems would thus modify the matrix structure. In addition, the presence of a water soluble drug might improve the surface wetting of the periodontal strip (Wan et al, 1995). The rate of swelling of the PVA periodontal strip was comparatively faster than the HPMC periodontal strips. The swelling state of the polymer was reported to be crucial for its bio-adhesive behavior (Chen and Cyr, 1970). Adhesion occurs shortly after the beginning of the

swelling but the bond formed is not very strong (Chen and Cyr, 1970). The adhesion will increase with increase in the degree of hydration until a point where over hydration leads to an abrupt drop in adhesion strength due to disentanglement at the polymer/ tissue interface.

Figure: 5.01: Swelling index of plain periodontal strips in PBS pH 6.75

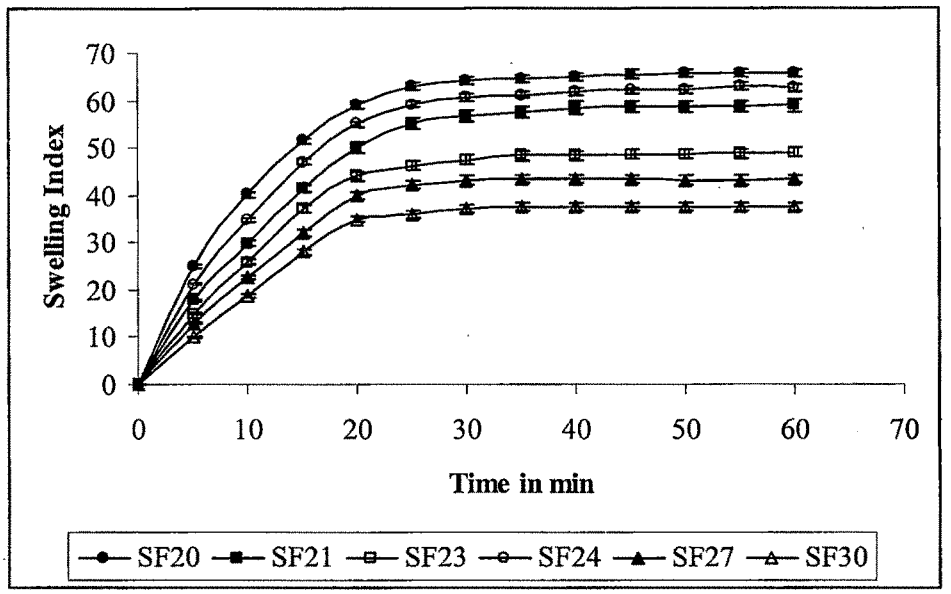


Figure: 5.02: Swelling index of plain periodontal strips in distilled water

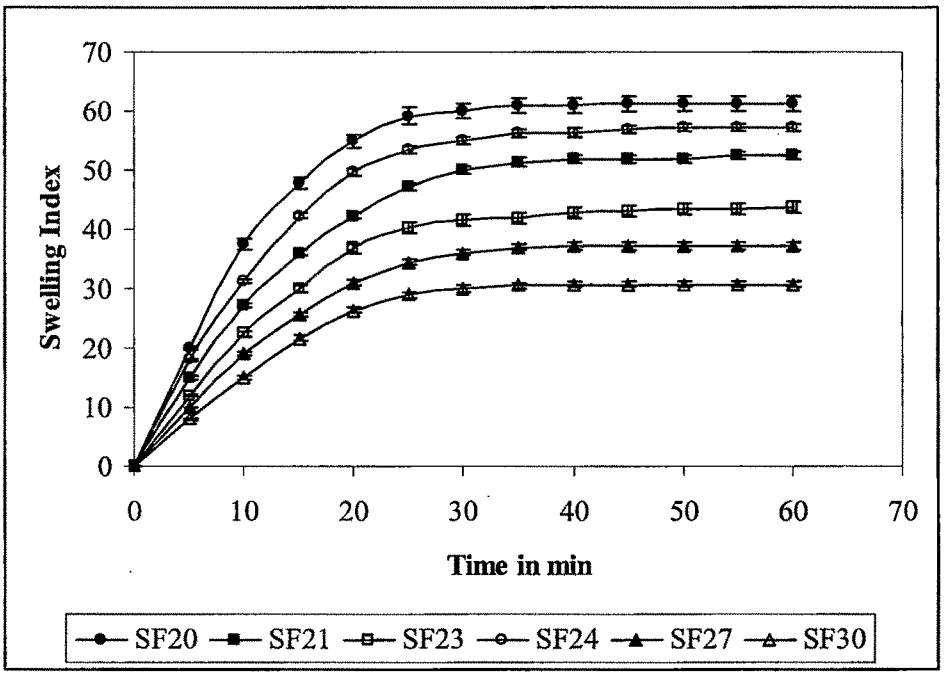


Figure: 5.03: Swelling index of minocycline hydrochloride loaded periodontal strips in PBS pH 6.75

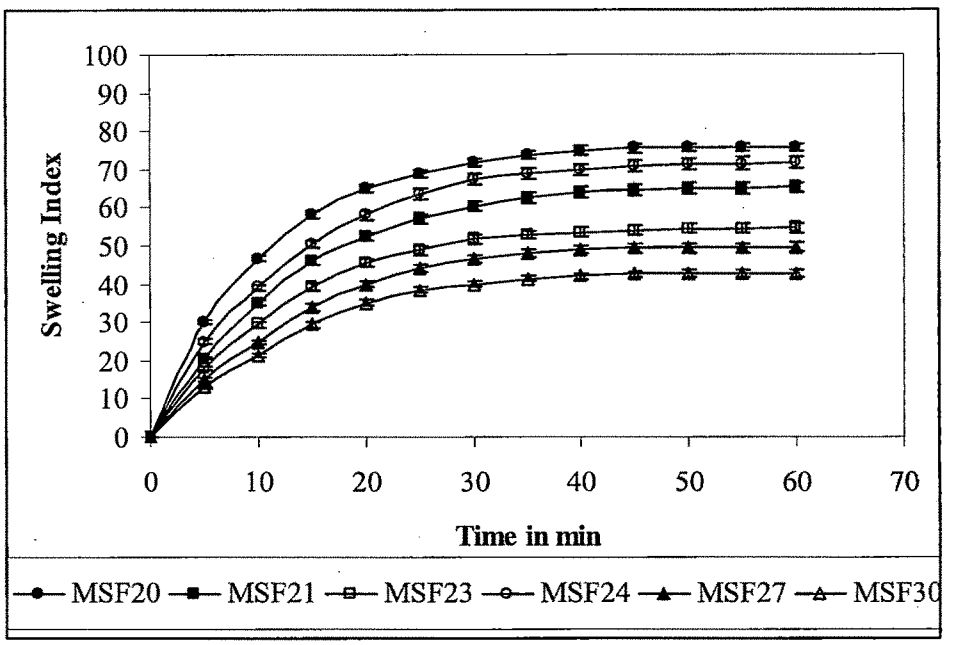


Figure: 5.04: Swelling index of minocycline hydrochloride loaded periodontal strips in distilled water

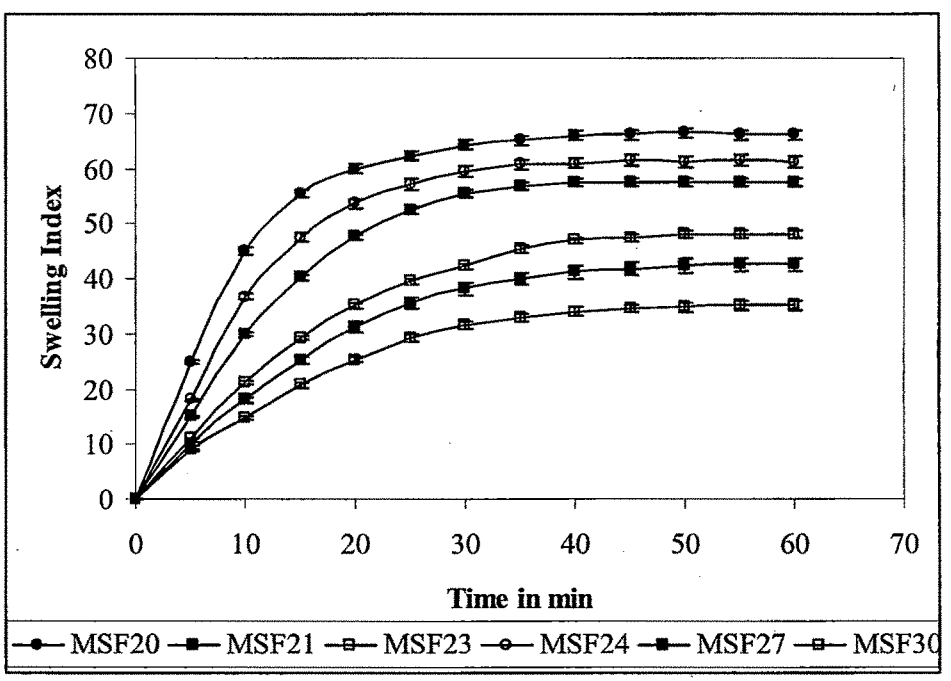


Figure: 5.05: Swelling index of clindamycin phosphate loaded periodontal strips in PBS pH 6.75

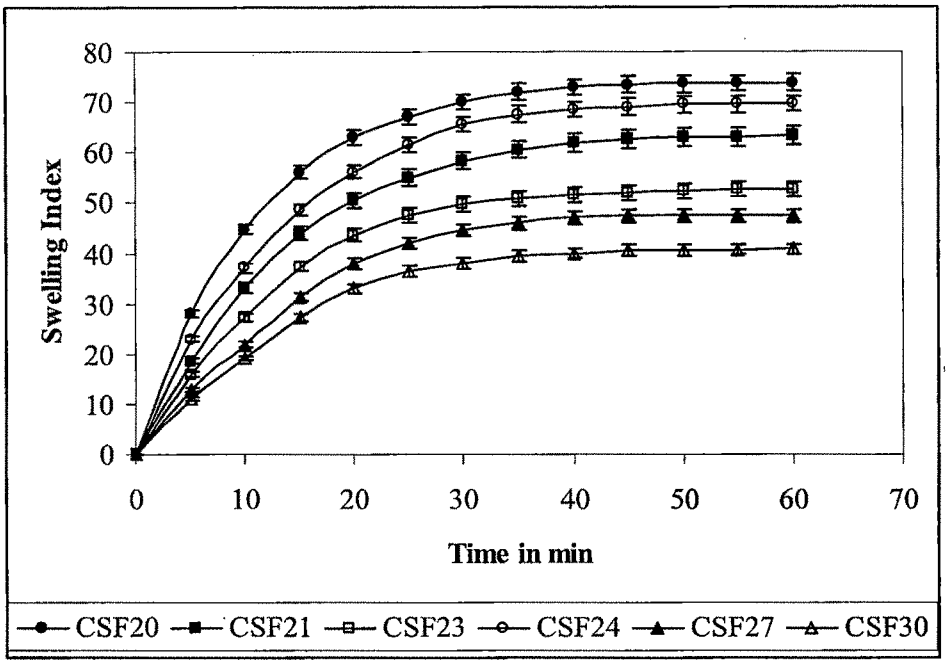
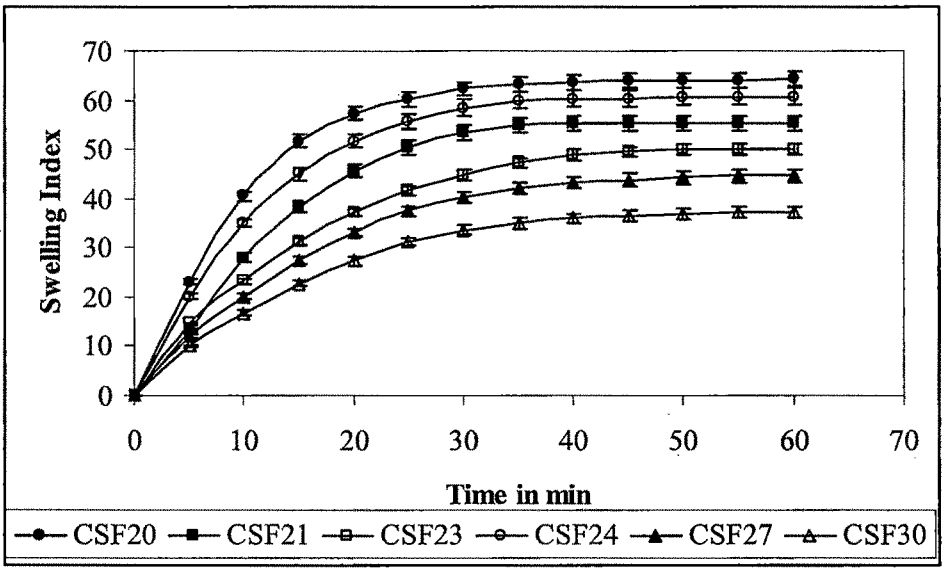


Figure: 5.06: Swelling index of clindamycin phosphate loaded periodontal strips in distilled water



5.4.10 Residence time

The in vitro residence time of the periodontal strips was determined using a modified USP disintegration apparatus (Nakamura et al, 1996) containing 800 ml PBS pH 6.75 maintained at 37±1^{0}C. The results recorded were the mean of three individual observations.

Results of the in vitro residence time of various plain and drug loaded periodontal strips are reported in Table 5.06, 5.07 and 5.08. All the periodontal strips remained attached to the mucosal surface until complete erosion. PVA periodontal strips showed convenient duration for complete erosion between 2.25 to 4.55 h, where as HPMC strips showed erosion time between 1.75 to 3.55 h. In vitro residence time of periodontal strips were higher compared to the ex vivo. Values of the in vitro residence time of the periodontal strips increased on addition of mucoadhesive polymer. All the periodontal strips reside on the mucosal membrane until complete erosion. The presence of minocycline hydrochloride/ clindamycin phosphate was found to be slightly affecting the residence time of the drug loaded periodontal strips.

5.4.11 Mucoadhesive force

The tensile strength, required to detach the drug loaded mucoadhesive periodontal strips from the mucosal surface, was applied as a measure of the mucoadhesive performance. The apparatus was locally assembled and was a modification of the apparatus previously applied by Parodi (Parodi et al, 1996) using sheep cheek mucosal membrane. The adhesion force data reported represents the mean of six determinations.

Figure 5.07 and 5.08 represents the bar diagram of plain and drug loaded periodontal strips containing PVA and HPMC respectively. Table 5.06, 50.7 and 5.08 represents the mean values of in vitro mucoadhesive strength of the periodontal strips. Increase in mucoadhesion strength was observed on addition of mucoadhesive polymer carbopol 934P to all the periodontal strip formulations. Maximum mucoadhesion without addition of mucoadhesive polymer was recorded for formulations prepared with 10.0 % w/v PVA along with 0.5 % w/v carbopol 934P (467.26 × 10^2 kg m^{-1} s^{-2}) than compared with the 1.50 % w/v HPMC along with 0.5 % w/v carbopol 934P (429.75 × 10^2 kg m^{-1} s^{-2}). Various mechanisms have been proposed to explain the in vitro mucoadhesion phenomena. These included electrical double

layers, electrostatic attractions, hydrogen bonding, Vander Walls force, hydrophobic bonding, wetting, diffusion interpenetration, physical entanglements, and surface free energy (Park and Robinson, 1985; Pappas and Buri, 1985; Jimenez-Castellanos et al, 1993). Although non-ionic, the polymeric nature of PVA provides the polymer with unique gelling characteristics, which in turn are responsible for its adhesive properties, in addition to its high mechanical strength, tack and high elasticity. Linear chains of PVA exhibit strong mucoadhesive behavior either because of hydrogen bonding due to hydroxyl group or because of significant chain penetration or both (Peppas and Mongia, 1997). The PVA periodontal strips had a faster hydration rate which could promote interpenetration of the polymer chain with the tissue. All these factors may have contributed to higher mucoadhesive strength of PVA strips.

One experimental result showed that all the periodontal polymer strips tested adhered to the oral mucosa for a significant period of time, which indicated that the mucoadhesive values of all the formulations were satisfactory to retain on the periodontal mucosa.

Table no: 5.06: Mechanical and biological property of plain periodontal strips

Composition/ Characteristics	Batch code					
	SF20	SF21	SF23	SF24	SF27	SF30
In vitro residence time (h)	2.25 ± 0.35	2.95 ± 0.62	1.75 ± 0.54	2.54 ± 0.75	4.55 ± 0.84	3.55 ± 0.56
Ex vivo residence time(h)	2.55± 0.95	3.52 ± 1.05	1.85 ± 1.05	2.75 ± 0.85	5.20 ± 1.22	4.32 ± 1.02
Mucoadhesive force (10^2, kg m^{-1} s^{-2})	145.65 ± 1.31	302.15 ± 1.32	130.98 ± 1.42	292.54 ± 1.40	467.26 ± 1.35	429.75 ± 1.75
Moisture absorbed (%) after 1 day	3.48 ± 0.24	2.94 ± 0.16	4.46 ± 0.34	3.08 ± 0.78	1.78 ± 0.17	2.53 ± 0.26
Moisture absorbed (%) after 7 days	9.59 ± 0.62	8.05 ± 0.73	11.54 ± 0.51	8.31 ± 0.93	6.10 ± 0.62	7.05 ± 0.43
Tensile strength ($kgmm^{-2}$)	4.35 ± 0.65	8.65 ± 0.95	3.45 ± 0.29	5.35 ± 0.72	10.95 ± 0.69	9.21± 0.78
Elastic modulus ($kgmm^{-2}$)	20.52 ± 1.78	45.52 ± 1.42	20.65 ± 1.64	25.35 ± 1.48	55.85 ± 1.25	48.78 ± 1.64
Elongation at break (% mm^{-2})	22.25 ± 1.43	13.24 ± 1.55	23.15 ± 1.64	26.32± 1.38	19.25 ± 1.95	17.91 ± 1.44
Strain	0.20 ± 0.02	0.30 ± 0.03	0.43 ± 0.05	0.27 ± 0.01	0.24 ± 0.01	0.19 ± 0.02

Table no: 5.07: Mechanical and biological property of minocycline hydrochloride loaded mucoadhesive periodontal strips

Composition / Characteristics	Batch code					
	MSF20	MSF21	MSF23	MSF24	MSF27	MSF30
In vitro residence time (h)	2.10 ± 0.45	2.75 ± 0.53	1.55 ± 0.35	2.35 ± 0.65	4.25 ± 0.89	3.25 ± 0.42
Mucoadhesive force (10^2, kg m^{-1} s^{-2})	142.25 ± 1.12	289.25 ± 1.25	125.32 ± 1.26	285.26 ± 1.45	460.25 ± 1.27	420.41 ± 1.85
Moisture absorbed (%) after 1 day	3.61 ± 0.27	3.15 ± 0.10	4.71 ± 0.44	3.10 ± 0.66	1.90 ± 0.19	2.64 ± 0.27
Moisture absorbed (%) after 7 days	10.05 ± 0.44	8.83 ± 0.70	11.94 ± 0.32	8.90 ± 0.93	6.48 ± 0.34	7.26 ± 0.42
Tensile strength ($kgmm^{-2}$)	4.25 ± 0.55	8.55 ± 0.98	3.25 ± 0.39	5.25 ± 0.82	10.73 ± 0.73	9.10± 0.87
Elastic modulus ($kgmm^{-2}$)	19.57 ± 1.54	43.28 ± 1.15	19.26 ± 1.35	23.87 ± 1.62	53.25 ± 1.67	46.52 ± 1.59
Elongation at break (% mm^{-2})	21.15 ± 1.29	12.55 ± 1.39	22.17 ± 1.61	24.78 ± 1.32	18.67 ± 1.87	16.29 ± 1.52
Strain	0.19 ± 0.04	0.28 ± 0.03	0.41 ± 0.04	0.25 ± 0.02	0.23 ± 0.03	0.17 ± 0.03

Table no: 5.08: Mechanical and biological property of clindamycin phosphate loaded mucoadhesive periodontal strips

Composition / Characteristics	Batch code					
	CSF20	CSF21	CSF23	CSF24	CSF27	CSF30
In vitro residence time (h)	2.12 ± 0.35	2.65 ± 0.44	1.45 ± 0.65	2.38 ± 0.75	4.35 ± 0.80	3.22 ± 0.72
Mucoadhesive force (10^2, kg m^{-1} s^{-2})	140.62 ± 1.35	285.67 ± 1.55	122.52 ± 1.36	284.12 ± 1.65	457.29 ± 1.29	418.26 ± 1.15
Moisture absorbed (%) after 1 day	3.68 ± 0.27	3.32 ± 0.11	4.83 ± 0.43	3.19 ± 0.70	2.01 ± 0.22	2.74 ± 0.26
Moisture absorbed (%) after 7 days	10.29 ± 0.63	8.97 ± 0.72	12.42 ± 0.57	9.12 ± 0.85	6.82 ± 0.30	7.46 ± 0.30
Tensile strength ($kgmm^{-2}$)	4.22 ± 0.48	8.50 ± 0.92	3.20 ± 0.45	5.21 ± 0.78	10.63 ± 0.62	8.98± 0.67
Elastic modulus ($kgmm^{-2}$)	19.48 ± 1.24	43.18 ± 1.05	19.06 ± 1.55	23.67 ± 1.42	53.15 ± 1.47	46.32 ± 1.79
Elongation at break (% mm^{-2})	21.05 ± 1.39	12.25 ± 1.42	22.07 ± 1.41	24.48 ± 1.72	18.37 ± 1.57	16.09 ± 1.72
Strain	0.18 ± 0.06	0.27 ± 0.02	0.39 ± 0.05	0.24 ± 0.04	0.22 ± 0.05	0.16 ± 0.07

Figure 5.07: The diagrammatic representation of mucoadhesive strength of plain, minocycline hydrochloride/ clindamycin phosphate loaded PVA periodontal strips

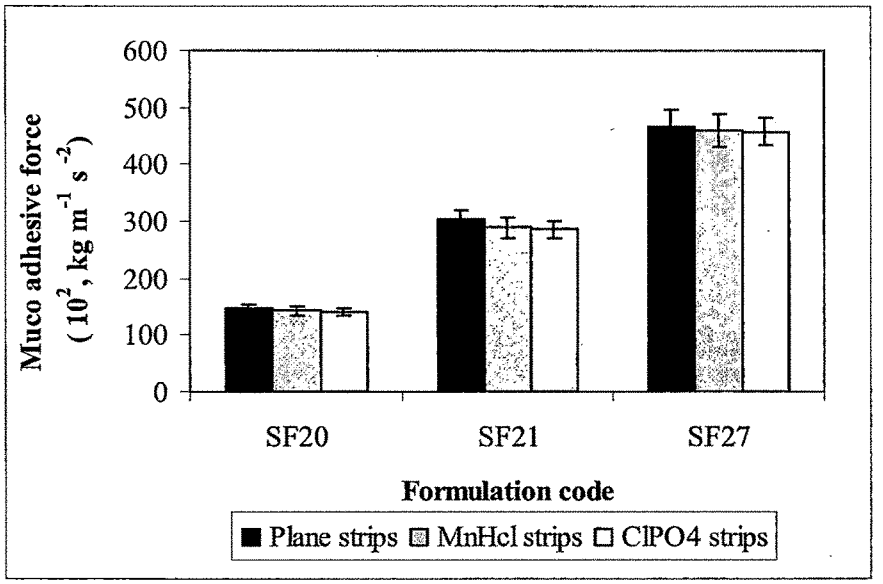
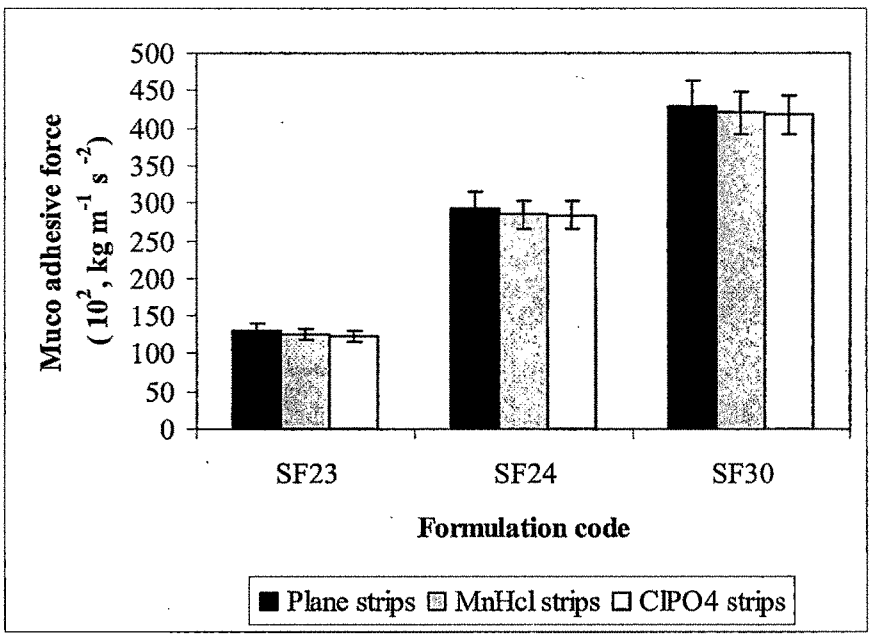


Figure: 5.08: The diagrammatic representation of mucoadhesive strength of plain, minocycline hydrochloride/ clindamycin phosphate loaded HPMC periodontal strips



5.4.12 In vitro release study

The drug loaded mucoadhesive periodontal strips were evaluated for in vitro drug release using Franz-diffusion cell by treating cellophane sheets in 5% w/v of glycerin (Viegas et al, 1988; Anders et al, 1989). The experiment was carried out using phosphate buffer pH 6.75 at 100 rpm and at a temperature 37±1°C by help of a circulating water bath. At predetermined time interval samples were withdrawn and an equal volume of pre-warmed buffer was replaced. Results were recorded by analyzing the samples after appropriate dilution to determine the minocycline hydrochloride/ clindamycin phosphate content.

The results of in vitro release studies indicated that the main factors affecting the release of minocycline hydrochloride/ clindamycin phosphate from the periodontal strips were the polymer concentration as shown in table no 5.09 and 5.11 respectively. There was a decrease in the drug release with an increase in the film forming polymer (HPMC/ PVA) concentration. The increase in concentration of mucoadhesive polymer concentration adds no value in the drug release.

Table no: 5.09: In vitro release study of the minocycline hydrochloride loaded mucoadhesive periodontal strips

Time in (h)	Cumulative % release					
	MSF20	MSF21	MSF23	MSF24	MSF27	MSF30
1	18.635± 0.34	11.932 ± 0.34	10.088 ± 0.03	8.077 ± 0.07	5.060 ± 0.07	3.217 ± 0.33
2	31.446 ± 0.35	23.134 ± 0.35	19.217 ± 0.05	16.611 ± 0.34	12.804 ± 0.34	8.708 ± 0.69
4	48.762 ± 0.36	39.122 ± 0.36	33.421 ± 0.52	29.664 ± 0.35	25.039 ± 0.69	20.112 ± 1.05
6	61.582 ± 0.55	52.363 ± 0.38	46.218 ± 0.36	40.866 ± 0.36	35.955 ± 0.89	29.612 ± 0.42
8	69.812 ± 1.33	61.715 ± 0.39	54.672 ± 0.37	48.784 ± 0.38	43.471 ± 0.41	37.449 ± 0.76
12	78.615 ± 0.44	71.027 ± 1.273	64.735 ± 0.39	58.633 ± 0.39	52.126 ± 6.79	45.555 ± 1.13
24	90.126 ± 0.46	84.978 ± 0.45	79.477 ± 1.74	74.165 ± 0.40	68.436 ± 1.36	60.296 ± 0.50

Table no: 5.10: Release kinetics parameters of minocycline hydrochloride loaded mucoadhesive periodontal strips

Batch Code	Correlation coefficient				N (Release exponent)	K (Release rate constant)
	Zero order	Higuchi	First order	Peppas		
MSF20	0.730	0.913	0.937	0.778	0.379	2.393
MSF21	0.790	0.938	0.891	0.781	0.391	2.460
MSF23	0.820	0.955	0.840	0.755	0.375	2.371
MSF24	0.847	0.967	0.777	0.731	0.355	2.265
MSF27	0.866	0.973	0.686	0.723	0.340	2.188
MSF30	0.880	0.975	0.539	0.733	0.310	2.042

The in vitro release profile of minocycline hydrochloride/ clindamycin phosphate is illustrated in figure 5.09 and 5.10. The maximum release of minocycline hydrochloride/ clindamycin phosphate from the periodontal strips was shown by the formulation containing 10.0 % w/v PVA along with 0.5% w/v carbopol 934P where as the least was shown by the formulation containing 1.25 % w/v HPMC after 24 h. The higher release of minocycline hydrochloride/ clindamycin phosphate from PVA patches can be explained by the viscosity of the polymer solution. A preliminary study showed that 10% w/v solution of PVA had lower viscosity than 1.5 % w/v solution of HPMC. As the viscosity is related to the strength and durability of the gel layer, the diffusion of the drug will be easier in case of PVA patches. Addition of carbopol 934P increases the drug release from the periodontal strip, which may be due to increase in water retention capacity of the periodontal strips, resulting in increase in the driving force for the drug molecule to come out of the gel layer. In addition, the relatively high swelling of the HPMC increased gel layer thickness and consequently increased the diffusion pathways (Tan et al, 2001), resulting in the slower drug release from these periodontal strips compared to the PVA periodontal strips.

The release of the clindamycin phosphate from the periodontal strips was found to be faster compared to the minocycline hydrochloride loaded periodontal strips. Formulation containing clindamycin phosphate showed higher release profile with sustained release effect. At pH 6.75 clindamycin phosphate possess the pKa of 7.7 which was partly positively charged, thus inducing an electrostatic repulsion, which enhances the drug release rate. To examine the kinetics of drug release and mechanism, the release data were fitted to models

representing zero order, first order, Higuchi's square root of time (Sankar and mishra, 2003) and korsemeyer and peppas model. The coefficient of correlation values (calculated from the plot of Q vs t for zero order, Log (Qo-Q) vs t for first order and Q vs $t^{1/2}$ for Higuchi model, Log (Q/Qα) vs log t for korsemeyer and peppas model where Q is the amount of drug release at time t, Qα is the amount of drug release at time α and Qo-Q is the amount of drug remaining after time t) were as shown in table no 5.10 and 5.12. Thus it can be concluded that the minocycline hydrochloride/ clindamycin phosphate release from the periodontal strips can be best explained by Higuchi model. The mechanism of the drug release is further investigated by the well-known exponential equation, which is often used to describe the drug release behavior from polymeric systems;

$$Mt / M\alpha = kt^n$$

Where, Mt/Mα is the fractional drug release at time't'. 'k' is a constant incorporating the properties of the macromolecular polymeric systems and the drug and 'n' is the kinetic constant which depends on and is used to characterize the transport mechanism. When 'n' 0.5, this indicates a quasi diffusion mechanism, when 'n' > 0.5, an anomalous non-fickian diffusion is observed, when 'n' = 1 indicates a zero order release (Sankar and Mishra 2003). The values of 'n' and 'k' were obtained from the plot of Q vs $t^{1/2}$. The values of 'n' obtained for all the batches are less than 0.5, which indicates that the drug release followed quasi fickian diffusion.

The values of the diffusional exponent 'n' and regression are shown in table no 5.10 and 5.12, indicating higuchi order of kinetics. The release was, thus controlled by the visco-elastic relaxation of the matrix during the solvent penetration as well as the diffusivity of the drug in the gel layer formed as the periodontal strip swelled. In this case, the relative rates at which the swelling and erosion fronts moved relative to each other were synchronized and a constant diffusion path length was obtained. For PVA periodontal strips r^2 was 0.913, 0.938 and 0.973 for minocycline hydrochloride and 0.952, 0.947 and 0.975 for clindamycin phosphate, and for HPMC periodontal strips r^2 was 0.955, 0.967 and 0.975 for minocycline hydrochloride and 0.966, 0.973 and 0.973 for clindamycin phosphate, indicating higuchi order of release behavior. When swelling is predominant, drug diffusion probably occurs through the solvent filled pathways of the swollen periodontal strips. The periodontal strip

formulations MSF24, MSF27, MSF30, CSF24, CSF27 and CSF30 were selected for the further study.

Figure: 5.09: Cumulative release profile of minocycline hydrochloride in mcg in periodontal strips

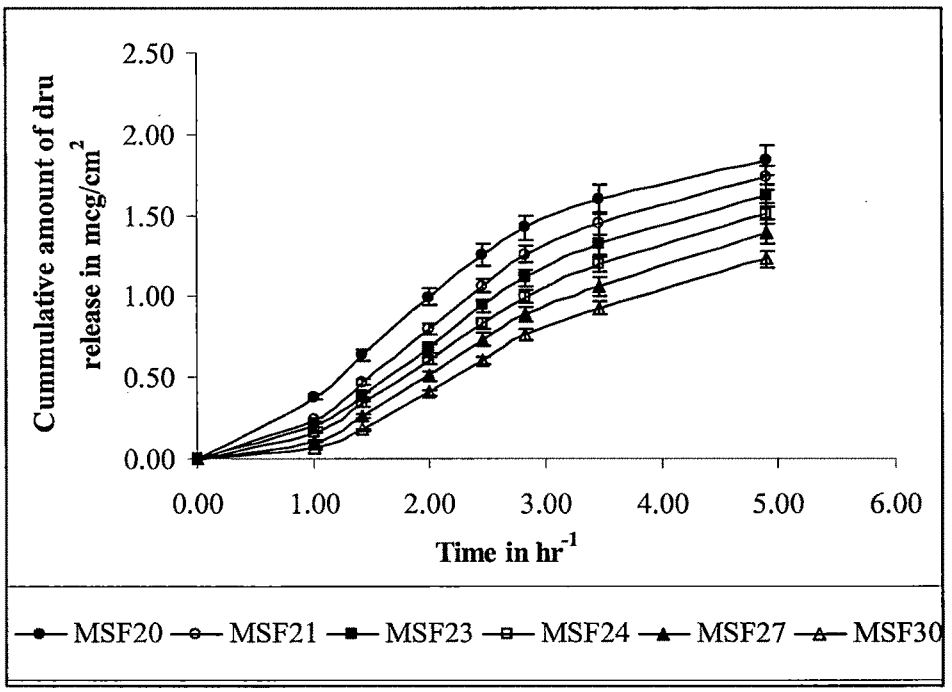


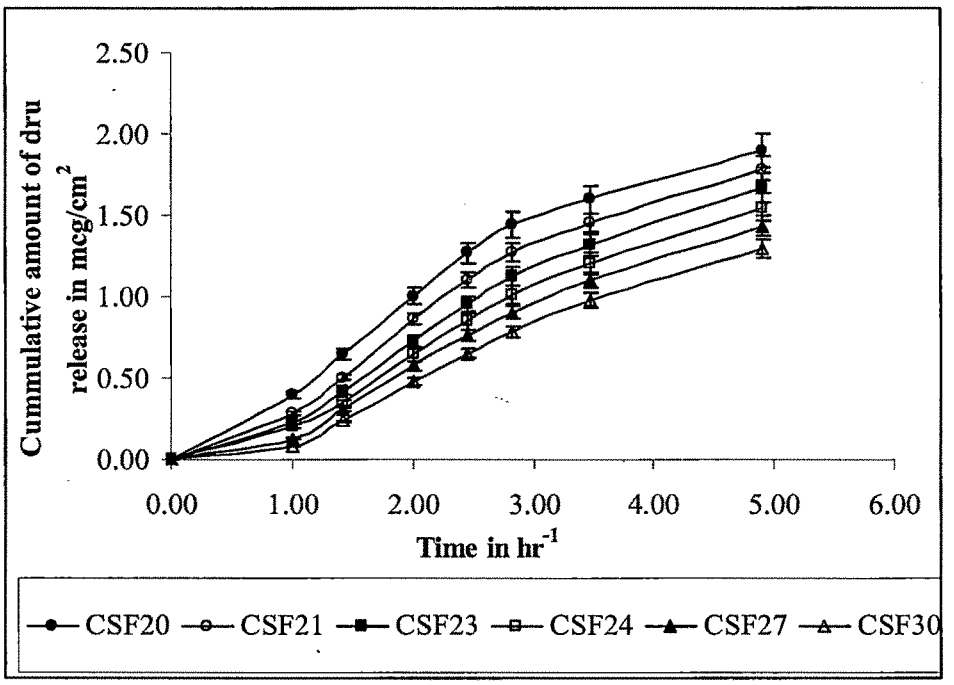
Table no: 5.11: In vitro release study of the clindamycin phosphate loaded mucoadhesive periodontal strips

Time in (h)	Cumulative % release					
	CSF20	CSF21	CSF23	CSF24	CSF27	CSF30
1	19.871 ± 0.32	14.102 ± 3.21	11.538 ± 0,32	10.256 ± 0.32	6.410 ± 0.32	4.001 ± 0.06
2	32.525 ± 0.65	25.243 ± 0.77	20.974 ± 3.22	17.397 ± 0.333	15.320 ± 0.653	11.698 ± 0.64
4	50.141 ± 1.00	43.217 ± 1.12	36.431 ± 0.95	32.179 ± 0.66	28.743 ± 1.00	24.019 ± 0.35
6	63.388 ± 0.57	55.141 ± 0.51	47.773 ± 1.30	42.397 ± 0.69	38.192 ± 0.40	32.647 ± 1.00
8	72.068 ± 0.73	63.628 ± 0.85	56.094 ± 0.86	50.730 ± 0.72	45.089 ± 0.73	39.339 ± 3.28
12	79.931 ± 1.25	72.692 ± 1.19	66.170 ± 0.88	60.294 ± 1.06	55.089 ± 0.756	48.814 ± 1.81
24	94.841 ± 0.49	89.397 ± 0.59	83.512 ± 0.76	77.538 ± 1.10	71.833 ± 0.78	65.019 ± 3.48

Table no: 5.12: Release kinetics parameters of clindamycin phosphate loaded mucoadhesive periodontal strips

Batch Code	Correlation coefficient				N (Release exponent)	K (Release rate constant)
	Zero order	Higuchi	First order	Peppas		
CSF20	0.747	0.952	0.959	0.707	0.413	2.588
CSF21	0.794	0.947	0.920	0.661	0.391	2.460
CSF23	0.833	0.966	0.869	0.656	0.377	2.382
CSF24	0.852	0.973	0.804	0.547	0.356	2.270
CSF27	0.863	0.975	0.724	0.675	0.340	2.188
CSF30	0.880	0.973	0.606	0.686	0.293	1.964

Figure: 5.10: Cumulative release profile of clindamycin phosphate in mcg in periodontal strips



5.4.13 In-vitro Permeation studies

5.4.13.1 Determination of saturated drug concentration

A saturated minocycline hydrochloride/ clindamycin phosphate solution in phosphate buffer pH 6.75 was prepared separately by equilibrating the excess minocycline hydrochloride/ clindamycin phosphate with the vehicle for 2 hours. The temperature of the solution was

maintained at 25^0C using a circulating water bath. The sample was filtered and appropriately diluted for estimation of saturation solubility of minocycline hydrochloride/ clindamycin phosphate. The saturated concentration of minocycline hydrochloride/ clindamycin phosphate in phosphate buffer pH 6.75 was found to be 106.994 mg ml^{-1} & 103.900 mg ml^{-1} respectively.

5.4.13.2 Preparation of mucosal tissue

The animal was sacrificed in the slaughter house and the sheep cheek pouch was excised. It was washed thoroughly with distilled water. The mucosal membrane so separated was cut into pieces of 3×3 cm. A piece of the mucosal membrane was washed with isotonic phosphate buffer pH 6.75 and kept in the phosphate buffer pH 6.75 in order to remove any soluble components. The integrity of the mucosal surface was tested microscopically (Raykar et al, 1998) before to confirm the absence of any significant change.

5.4.13.3 Measurement of thickness of sheep cheek mucosal membrane

The mucosal thickness of cheek mucous membrane was measured microscopically after staining with hematoxylin-eosin. A wax block of skin was prepared by using steel molds. Molten wax was poured into the steel mold from a paraffin dispenser heated within 68 to 70^0C. The skin was pushed down to the bottom of the mold so that it was positioned on the cutting surface. After cooling, the block was removed by slightly reheating the mold. The wax block was held on the holder of the microtome. The sections were cut at about 5 to 7μm thickness with a dispersible microtome blade. The section was transferred to a glass slide and affixed. The glass slide was put in a caplin jar containing hematoxylin-eosin for 10 minutes, then rinsed with isopropyl alcohol, and kept under running water for 5 to 7 minutes. The glass slide was dipped 30 times in a caplin jar containing 1% eosin and then again rinsed with isopropyl alcohol. The glass slide was then allowed to dry completely and kept in a caplin jar containing xylene for 7 to 10 minutes. Finally the glass slide was air dried and observed under a microscope and the thickness was measured using a micrometer. The average thickness was found to be $1.52 \pm 0.325 \times 10^{-2}$ μm, which is the mean of three measurements.

In vitro permeation studies of various drug loaded mucoadhesive periodontal strips were done as described by many research groups (Caschel et al, 2000; Pisal et al, 2004). From the

results of permeation it is evidenced that the periodontal strip formulations prepared with 1.5% w/v HPMC posses sustain release compared to the other formulations. This may be due to low surface wetting ability and swelling of the periodontal strips. The swelling of the polymers was affected by the ionic strength and pH (Park and Robinson, 1985). PVA periodontal strips seemed to wet faster than the HPMC periodontal strips. The swelling of the polymers may be due to the solvent front on each surface, which may be allowing a small quantity of solvent to diffuse into the inner core of the coated periodontal strip and the resistance of the matrix network structure (hydrogen bond) to the movement of water molecules.

Cumulative amount of drug permeated as function of inverse of time is given in figure 5.11 and 5.12. Different drug permeation kinetics is presented in table no 5.14 for minocycline hydrochloride/ clindamycin phosphate containing periodontal strips. It was evidenced that cumulative amount of drug permeated with time was reduced for all the formulations compared to the pure drug solution. Effective permeability (Permeability coefficient) of the pure minocycline hydrochloride and clindamycin phosphate was found to be 38.961 and 39.713 respectively. For minocycline hydrochloride containing periodontal strips the effective permeability was found to be 10.094, 10.809 and 9.287 ($\times 10^{-8}$cm.sec^{-1}) for the formulation MSF24, MSF27 and MSF30 respectively. Similarly for clindamycin phosphate containing periodontal strips the effective permeability was found to be 10.893, 11.470 and 10.247 ($\times 10^{-8}$cm.sec^{-1}) for the formulation CSF24, CSF27 and CSF30 respectively. It was also found that effective permeability coefficient for minocycline hydrochloride and clindamycin phosphate is significantly lower for periodontal strips prepared using HPMC ($P< 0.001$) as compared to that of pure drug solution. Since strips need to be wet for effective permeability, it was hypothesized that the drug permeation may be due to diffusion through the water channel of the gel matrix of the periodontal strips. PVA strips shows higher permeability due to faster wetability compared to the HPMC periodontal strips. HPMC periodontal strips showed higher lag time compared to the PVA periodontal strips which conforms the higher time taken by the HPMC periodontal strips compared to the PVA periodontal strips for wetting. Permeation flux of the drugs are higher in formulations containing 0.5% w/v carbopol 934P, which may be due to faster swelling of the periodontal strips.

Table no: 5.13: In vitro permeation study of the minocycline hydrochloride and clindamycin phosphate loaded mucoadhesive periodontal strips

Time in (h)	Cumulative % permeated					
	MSF24	MSF27	MSF30	CSF24	CSF27	CSF30
1	11.261 ± 0.67	7.574 ± 1.00	4.558 ± 0.67	13.140 ± 0.64	10.256 ± 0.64	6.410 ± 0.96
2	20.090 ± 1.36	15.251 ± 1.38	10.890 ± 0.77	23.923 ± 0.98	18.358 ± 0.98	14.049 ± 0.98
4	33.612 ± 1.42	28.250 ± 3.44	21.926 ± 1.06	40.243 ± 1.02	32.431 ± 1.18	27.410 ± 1.35
6	45.632 ± 1.13	38.728 ± 1.23	30.488 ± 1.10	50.128 ± 0.74	43.405 ± 1.07	37.45 ± 0.77
8	52.719 ± 1.17	45.560 ± 1.60	38.017 ± 1.47	56.820 ± 1.41	50.495 ± 1.10	44.641 ± 1.11
12	60.691 ± 0.88	53.612 ± 1.32	47.477 ± 0.86	63.705 ± 1.14	58.444 ± 3.39	52.385 ± 0.83
24	69.909 ± 0.91	64.935 ± 1:03	59.269 ± 0.88	74.948 ± 0.86	70.162 ± 1.91	65.179 ± 1.50

Figure 5.11: Cumulative permeation profile of minocycline hydrochloride in mcg in periodontal strips

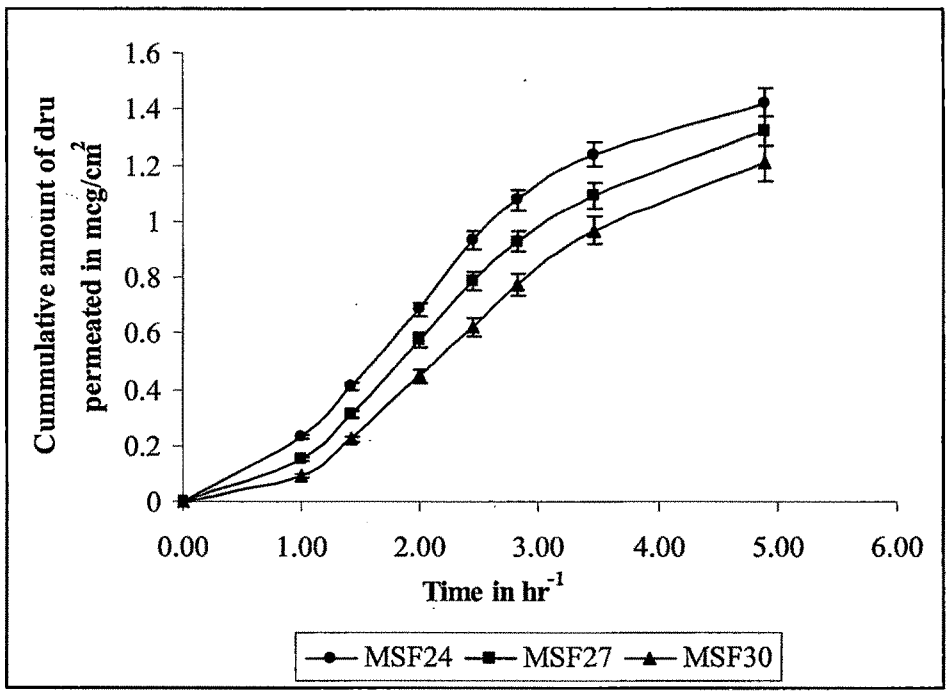


Figure 5.12: Cumulative permeation profile of clindamycin phosphate in mcg in periodontal strips

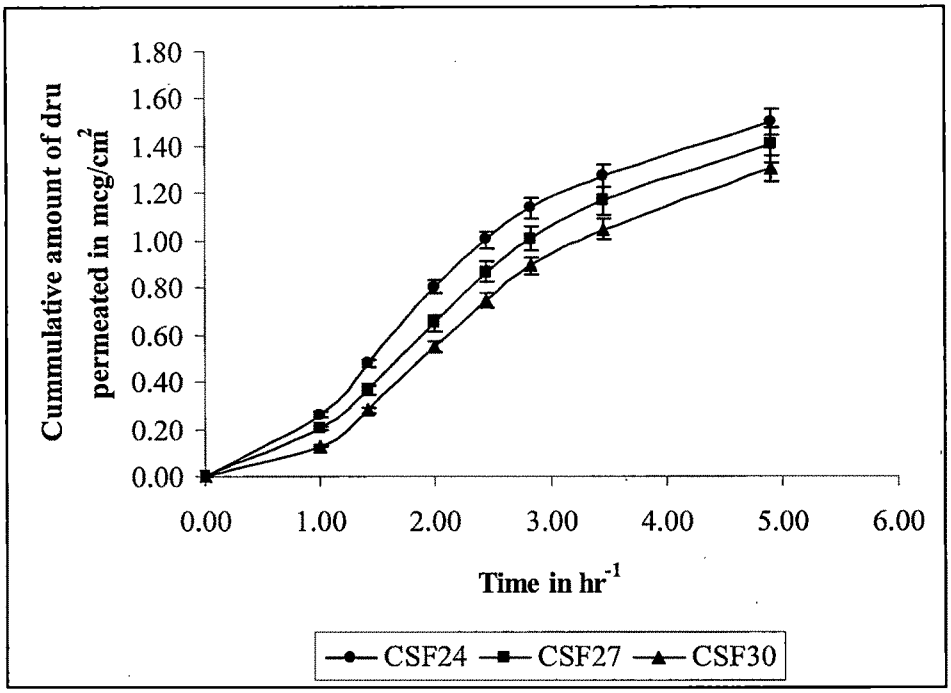


Table no: 5.14: Drug permeation kinetics of various drug loaded periodontal strip formulations

Formulations	Permeation flux $J(mg.cm^{-2}.hr^{-1})$	Lag time ($t_L$hr)	Diffusion coefficient ($D\times10^{-8}$ $cm^2.sec^{-1}$)	Permeability coefficient ($P\times10^{-8}$ $cm.sec^{-1}$)
MSF24	0.301674	0.80	1.337	10.094
MSF27	0.323076	0.50	2.139	10.809
MSF30	0.277552	1.00	1.069	9.287
Minocycline Hydrochloride	0.150	0.01	1.06	38.961
CSF24	0.316151	0.55	1.944	10.893
CSF27	0.332918	0.40	2.674	11.470
CSF30	0.297376	0.75	1.426	10.247
Clindamycin Phosphate	0.1485	0.02	0.534	39.713

5.4.14 FTIR studies

FTIR spectral measurements of drug loaded periodontal mucoadhesive strips were performed using a Shimadzu FTIR spectrometer. Periodontal strips grounded with KBR and FTIR spectra were taken in the range 4500-500cm^{-1}.

From the FTIR spectral studies, the characteristic bands of two important functional groups of the pure drug as well as that of the polymer were identified. The FTIR spectra showed that the characteristic bands of the drug (Minocycline hydrochloride/ clindamycin phosphate) were not altered after the formulation. No change in the positions of the important functional groups reveals the absence of any chemical interaction occurred among the drug and the polymer.

The interpretation of IR spectra of the PVA with minocycline hydrochloride reveals as follows: IR (KBr) cm^{-1}: 3344.66, 3474.21 (OH Str.), 3268.29 (NH Str.), 2937.98 (CH_2 Str.), 1651.54 (C=O Str.), 1560.04 (OH Str.), 1452.96-1459.87 (CH=CH Str.), 1272.20 (CN Str.), 829.21 (CH of Ar-H).

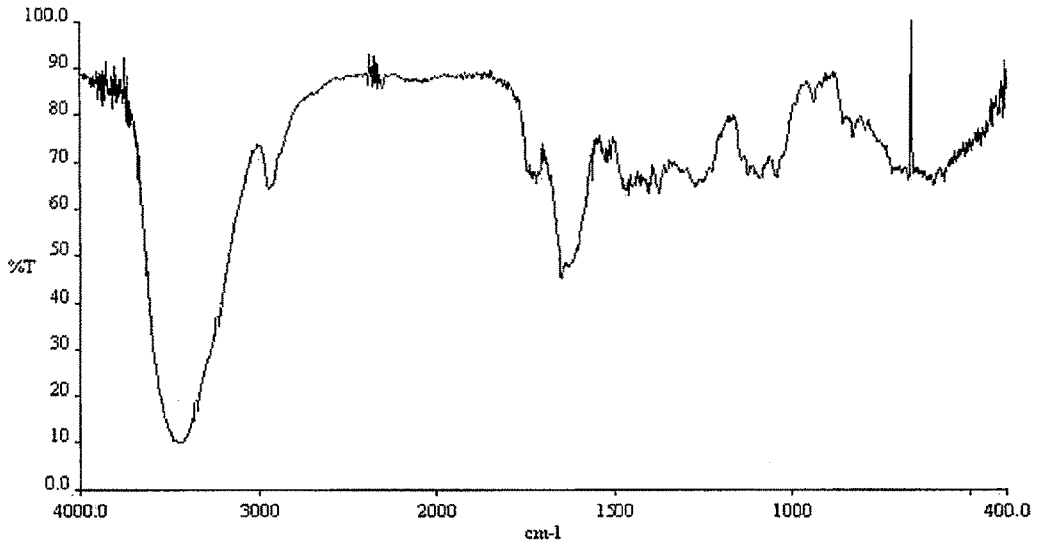
The interpretation of IR spectra of the PVA with clindamycin phosphate reveals as follows: IR (KBr) cm^{-1}: 3627.87 (OH Str.), 3390.41 (NH Str.), 2930.42 (CH_2 Str.), 1698.66 (C=O Str.), 1579.99 (CN Str.), 1458.05 (CH=CH Str.), 673.02 (C-Cl Str.).

The interpretation of IR spectra of the HPMC with minocycline hydrochloride reveals as follows: IR (KBr) cm^{-1}: 3476.76(OH Str.), 3345.51(NH Str.), 2936.40 (CH_2 Str.), 1651.99 (C=O Str.), 1560.65(OH Str.), 1460.67 (CH=CH Str.), 1316.68(CN Str.), 852.77(CH of Ar-H).

The interpretation of IR spectra of the HPMC with clindamycin phosphate reveals as follows: IR (KBr) cm^{-1}: 3464.55 (OH Str.), 3383.03 (NH Str.), 2933.11 (CH_2 Str.), 1646.68 (C=O Str.), 1540.19 (CN Str.), 1456.78 (CH=CH Str.), 1317 (CN Str.), 849.29 (CH of Ar-H), 671.31 (C-Cl Str.).

The above data is compared with the standard peaks of the drug and the polymer and interpretation of all these in our spectra satisfies and agreed with the above conditions indicating no chemical interaction between the drug and the Polymer.

Figure 5.13: FTIR data of MnHCl-PVA periodontal strip



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Comments: KBr pellet

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End: 400.00
Interval: -1.000000

Ordinate: (%T)
Maximum: 100.00
Minimum: 10.00
Points: 3601

Instrument Model: Spectrum One
Instrument Serial Number: 69888
Instrument Software Version: CPU32 Main 0002
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Detector: LiTaO3
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Beamsplitter: OptKBr
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Beam type: Ratio
Phase Correction: Background
OPD Velocity: 0.20 cm/sec
I-Stop Size: 8.94mm
IR Accessory: Slide Holder
Igram Type: Double
Scan Direction: Combined
Filterwheel Position: 1
IR Type: FT
IR-Laser Wavenumber: 15798.00 cm-1

Accessories:
Manufacturer: P
Part Number: L1200301
Description: Standard sample wealkit
Scan Range / cm-1: 4000 450
Temperature / C: Not Specified

MPVApk

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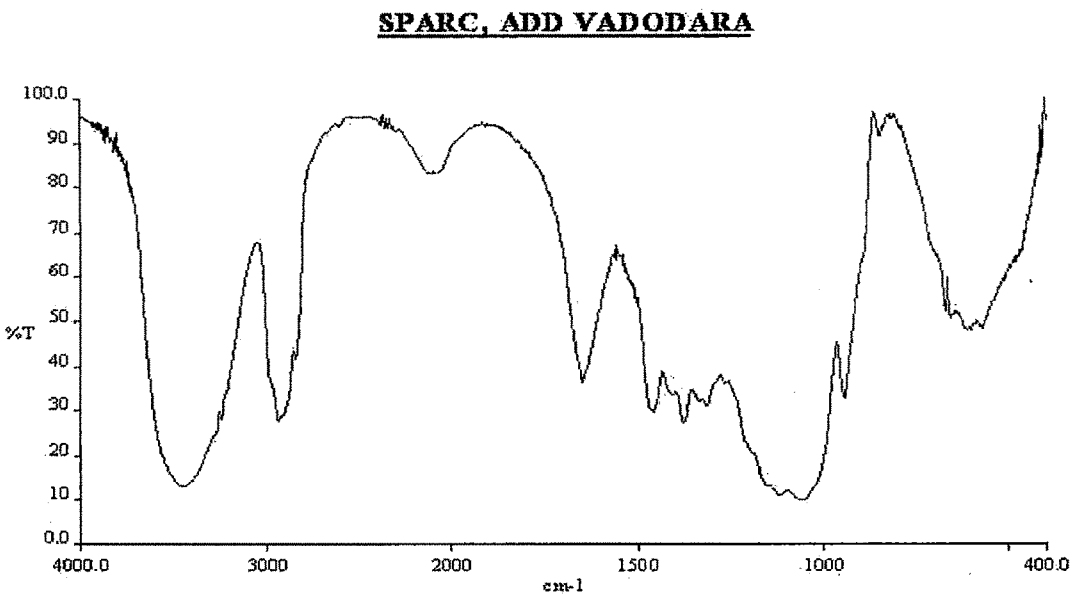
3779.66 83.70 3765.23 82.73 3760.83 82.50 3756.76 82.23 3748.76 83.91
3744.32 77.99 3739.87 79.17 3732.08 78.06 3726.97 79.13 3722.12 77.39
3688.23 73.52 3474.21 66.02 3344.66 65.20 3268.29 9.99 2937.98 64.15
2382.36 86.30 2369.94 88.02 2357.24 85.97 2342.40 86.60 2325.30 85.67
2299.95 85.86 1718.11 65.10 1698.68 69.46 1651.54 44.87 1560.04 66.09
1522.20 69.58 1517.54 69.48 1508.35 70.12 1459.87 62.79 1452.96 64.49
1405.17 63.17 1375.17 62.98 1272.20 64.65 1125.24 67.02 1092.37 66.20
1043.92 66.55 940.91 82.52 829.21 74.83 797.00 76.56 674.22 65.88
604.66 64.84 576.14 65.49 544.27 69.52 519.90 70.84 500.93 72.31
484.00 73.74 472.48 73.29 455.96 75.75 441.05 77.00 424.49 79.47
420.29 79.54 416.77 82.93 411.97 79.19 408.73 78.74 403.88 85.20

Figure 5.14: FTIR data of MnHCl-HPMC periodontal strip



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Minimum: 10.00
Points: 3601

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Accumulations: 8
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Resolution: 4.00 cm-1
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Beam type: Ratio
Phase Correction: Background
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I-Stop Size: 8.94 mm
IR Accessory: Slide Holder
Igram Type: Double
Scan Direction: Combined
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IR Laser Wavenumber: 15798.00 cm-1

Accessories:
Manufacturer: p
Part Number: L1200301
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Temperature / C: Not Specified

MHPMC.pk

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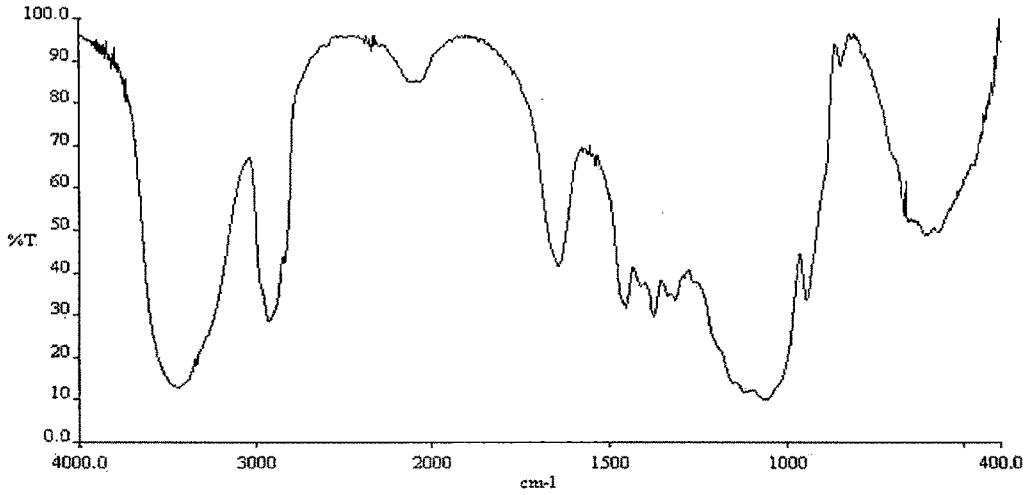
3815.42 88.37 3800.93 86.76 3753.01 82.88 3748.08 82.48 3476.76 79.67
3345.51 13.25 2936.40 27.79 2357.31 93.09 2342.88 93.10 2120.10 83.04
1651.99 36.43 1560.65 63.68 1557.88 64.16 1538.95 60.95 1460.67 29.68
1376.58 27.23 1316.68 31.18 1059.78 999 945.53 33.09 852.77 91.21
672.07 52.20 612.69 47.95 420.21 84.27 412.15 86.48

Figure 5.15: FTIR data of $ClPO_4$-HPMC periodontal strip



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Comments: KBr pellet

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Ordinate: (%T)
Maximum: 100.00
Minimum: 10.00
Points: 3601

Instrument Model: Spectrum One
Instrument Serial Number: 69888
Instrument Software Version: CPU32 Main 00.02
Accumulations: 8
Detector: LiTM03
Source: MIR
Beamsplitter: Opt.KBr
Resolution: 4.00 cm-1
Apodization: Weak
Spectrum Type: Spectrum
Beamtype: Ratio
Phase Correction: Background
OPD Velocity: 0.20 cm/sec
I-Stop Size: 8.94 mm
IR Accessory: Slide Holder
IgramType: Double
Scan Direction: Combined
Filterwheel Position: 1
IRType: FT
IR-Laser Wavenumber: 15798.00 cm-1

Accessories:
Manufacturer: P
Part Number: L1200301
Description: Standard sample area kit
Scan Range / cm-1: 4000 450
Temperature / C: Not Specified

CHPMC.pk

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3383.03 12.96 2933.11 28.57 2342.86 92.46 2118.96 84.84 1646.68 41.34
1540.19 65.14 1456.78 31.92 1378.38 29.86 1317.00 33.76 1062.96 9.99
946.67 33.46 849.29 88.88 671.31 53.42 609.09 48.94 420.31 81.56
416.05 88.62

5.4.15 Stability study

The optimized batch was subjected to stability studies. Formulations were stored in pouches for a period of 180 days at room temperature and at 4^0C. The strips were determined for the drug content, biological and mechanical property such as mucoadhesive force, tensile strength, elastic modulus, elongation at break and strain were determined after 6 months. Values of mechanical and biological properties of various minocycline hydrochloride/ clindamycin phosphate loaded periodontal strips were tabulated in the table no 5.15 to 5.18. The results showed that the periodontal strips did not have any significant change in the drug content and other biological and mechanical property. Basing on the various mechanical and biological properties and preformulation parameters among all the selected six formulations, MSF27, MSF30, CSF27 and CSF 30 were selected for further study. Selected formulations also showed better sustained permeation over a period of 24h.

Table no: 5.15: Mechanical and biological property of minocycline hydrochloride loaded mucoadhesive periodontal strips after 180 days storage at room temperature

Composition / Characteristics	Batch code					
	MSF20	MSF21	MSF23	MSF24	MSF27	MSF30
Drug content (%)	99.85	102.14	101.11	102.65	98.75	99.48
Mucoadhesive force (10^2, kg m^{-1} s^{-2})	140.62 ± 1.35	285.67 ± 1.55	122.52 ± 1.36	284.12 ± 1.65	457.29 ± 1.29	418.26 ± 1.15
Tensile strength ($kgmm^{-2}$)	4.22 ± 0.48	8.50 ± 0.92	3.20 ± 0.45	5.21 ± 0.78	10.63 ± 0.62	8.98± 0.67
Elastic modulus ($kgmm^{-2}$)	19.48 ± 1.24	43.18 ± 1.05	19.06 ± 1.55	23.67 ± 1.42	53.15 ± 1.47	46.32 ± 1.79
Elongation at break (% mm^{-2})	21.05 ± 1.39	12.25 ± 1.42	22.07 ± 1.41	24.48 ± 1.72	18.37 ± 1.57	16.09 ± 1.72
Strain	0.18 ± 0.06	0.27 ± 0.02	0.39 ± 0.05	0.24 ± 0.04	0.22 ± 0.05	0.16 ± 0.07

Table no: 5.16: Mechanical and biological property of clindamycin phosphate loaded mucoadhesive periodontal strips after 180 days storage at room temperature

Composition / Characteristics	Batch code					
	CSF20	CSF21	CSF23	CSF24	CSF27	CSF30
Drug content (%)	98.15	97.56	101.14	99.98	100.25	104.52
Mucoadhesive force (10^2, kg m^{-1} s^{-2})	140.62 ± 1.35	285.67 ± 1.55	122.52 ± 1.36	284.12 ± 1.65	457.29 ± 1.29	418.26 ± 1.15
Tensile strength ($kgmm^{-2}$)	4.22 ± 0.48	8.50 ± 0.92	3.20 ± 0.45	5.21 ± 0.78	10.63 ± 0.62	8.98± 0.67
Elastic modulus ($kgmm^{-2}$)	19.48 ± 1.24	43.18 ± 1.05	19.06 ± 1.55	23.67 ± 1.42	53.15 ± 1.47	46.32 ± 1.79
Elongation at break (% mm^{-2})	21.05 ± 1.39	12.25 ± 1.42	22.07 ± 1.41	24.48 ± 1.72	18.37 ± 1.57	16.09 ± 1.72
Strain	0.18 ± 0.06	0.27 ± 0.02	0.39 ± 0.05	0.24 ± 0.04	0.22 ± 0.05	0.16 ± 0.07

Table no: 5.17: Mechanical and biological property of minocycline hydrochloride loaded mucoadhesive periodontal strips after 180 days storage at 4° C

Composition / Characteristics	Batch code					
	MSF20	MSF21	MSF23	MSF24	MSF27	MSF30
Drug content (%)	99.56	101.24	99.65	98.25	101.52	103.21
Mucoadhesive force (10^2, kg m^{-1} s^{-2})	140.62 ± 1.35	285.67 ± 1.55	122.52 ± 1.36	284.12 ± 1.65	457.29 ± 1.29	418.26 ± 1.15
Tensile strength ($kgmm^{-2}$)	4.22 ± 0.48	8.50 ± 0.92	3.20 ± 0.45	5.21 ± 0.78	10.63 ± 0.62	8.98± 0.67
Elastic modulus ($kgmm^{-2}$)	19.48 ± 1.24	43.18 ± 1.05	19.06 ± 1.55	23.67 ± 1.42	53.15 ± 1.47	46.32 ± 1.79
Elongation at break (% mm^{-2})	21.05 ± 1.39	12.25 ± 1.42	22.07 ± 1.41	24.48 ± 1.72	18.37 ± 1.57	16.09 ± 1.72
Strain	0.18 ± 0.06	0.27 ± 0.02	0.39 ± 0.05	0.24 ± 0.04	0.22 ± 0.05	0.16 ± 0.07

Table no: 5.18: Mechanical and biological property of clindamycin phosphate loaded mucoadhesive periodontal strips after 180 days storage at 4° C

Composition / Characteristics	Batch code					
	CSF20	CSF21	CSF23	CSF24	CSF27	CSF30
Drug content (%)	98.15	97.54	101.24	103.15	101.42	102.15
Mucoadhesive force (10^2, kg m^{-1} s^{-2})	140.62 ± 1.35	285.67 ± 1.55	122.52 ± 1.36	284.12 ± 1.65	457.29 ± 1.29	418.26 ± 1.15
Tensile strength ($kgmm^{-2}$)	4.22 ± 0.48	8.50 ± 0.92	3.20 ± 0.45	5.21 ± 0.78	10.63 ± 0.62	8.98± 0.67
Elastic modulus ($kgmm^{-2}$)	19.48 ± 1.24	43.18 ± 1.05	19.06 ± 1.55	23.67 ± 1.42	53.15 ± 1.47	46.32 ± 1.79
Elongation at break (% mm^{-2})	21.05 ± 1.39	12.25 ± 1.42	22.07 ± 1.41	24.48 ± 1.72	18.37 ± 1.57	16.09 ± 1.72
Strain	0.18 ± 0.06	0.27 ± 0.02	0.39 ± 0.05	0.24 ± 0.04	0.22 ± 0.05	0.16 ± 0.07

5.5 CONCLUSION

From the above study it can be concluded that the non ionic polymer PVA and HPMC can be used for formulating the mucoadhesive periodontal strips for the treatment of dental infectious diseases. Formulations were tried using different concentrations of strip forming polymer HPMC and PVA alone and along with the addition of mucoadhesive polymer carbopol 934P. All the formulations showed good mechanical and mucoadhesive property. Addition of mucoadhesive polymer carbopol 934P improves the mechanical and mucoadhesive property of the periodontal strips. Optimized periodontal drug loaded strip formulations were found to be more flexible in nature compared to that of the plain periodontal strips. Addition of carbopol 934P also increases the swelling index of the periodontal strips. The rate of swelling of the PVA periodontal strip was comparatively faster than the HPMC periodontal strips. The swelling state of the polymer was reported to be crucial for its mucoadhesive behavior. Adhesion occurs shortly after the beginning of the swelling but the bond formed is not very strong. The adhesion will increase with increase in the degree of hydration until a point where over hydration leads to an abrupt drop in adhesion strength due to the disentanglement at the polymer/ tissue interface. Mucoadhesive periodontal strips prepared using 1.5 % w/w HPMC and 10% w/w PVA along with 0.5% w/w carbopol 934P (MSF27, MSF30, CSF27, CSF30) were found to be more suitable basing

on their mechanical and mucoadhesive property. PVA periodontal strips showed good mucoadhesive property compared to that of the HPMC periodontal strips, which may be because of hydrogen bonding due to hydroxyl group or because of significant chain penetration or both. The PVA periodontal strips had a faster hydration rate which could promote interpenetration of the polymer chain with the mucosal tissue. Mucoadhesive periodontal strip formulations containing carbopol 934P showed improved in vitro residence time compared to the plain periodontal strips. PVA periodontal strips showed comparatively improved in vitro residential time compared to that of the HPMC periodontal strips. In vitro release and permeation showed a sustain release of the drug over a period of 24 hours compared to plain drugs. The release exponent of minocycline hydrochloride/ clindamycin phosphate was found to be more sustained in the formulations prepared using 1.5% w/w HPMC along with 0.5% carbopol 934P followed by the formulation prepared using 10% w/w PVA along with 0.5% w/w carbopol 934P. The investigation of in vitro release and permeation data showed that the diffusion is the mechanism of drug release which followed higuchi order of release model. The main advantages of this formulation is that it contains a lower drug dose, sufficient for the therapeutic effect as it is located directly onto the site of the periodontal infection, compared to traditional systemic therapies. Moreover periodontal strip is comfortable as non-irritant, biodegradable and may be preferred over other dosages forms in terms of elasticity, flexibility and capability to protect the inflamed surface. Results of the stability study showed satisfactory stability during the storage period of 6 months, and their chemical and mechanical property does not change significantly.

It may also be concluded that the periodontal strips to be placed locally into the periodontal pocket are the promising drug delivery systems against the infectious periodontal diseases. The anionic polymer PVA showed good mucoadhesive, physico-chemical and mechanical properties than compared to the HPMC periodontal strips. Both medicated PVA and HPMC periodontal strips maintained a satisfactory residence time in the periodontal cavity and ensured higuchi order of release of the drug over relatively longer period, which made them a good candidate for the drug delivery system through periodontal route for the treatment of infectious periodontal diseases.

5.6 REFERENCES

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