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Formulation and Evaluation of Cefpodoxime Proxetil Buccal Film

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ABSTRACT

A new method of administering drugs is through the buccal mucosa. Compared to pills, buccal films are more flexible and easier for patients to tolerate. Therefore, it was intended to use chitosan, gelatin, and pectin as the primary polymeric substrates to create buccal films containing cefpodoxime proxetil. It can be used to treat infections of the skin, soft tissues, urinary tract, and respiratory system brought on by both gram-positive and gram-negative bacteria. Seven formulations were created using the solvent casting process after a number of pre-formulation investigations, including solubility and infrared spectroscopy, were completed. In addition to mechanical evaluations like tensile strength and elongation at break, physical evaluations including physical appearance and surface texture, weight variation, mean thickness, swelling index, folding endurance, surface pH, and moisture loss & moisture absorption investigations were conducted. Using the polymers chitosan, hydroxypropyl methyl cellulose, polyvinylpyrrolidone, and propylene glycol as plasticizers, F6 was chosen as the optimal film based on the in vitro dissolution investigations, which showed a maximum cumulative drug release of 98.91% for up to 390 minutes. Additional tests, including stability, antimicrobial, and release kinetics, were computed for the optimized film and were determined to be within the limit.

Keywords: In vitro drug release, chitosan, solvent casting method, cefpodoxime proxetil, swelling index, antimicrobial research, and stability analysis.

INTRODUCTION

The intestinal mucosa absorbs and deesters the oral active ester prodrug Cefpodoxime proxetil, releasing the third-generation cephalosporin Cefpodoxime. There are oral tablet and oral suspension formulations of cefpodoxime proxetil on the market. This particular molecule is extremely insoluble in water. Consequently, the tablet form's oral bioavailability is just 50%. Numerous bioadhesive mucosal dosage forms, such as adhesive tablets, gels, ointments, patches, and more recently, films, have been produced. When it comes to patient comfort and flexibility, buccal films are better than sticky tablets.

METHODS AND MATERIALS Materials: Chitosan from India Sea Foods, Cochin, Kerala, and cefpodoxime proxetil, a gift sample from Sance Laboratories Pvt Ltd, Kerala. We bought gelatin, pectin, HPMC, NaCMC, PVP, PVA, and PG from Chemdyes.

The pre-formulation study, infrared spectroscopy1, solubility analysis, and calibration data preparation of cefpodoxime proxetil using methanol2 were the methods used.

Buccal films were created using the solvent casting method, which involved dissolving the water-

soluble components to create a transparent, viscous solution, then mixing and stirring the drug (Cefpodoxime proxetil) and other excipients in the appropriate solvent before casting the mixture onto a petri plate and allowing it to dry. Using a sharp knife, the film was removed once it had dried and stored in a self-sealing lid.
To create Cefpodoxime proxetil buccal film, several formulations (F1–F7) were tested utilizing different combinations of polymers such as Pectin, Gelatin, Chitosan, Sodium CMC, HPMC, Polyvinyl pyrrolidone, Polyvinyl alcohol, and Propylene glycol. In Table 1, the formulation chart is displayed.

Table 1- formulation chart

INGREDIENTS	FORMULATIONS						
	F1	F2	F3	F4	F5	F6	F7
CEFPODOXIME PROXETIL (mg)	50	50	50	50	50	50	50
PECTIN (% w/v)	4	4	-	-	-	-	-
GELATIN (% w/v)	-	-	3	3	-	-	-
CHITOSAN (% w/v)	-	-	-	-	2	2	2
SODIUM CMC (% w/v)	1.5	-	1.5	-	-	-	-
HPMC (% w/v)	-	1.5	-	1.5	-	1.5	1.5
POLYVINYL PYRROLIDONE (% w/v)	-	-	-	-	1	1	-
POLYVINYL ALCOHOL (% w/v)	-	-	-	-	1	-	1
PROPYLENE GLYCOL (% v/v)	5	5	5	5	5	5	5
PEPPERMINT FLAVOR (% v/v)	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Pectin films (F1-F2)3: At 25 oC, 1.5% w/v NaCMC was dissolved in 3/4 the amount of distilled water. The remaining 1/4 of the volume of distilled water was then added. For F2, HPMC was dissolved at 90 oC in one-third the volume of distilled water. Next, two-thirds of the volume of 5ºC distilled water was added. At pH 3, pectin (4% w/v) was dissolved in a diluted 0.1N HCl solution. After that, the solution was heated to 50ºC and calcium chloride (0.1%w/v) was added. Next, the polymeric solution was mixed with plasticizer (5% w/v propylene glycol) and medication (50 mg of cefpodoxime proxetil dissolved in methanol). To create a clear, bubble-free gel, the medicated gel was left at room temperature for the entire night. This gel will then be put into glass petri dishes and dried in an oven set between 60 and 70 degrees Celsius.

Gelatin films (F3-F4)4: Using a glass pestle and mortar, all components were precisely weighed and triturated. After that, the mixture was progressively introduced to the solvent system (distilled water) that included the plasticizer and was magnetically agitated. Until a clear solution was achieved, stirring was continued. Cefpodoxime proxetil films were made by dissolving the drug's calculated dosage (50 mg) in 5 milliliters of methanol. While stirring, the drug solution was added to the polymer solution. After that, the solution was quantitatively moved to a petri dish. To enable controlled solvent evaporation, inverted funnels were placed above the petri dishes. Depending on the solvent system, these were kept undisturbed for one to two days at temperatures between 20 and 250C.
Films of chitosan (F5-F7) 5,6: Chitosan was dissolved in 1.5% acetic acid and agitated for two hours to create a 2%w/v chitosan solution. To get rid of particles, this solution was filtered through a muslin cloth. The other ingredients were added to this polymeric solution and agitated for two hours. After being left overnight to eliminate air bubbles, this polymeric solution was evenly applied to a petri plate. After that, the plate was placed in an oven set at 450°C for four hours.
A sharp blade was used to remove the film when it had dried, and it was then stored in a self-sealing cover. To enhance the flavor of the formulation, peppermint flavor (1.5 % v/v) is additionally added to all of the aforementioned formulations.
Assessment of the Prepared Films' Mechanical and Physical Properties
a) Physical Assessment: I) Surface texture and physical appearance II) Weight fluctuation III) Mean thickness IV) Swelling index V) Folding endurance
VI) pH of the surface VII) Studies of moisture absorption and loss a) Mechanical evaluation: I) Tensile strength II) Stretching at break

a) Physical Assessment
The following characteristics of the buccal films were assessed:

I) Surface Texture and Physical Appearance Evaluation of surface texture and physical appearance encompasses both visual inspection and tactile or feel-based texture assessment. 7. II) Variation in weight
Ten 1 cm2 films were weighed separately, and the average of those films was calculated. 8. III) Thickness 1
A screw gauge with a minimum count of 0.01 mm was used to measure the film's thickness at various locations. Five separate locations on the film were used to determine its thickness, and an average was calculated.
IV) Swelling Index (percentage method) 9. The polymeric films were divided into tiny pieces with a diameter of 1.5 cm. This movie was set on
Up to five hours were spent measuring the agar plate's surface and diameter, and the percentage swelling index was computed using the following formula:

I) 9,7 Folding Endurance
A tiny piece of film (about 2 by 2 cm) was folded repeatedly in the same spot until it broke to test the film's folding endurance. The value of folding endurance is determined by how many times the film could be folded in the same spot without breaking.

II) pH 1 on the surface
The agar plate was made by dissolving 2% (w/v) agar in heated isotonic phosphate buffer of pH 6.6 while stirring, then pouring the solution into a petri dish and letting it stand until it solidified to form a gel at room temperature. Buccal films were then allowed to swell on the agar plate's surface for an hour. A pH paper was applied to the surface of the swollen area in order to determine the surface pH.

III) Studies on moisture absorption and loss 10 a. Loss of moisture
The buccal films were stored in desiccators with anhydrous calcium chloride after being precisely weighed. The films were removed and weighed three days later. Moisture loss was calculated using the following formula to determine the moisture loss (%):

b. Absorption of moisture
After precisely weighing the buccal films, they were put in desiccators with 100 milliliters of saturated aluminum chloride solution, which keeps the relative humidity (RH) at 76%. The films were removed and weighed three days later. The following formula was used to determine the percentage of moisture absorption:

I) Mechanical Assessment

Strength of Tension11
The force or tension needed to split the patch in two is known as the buccal films' tensile strength. An apparatus built in the lab was used to measure tensile strength.

Instrument
The tensile strength measuring device was created in our lab specifically for this project. The test film can be held in place between two horizontal hooks thanks to the instrument's construction. One side hook of the balance had a 2.5 cm long film fastened to it, while the other side hook was fastened to a plate that was connected to the pan. Figure 1 depicts the configuration.

A modified tool for measuring tensile strength is shown in Figure 1.

Calculation Method
According to the American Standard for Testing Materials (ASTM) standard test principles, tensile strength is defined as "the maximum load during the tensile strength test divided by the original minimum cross-sectional area of the specimen." Tensile strength, hence

T is the force at break divided by the sample's initial cross-sectional area.

ii) Percent Elongation at Break[12]
The percentage of elongation at break is calculated by dividing the specimen's elongation at the time of rupture by its starting gauge length, then

multiplying the result by 100.

Cefpodoxime Film Evaluation.
i) Determining Drug Content13

The total weight of the movie was calculated. One piece of film was extracted and smashed with a pestle and mortar to determine the drug content. The medication was diluted to 100ml after methanol was added and triturated to fully dissolve it. Filtration was done on the solution. A UV spectrophotometer was used to detect the solution's absorbance at 235 nm, and the drug loading was computed. The drug-free polymer solution acts as a blank. A formula was used to determine the percentage of medication loading.
ii) In vitro release investigation 5
Utilizing USP dissolving equipment type 2 in 400 ml phosphate buffer pH 6.8 at 50 rpm and 37 ± 0.5°C, the in vitro release investigation was conducted. To avoid the film floating over the dissolving media, a film was taken and affixed to a glass slide. For seven hours, the in vitro release research was conducted. At different intervals, 5 ml of samples were taken out and replaced with fresh medium. The samples' absorbance was measured at 235 nm, and the cumulative percentage release was computed.
The optimized film is further assessed under the following headings:
1. Kinetics of Release 14 i) Using the graphic approach to determine the drug's order of release from the buccal film
A graph showing the cumulative percentage of drug release vs time was created using the dissolving data to graphically determine the order of drug release from buccal film. Nothing If a straight line or linearity is found, order release can be verified. The correlation between X and Y was verified by calculating the regression coefficient of the curve.

ii) Drug release study mechanism
The in vitro release data must be fitted into an appropriate model in order to forecast and correlate the drug's release behavior from the buccal film. The cumulative percentage of medication release vs √time was shown on a graph. Higuchi's diffusion is the releasing mechanism if linearity is seen.

2. Determining the Optimized Films' Bioadhesive Strength

Bioadhesive Strength Measurement15
The bioadhesive performance was measured using the tensile strength needed to separate the polymeric film from the mucosal surface.

Instrument
The device was a modification of the physical balance and was put together locally. A two-arm balance made up the majority of the apparatus. A tiny, vertically hanging stainless steel lamina took the role of the balance's left arm. In order to secure the model mucosal membrane, a platform was kept at the bottom on the same side.

Approach
A two-arm balance made up the majority of the apparatus. A tiny, vertically hanging stainless steel lamina took the role of the balance's left arm. In order to secure the model mucosal membrane, a platform was kept at the bottom on the same side. After being removed and cleaned, the bovine cheek pouch was affixed to the platform. Using an adhesive, the 3 cm^2 mucoadhesive patch was adhered to the stainless steel lamina. For initial hydration and swelling, 1 milliliter of isotonic phosphate buffer was applied to the exposed patch area for 30 seconds. After then, the platform was lifted until the hydrated patch made contact with the mucosal surface.
For three minutes, a preload of twenty grams was applied as beginning pressure over the stainless steel lamina. After that, the right pan's weight was gradually raised till the patch
breaks away from the mucosal layer. The bioadhesive strength of the mucoadhesive patch is determined by the force needed to separate it from the mucosa. For every patch, the process is performed three times, and the average of the three

trials was calculated for every formulation set. Before taking a reading, the tissue was thoroughly and gently cleaned with isotonic phosphate buffer after each measurement. It was then left for five minutes.

1. Analysis of Optimized Film16's Antibacterial Properties

To produce the agar plates for this investigation, 28 g of nutritional agar was dissolved in

1 L of distilled water was autoclaved for 15 minutes at 121 °C and 15 lbs of pressure to sterilize it. Sterile Petri dishes were filled with the agar solution. The agar plates were then inoculated (cultured) with S after being left to cool and solidify at room temperature. E. coli and aureus.

Diffusion Assay on Agar

The optimized buccal film of Cefpodoxime (F6) was tested for antibacterial efficacy using the agar diffusion assay on an aliquot of in vitro drug release studies. Following the collection of an aliquot of the in vitro drug release sample, 6.5 hours. Carefully, a 0.1 mL sample was pipetted into the agar plates' evenly spaced wells. Pure Cefpodoxime Proxetil was likewise used to prepare the reference standard, which was then infected under the same circumstances. Following two hours of cold prediffusion, these plates were incubated for twenty-four hours. Each agar well that was inoculated with S. aureus and E. coli had its growth inhibition zone's diameter (in millimeters) measured.

2. Stability Study of the Optimized Film1

Optimized medicated films were submitted to stability testing. Films were placed in a beaker lined with aluminium foil and kept in a humidity room maintained at 40±20C and 75±5% relative humidity for 1 month. After 15 and 30 days, changes in the stored films' appearance, drug content, and in-vitro release were examined

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OUTCOMES AND CONVERSATION

Pre-formulation research:
a) Studies using IR spectroscopy IR spectra for pure drug and physical mixture of drug-polymers were collected and evaluated for primary peaks. These peaks, which were unaffected and clearly visible in the drug's infrared spectra along with polymers such pectin, chitosan, gelatin, sodium CMC, HPMC, PVP, and PVA, can be regarded as distinctive peaks of cefpodoxime proxetil. Cefpodoxime proxetil did not interact with the chosen polymers, according to the spectra. So the medicine and polymers are compatible with each other.

b) Studies on solubility Cefpodoxime Proxetil was discovered to be freely soluble in acetonitrile, isopropyl alcohol, methanol, and DMSO, while being insoluble in water and only weakly soluble in ether. Solubility research has been completed for Cefpodoxime proxetil and the results were within the pharmacopoeial standards.

c) Preparation of calibration data of cefpodoxime proxetil Using methanol The absorption readings of Cefpodoxime proxetil solution (25-150µg/ml) in methanol at the maximum wavelength of 235 nm were tabulated in table 7.2 and figure 7.2 depicts a calibration curve for the readings. It was discovered that the curve was linear within the 25–150 µg/ml concentration range. Table 2 provides the calibration data, and the curve seen in Figure 2.
Table: 2 - Calibration data of Cefpodoxime proxetil using methanol

Concentration (µg/ml)	Absorbanceat 235nm
0	0
25	0.2174
50	0.4231
75	0.6433
100	0.8639
125	1.0580
150	1.2860

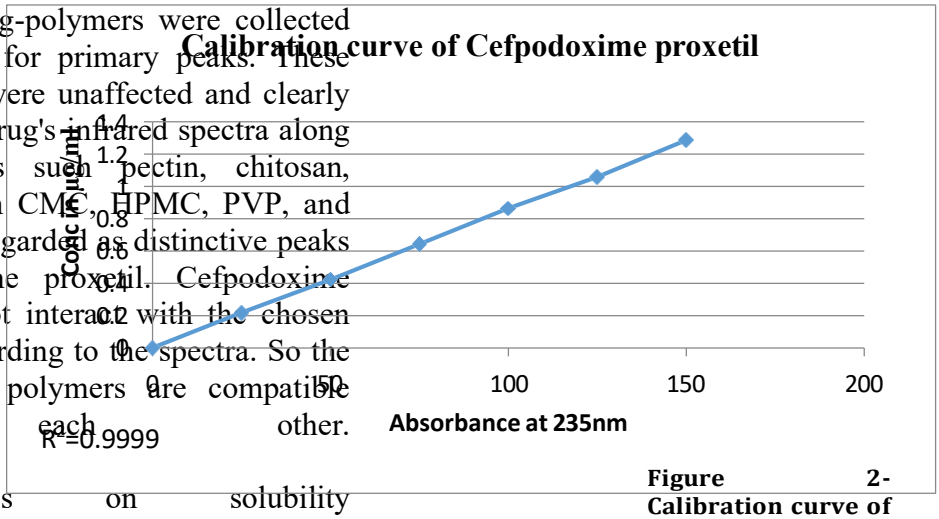

Figure 2- Calibration curve of Cefpodoxime using methanol.

Evaluation of Physical and Mechanical Characteristics of the Prepared Films

Physical evaluation

The seven prepared buccal films were evaluated for different physical parameters and the results were recorded in table 3.

Table 3 -Physical evaluation data of formulations

Physical characteristics	Formulations			
	F1	F2	F3	F4
Appearance	Less smooth	smooth	Less smooth	smooth
Surface texture	Less flexible	Flexible	Less flexible	flexible
Thickness (mm)	0.403 ±0.14	0.402 ±0.08	0.402 ±0.09	0.402 ±0.09
Average Weight (mg)	55 ±0.95	56 ±1.07	58 ±1.24	57 ±1.7
Swelling index after 6hr (%)	27.05 ±0.12	28.06 ±0.22	27.13 ±0.24	28.11 ±0.31
Folding endurance	291 ±5	>300	>300	>300
Surface pH	7	7	7	7

Moisture absorption (%)	4.35 ±0.01	4.15 ±0.03	5.92 ±0.02	5.64 ±0.03	5.35 ±0.01	5.16 ±0.02	5.94 ±0.03
Moisture loss (%)	1.85 ±0.08	1.88 ±0.06	1.91 ±0.03	1.94 ±0.04	1.48 ±0.05	2.02 ±0.04	2.09 ±0.06

Physical studies revealed that all seven formulations had improved texture and appearance. Comparatively less flexibility and smooth surface were displayed by Formulations F1 and F3. To a certain degree, physical appearance contributes to increased patient compliance. All of the films' average weight and thickness were measured, and the findings are displayed in a table. The formulations' average weight ranged from 55±0.95 to 58±1.44 mg, while their thicknesses fell between 0.401±0.11 and 0.403±0.14. The findings indicated that every formulation's weight and thickness fell within the permissible range. During release trials, this guarantees a consistent drug release. All of the formed films are within the normal ranges, according to swelling experiments of various films. The swelling index values for Formulations F2, F4, F6, and F7 were relatively similar, at about 28%. Out of all the films, F5 has the lowest swelling index, at about 26.5%. The presence of swellable polymers like HPMC may be the cause of an increased swelling index.

For buccal film, a folding endurance of greater than 300 is ideal. When seven distinct buccal films were tested for folding endurance, formulation F1 had the lowest folding endurance (291 times). The remaining six formulations are perfect for buccal films since they have a folding endurance value higher than 300. Since all of the formulations had a surface pH of 7, or neutral pH, no discomfort was anticipated when administered buccal. The moisture absorption % was calculated and recorded. The range of this is 4.15±0.03 to 5.94±0.03 percent. After calculating the % moisture loss of each of the seven formulations, it was discovered to be between 1.48±0.05 and 2.09±0.06. The minimal moisture loss observed in all tested formulations from F1 to F7 is beneficial for preserving the film's flexibility and other physical characteristics while it is being stored. All antibiotic buccal film formulations' physico-chemical characteristics were determined to be within acceptable bounds.

Mechanical evaluation

For mechanical evaluation tensile strength and percentage elongation at break were studied and the results were tabulated in table 4

Table 4 – Mechanical evaluation data of formulations

Formulations	Tensile strength (N/m^2)	% Elongation at break
F1	4.6 x10³± 0.14 x10³	44.1 ± 1.9
F2	4.7 x10³± 0.12 x10³	46.3 ± 1.5
F3	4.6 x10³± 0.16 x10³	48.1 ± 1.9
F4	4.9 x10³± 0.14 x10³	47.8 ± 1.8
F5	5.4 x10³± 0.13 x10³	50.4 ± 1.1
F6	5.6 x10³± 0.15 x10³	49.3 ± 1.8
F7	5.1 x10³± 0.11 x10³	48.6 ± 1.6

Film F7's highest tensile strength of 5.6 x103± 0.15 x103N/m2 indicates that the combination produced effective cross-linking. Additionally, it was found that other formulations' values were within the buccal film range. The elongation of the break, which is the outcome of the elongation at break test, indicates the film's strength and elasticity. The best films for buccal application are flexible and strong. Formulation F5 exhibited the highest elongation, measuring 50.4 ± 1.1%, according to the examination of the different formulations. The values from other formulas are within the range and good.

Drug Content Determination

The drug content of all formulations was consistent, ranging from 98.16 to 98.88%, according to research on the drug loading efficiency of each formulation. Formulations F4 and F6 were found to produce the highest drug loading. Formulation F1 produced the lowest medication loading. In

its formulations, the combination of HPMC with chitosan is providing a promising drug content. Table 5 displays the chart.

Table 5 – Percent drug content of formulations

FORMULATIONS	DRUG CONTENT (%)
F1	98.16 ± 0.14
F2	98.39 ± 0.21
F3	98.27 ± 0.19
F4	98.88 ± 0.01
F5	98.16 ± 0.24
F6	98.88 ± 0.03
F7	98.51 ± 0.16

In Vitro Drug Release

The release of drug from the dosage form plays important role in buccal drug delivery and in determining the therapeutic effect of the medication. The *in vitro* release study of all formulations of buccal film was carried out using USP dissolution apparatus type 2 in 400 ml phosphate buffer pH 6.8 at 50 rpm. A comparison of the 7 *in vitro* drug release is shown in table 6 and figure 3.

Table 6 - Comparison of *In vitro* drug release of formulations F1-F7

Time in minutes	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
30	33.6	15.5	24	10.5	10.75	9	9.5
60	69.49	32.98	43.56	21.99	22.00	16.08	16.11
90	96.26	49.17	68.14	32.18	35.12	24.65	26.11
120	96.54	69.70	85.79	45.70	45.77	29.83	35.24
150		83.83	98.87	52.14	52.37	40.73	43.80
180		96.86		62.83	68.26	45.89	49.39
210		98.25		76.32	75.90	52.37	60.32
240				88.36	90.34	63.07	68.38
270				97.41	97.43	68.42	85.30
300						75.90	91.93
330						83.90	97.44
360						90.43	98.98
390						98.91	

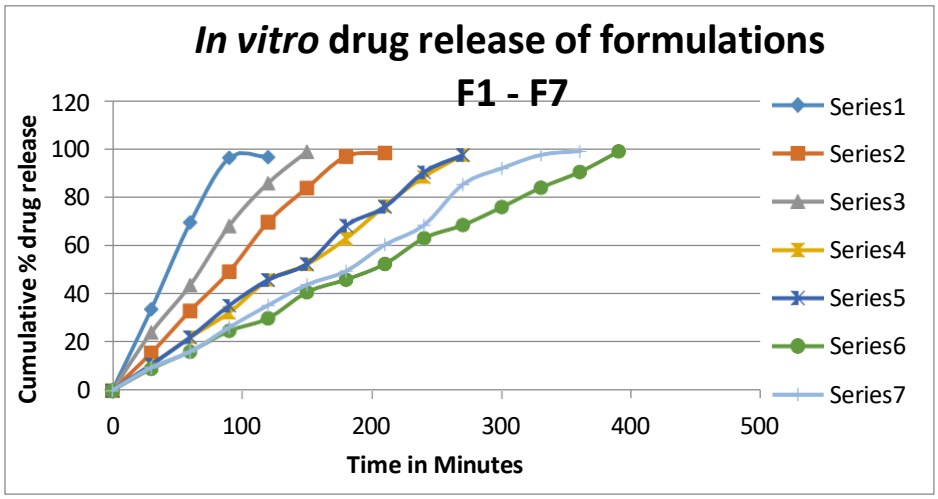

Figure 3 - Comparison of *In vitro* drug release graph of formulations F1-F7

Because of its greatest release over a 390-minute period, formulation F6, which contains chitosan, HPMC, and PVP, can be regarded as the optimal formulation based on the aforementioned in vitro release trials. The cumulative percentage of medication release plotted against time indicates linearity in release. Thus, this It was discovered that this mixture was perfect for buccal release. For release kinetics and subsequent research, the refined formulation F6 was then taken into consideration.

Release Kinetics

Release kinetic study of optimized film (F6)

The cumulative percentage of drug released versus time was shown on a graph to ascertain the sequence of drug release from buccal film using a graphical method based on the dissolving data. If linearity or a straight line is attained, zero order release has been verified. The correlation between X and Y was verified by calculating the regression coefficient of the curve. When plotting the cumulative percentage of medicine released vs time, formulation F6 produced a straight line with a r2 value of 0.9985, confirming the zero order release. Figure 4 displays the linearity and graph.

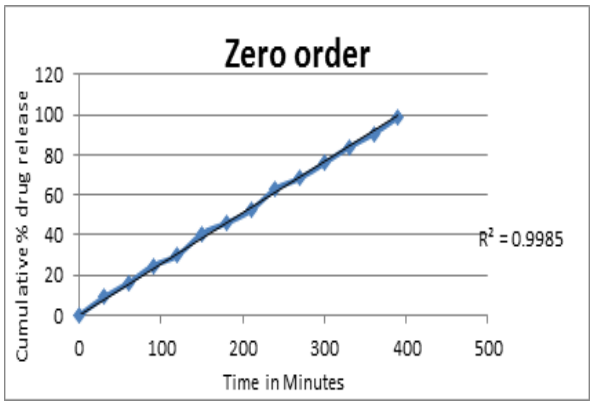

Figure 4: Release kinetics of formulation F6

Mechanism of Drug release of optimized film (F6)

In order to predict and correlate the release behavior of drug from the buccal film, a graph was plotted with cumulative % drug release vs. √time, figure 5.

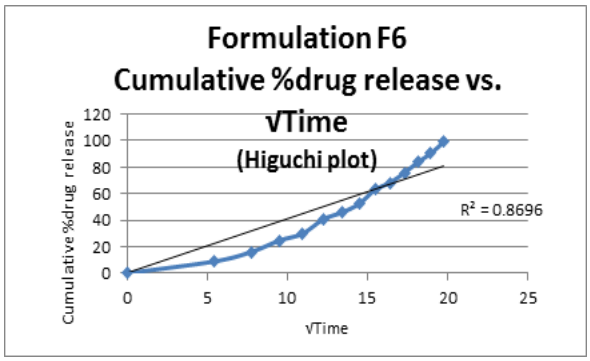

Figure 5 -Mechanism of Drug release of formulation F6

From the data shown in Table 7, the *in vitro* dissolution data were fit in to Higuchi's

diffusion plot with r^2 value 0.8696.from the result it is confirm that the prepared buccal film model for antibiotic Cefpodoxime proxetil follows zero order diffusion kinetics.

Table 7 – Higuchi plot Formulation F6

√Time	Cumulative %drug release
0	0
5.47	9
7.75	16.08
9.49	24.65
10.95	29.83
12.25	40.73
13.42	45.89
14.49	52.37
15.49	63.07
16.43	68.42
17.32	75.90
18.17	83.90
18.97	90.43
19.75	98.91

Determination of Bioadhesive Strength of Optimized Films

Mucoadhesion strength is generally influenced by a number of parameters, including the biological membrane employed in the study, the polymer's rate of swelling, and the duration of contact with mucus. Table 8 illustrates that the optimized formulation of buccal film yielded an adequate bioadhesive strength of 6.1±0.08 N.

Table: 8 – Bioadhesive strength of optimized film

Formulation	Bioadhesive strength(N)
F6	6.1±0.08

Antibacterial Study of Optimized Films

After 24 hrs of incubation the diameter of zone of inhibition was measured and the values were shown in the table 9.

Table 9 – Antibacterial study of formulation F6

Organism used	Zone of inhibition (mm)	
	Formulation - F6	Standard Cefpodoxime
E.coli	23 ± 0.08	24 ± 0.02
S.aureus	26 ± 0.06	28 ± 0.04

The drug extracted from buccal film showed better antimicrobial activity against the tested microorganisms. The zone diameter

Formulation F6 produced a zone diameter of 23 ± 0.08 mm against E. coli (figure 6) and 26 ± 0.06 mm against S. aureus (figure 7), which is about equivalent to the zone diameter generated by the medication cefpodoxime alone against the bacteria. This demonstrated unequivocally that Cefpodoxime proxetil's potency and activity are unaffected by its entrapment in the buccal film.

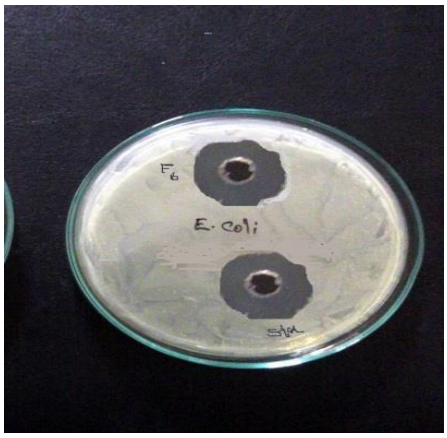

Figure 6 – Zone of inhibition against *E.coli*

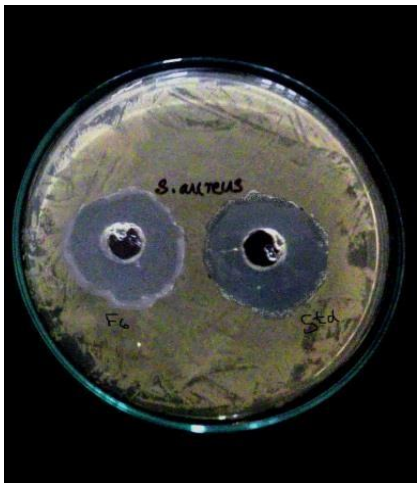

Figure 7 – Zone of inhibition against *S.aureus*

Stability Study of the Optimized Film For a month, films of formulation F6 were stored in a humidity chamber with a temperature of 40±20C and a relative humidity of 75±5%. At the end of 15 and 30 days, changes in the films' look and drug content were examined. Table 10 contains the tabulation of the readings. It was evident from the data analysis that there are no appreciable variations in the mechanical and physical evaluation values. Appearance, surface texture, thickness, average weight, swelling index, folding endurance, surface pH, moisture absorption, tensile strength, and percentage elongation at break were among the values taken into account. Even after 30 days of research, the readings appeared to be normal. The graphs for the optimized film and the findings of the invitro drug release investigation were created after 15 and 30 days, respectively, and are displayed in Table 11 and Figure 8.

Table 10 – Stability study evaluation of formulation F6

Evaluation Parameters		**After 15 days Formulation F6**	**After 30 days Formulation F6**
Physical characteristics	Appearance	Clear, smooth	Clear, smooth
	Surface texture	Flexible	Flexible
	Thickness (mm)	0.402 ± 0.14	0.402 ± 0.11
	Average Weight (mg)	58 ± 0.74	58 ± 0.61
	Swelling index after 6hr (%)	26.15 ± 0.12	26.11 ± 0.22
	Folding endurance	>300	>300
	Surface pH	7	7
	Moisture absorption (%)	5.15 ± 0.05	5.13 ± 0.02
	Moisture loss (%)	2.02 ±0.02	2.02 ±0.06
Mechanical evaluation	Tensile strength (N/m^2)	$5.6 \times 10^3 \pm 0.02 \times 10^3$	$5.5 \times 10^3 \pm 0.10 \times 10^3$
	% Elongation at break	49.2 ± 0.29	49.2 ± 0.91
Drug content determination (%)		98.46 ± 0.03	98.01 ± 0.12
***In vitro* drug release**	% Cumulative drug release	98.90	97.44
	Time (min)	390	390

Table 11 - *In vitro* drug release of formulation F6 after 15 days of stability study

Time (minutes)	**Absorbance 235nm**	**Amount of drug release (mg)**	**% drug release**	**Cumulative % drug release**
0	0	0	0	0
60	0.171	8	16	16
120	0.350	15.75	31.5	32.01
180	0.502	23.5	47	47.67
240	0.669	31.12	62.24	63.00
300	0.809	37.75	75.5	76.32
360	0.960	44.25	88.5	89.35
390	1.054	49	98	98.90

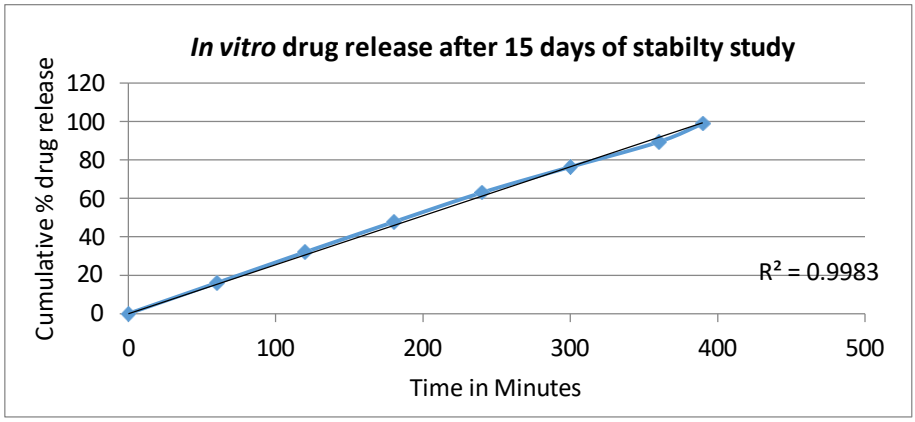

Figure 8 - *In vitro* drug release of formulation F6 after 15 days of stability study

Table 12 - *In vitro* drug release of formulation F6 after 30 days of stability study

Time (minutes)	Absorbance 235nm	Amount of drug release (mg)	% drug release	Cumulative % drug release
0	0	0	0	0
60	0.173	8	16	16
120	0.355	16.6	33.2	33.68
180	0.499	23.5	47	47.71
240	0.672	31.12	62.24	63.00
300	0.819	38.25	76.5	77.31
360	0.977	45.5	91	91.84
390	1.036	48.25	96.5	97.44

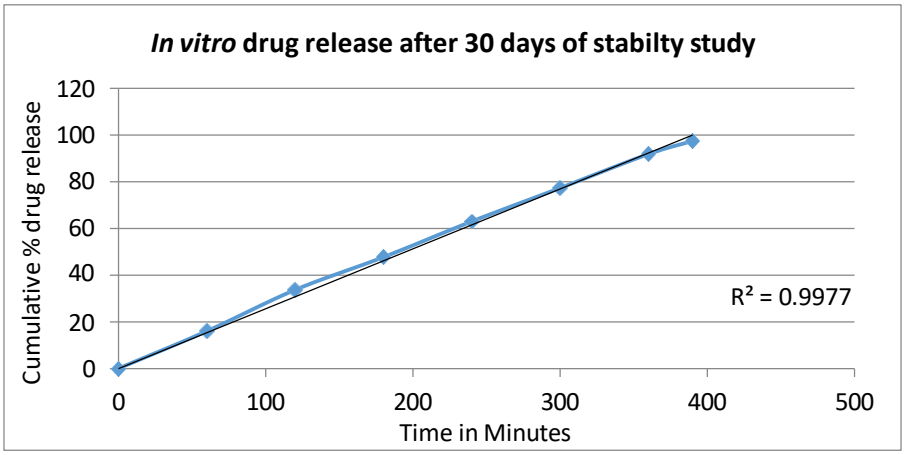

Figure 9- *In vitro* drug release of formulation F6 after 30 days of stability study

At 390 minutes, the cumulative percentage release was 98.90 after 15 days and 97.44 after 30 days. There is no discernible change from the prior values in the percentage release statistics, including the time of release and the cumulative percentage release.

FINAL RESULTS

Formulation F6 with Chitosan, HPMC, and PVP was determined to be the best combination for antibiotic buccal film based on pre-formulation research, physicochemical analyses, mechanical assessments, in vitro release, and stability studies. Additionally, the antibacterial study shows that carrying an antibiotic in this specific formulation combination is not problematic. to the buccal membrane. Thus, the current study's goal of creating an antibiotic buccal film was accomplished. This approach can be improved in the future with different polymer percentages for improved bioavailability and controlled release. With the right animal model, an in vivo investigation can also be carried out.

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