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DESIGN, DEVELOPMENT, AND CHARACTERIZATION OF BUCCAL MUCOADHESIVE PATCH LOADED WITH CLINDAMYCIN HYDROCHLORIDE AND CURCUMIN USING DESIGN EXPERT SOFTWARE FOR THE TREATMENT OF PERIODONTITIS

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Keywords:

Buccal patches, Poly vinyl alcohol, Hydroxy ethyl cellulose, Clindamycin hydrochloride, Curcumin, DoE

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ABSTRACT: Periodontitis is a widespread oral gum infection having multiple antibiotics for the treatment, but large oral doses and the emergence of antibiotic resistance constrain their usage. The goal of this study was to develop and characterize buccal mucoadhesive patches made of clindamycin and polymers for the treatment of Periodontitis. Patches were developed by solvent casting method using Clindamycin Hydrochloride, an herbal constituent of Curcumin, and polymers like Polyvinyl Alcohol, and Hydroxy Ethyl Cellulose. Eight trial patches were developed by keeping the drug ratio constant and varying the concentration of different polymers. The optimized patch concentration was chosen to formulate the buccal mucoadhesive patch to treat periodontitis. Optimization was conducted by Design Expert Software (DoE) using 2^3 full factorial designs by taking three independent variables as factors and two dependent variables *in-vitro* Drug release (Y1) and Drug content (Y2). Prepared buccal mucoadhesive patches were flexible and showed the highest efficacy in the inhibition of oral microorganism species like Porphyromonas, Streptococcus, Actinomyces, and Candida albicans. The optimized patch was analyzed for interaction study using FTIR and DSC analysis, the tensile strength was analyzed using a Tensiometer and other parameters like weight uniformity, film thickness, content uniformity, surface pH, folding endurance, and tensile strength. The *in-vitro* release study showed an initial burst release of the drug followed by a sustained release for up to 24 hours. The developed Buccal Mucoadhesive Patch gives sustained action for up to 24 hours compared to other dosage forms.

INTRODUCTION: Periodontitis is a bacterial infectious disease with a large geographic distribution. It begins by damaging the gingival tissue and if left untreated, extends to deeper tissues, disrupting the natural homeostasis of the bone and resulting in tooth loss [1].

QUICK RESPONSE CODE

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Periodontitis is a set of inflammatory diseases affecting the periodontium- that is, the tissues that surround and support the teeth [2]. Periodontitis involves progressive loss of the alveolar bone around the teeth [3].

The etiology of the illness is impacted by both local and systemic causes. One of the most widespread conditions affecting the mouth is periodontitis. The condition must be treated as soon as possible since it not only causes tooth loss but also has an impact on the patient's overall health [4]. Different approaches have been developed for the treatment

of periodontal disease, including traditional techniques, scaling, and root planning; however, these techniques are heavily dependent on the clinician's competence and capacity to get into wealthy backers or fraction areas [6]. Advanced drug-loaded biomaterials, such as micro/nanofibers, members, hydrogels, or nanoparticles, can address these constraints by providing precise and regulated drug release while also focusing on the bacteria invading intra-periodontal pockets.

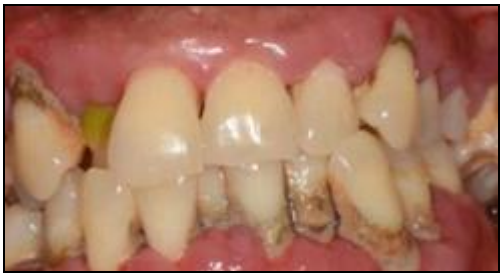


FIG. 1: CLINICAL PRESENTATION OF PERIODONTITIS [5]

Among these Buccal drug delivery systems (BDDS) have won a variety of exposure and attractions as they possess plenty of advantages and benefits as compared to different mucosal drug delivery systems. Muco-adhesion is the attachment of the drug along with a suitable carrier to the mucous membrane. Muco-adhesion has the following mechanism [7].

1. Intimate contact between a bio-adhesive and a membrane (wetting or swelling phenomenon).
2. Penetration of the bio-adhesive into the tissue or the surface of the mucous membrane (interpenetration) [8].

The mucosa has a rich blood supply, and it is relatively permeable. Drug release is controlled and prolonged when it occurs through the oral mucosa, which also aids in overcoming hepatic metabolism. Various synthetic and natural polymers have been used to formulate buccal patches. Hydroxy ethyl cellulose (HEC) is a polysaccharide derivative. It is a water-soluble polymer and is used in pharmaceutical formulations with excellent properties of bio-compatibility, oxygen and nutrient permeability, and high porosity [9]. Due to the great chemical and thermal stability and affordable manufacture, PVA is utilized in a wide range of industries. In addition, it is a well-liked water-soluble polymer with high strength and great optical transparency. Clindamycin is a parenteral, topical, and oral broad-spectrum antibiotic used to treat sensitive organism-caused bacterial infections. Curcumin has a wide range of medically validated advantages, including the capacity to enhance heart health and defend against Alzheimer's and cancer. It works well as an antioxidant and anti-inflammatory. Additionally, it might lessen arthritis and depression symptoms [10].

MATERIALS AND METHODS:

Materials: Clindamycin hydrochloride was purchased from Carbanio.com, Polyvinyl Alcohol from Thermo Fischer Scientific India Pvt., Ltd (India), and Curcumin from Loba Chemie Pvt. Ltd (Maharashtra, India), Hydroxy Ethyl Cellulose from Carbanio.com, and Glycerol from Jiangyin Tenghua Import & Export Co., Ltd. All reagents were of analytical grade and used as received.

Methods:

Preparation of Buccal Mucoadhesive Patches: The buccal mucoadhesive patches were prepared by using the solvent casting technique. The trial batch concentrations are mentioned in Table 1. Polyvinyl alcohol powder 10% w/v was dissolved in hot water at 70 – 80 ° C and 0.1g of Hydroxy ethyl cellulose was added after cooling. Then Glycerol was added under stirring. Finally, 10% w/v of clindamycin was incorporated in the above polymeric solution with continuous stirring, and to this 0.1g Curcumin was added.

The medicated gel was kept overnight at room temperature to ensure the gel was free from air bubbles. Then the gel was cast into a glass Petri dish and allowed to dry in an oven maintained at 40° C for 4 to 5 hrs till flexible film was formed. The dried film was cut into patches of 1cm x 1cm area. Various concentrations of polymers underwent trial formulation, and from that the optimum formulation was obtained and the best patch is represented in **Fig. 2.**

FIG. 2: BUCCAL PATCH OF F7 FORMULATION

TABLE 1: FORMULATION CHART OF CLINDAMYCIN HYDROCHLORIDE BUCCAL MUCOADHESIVE PATCHES

Ingredients(25ml)	Formulation code							
	F1	F2	F3	F4	F5	F6	F7	F8
Clindamycin HCl (mg)	1000	1000	1000	1000	1000	1000	1000	1000
Curcumin (mg)	1	0.5	0.1	0.1	0.1	0.1	0.1	0.1
PVA (mg)	600	500	650	700	850	900	1000	800
HEC (mg)	0.01	0.01	0.01	0.1	0.1	0.1	0.1	0.1
Glycerol (mg)	1	1	0.5	0.5	0.5	0.5	0.5	0.5
Water (mg)	Quantity sufficient to 25 ml							

Optimization Studies [11]: Optimization was carried out by Design Expert Software (DoE) using 2^3 full factorial designs by taking three independent variables as factors and two dependent variables *In-vitro* Drug release (Y1) and Drug content (Y2) as factors **Table 2.**

TABLE 2: INDEPENDENT AND DEPENDENT VARIABLES USED IN THE DESIGN

Independent Variables	Levels (-1 to +1)	
PVA (mg)	-1	+1
HEC (mg)	-1	+1
Curcumin (mg)	-1	+1
Dependent variables	Y1 = In Vitro Drug Release Y2 = Drug Content	

Effect of Independent Variables on *In-vitro* Drug Release (Y1): ANOVA test for the observed data of In Vitro Drug Release indicated that the 2-level factorial model was significant with an F value of 14.52 and P value < 0.0500 are fitting for the data. The resulting equation with coded values is as follows:

Log10 (*In-vitro* drug release) = 1.94-0.0051B-0.0275C-0.0213BC

From the equation, it was observed that the HEC and Curcumin react and release the drug slowly. From the contour plot, we can observe that 95% of the drug was released from the formulation by the 24th hour.

The model suggests that the polymers PVA and HEC are more effective in the In vitro drug release. The Model F-value of 14.52 implies the model is significant. There is only a 1.29% chance that an F-value this large could occur due to noise. P-values less than 0.0500 indicate model terms are significant. In this case, C and BC are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model. The following **Table 3** and **Fig. 3** depict the optimized value for the *in-vitro* drug release.

TABLE 3: ANOVA TABLE FOR RESPONSE 1

Response 1: In vitro drug release
Transform: Base 10 Log
Constant: 0

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	0.0099	3	0.0033	14.52	0.0129	significant
B-HEC	0.0002	1	0.0002	0.9070	0.3948	
C-curcumin	0.0060	1	0.0060	26.65	0.0067	
BC	0.0036	1	0.0036	16.00	0.0161	
Residual	0.0009	4	0.0002			
Cor Total	0.0108	7				

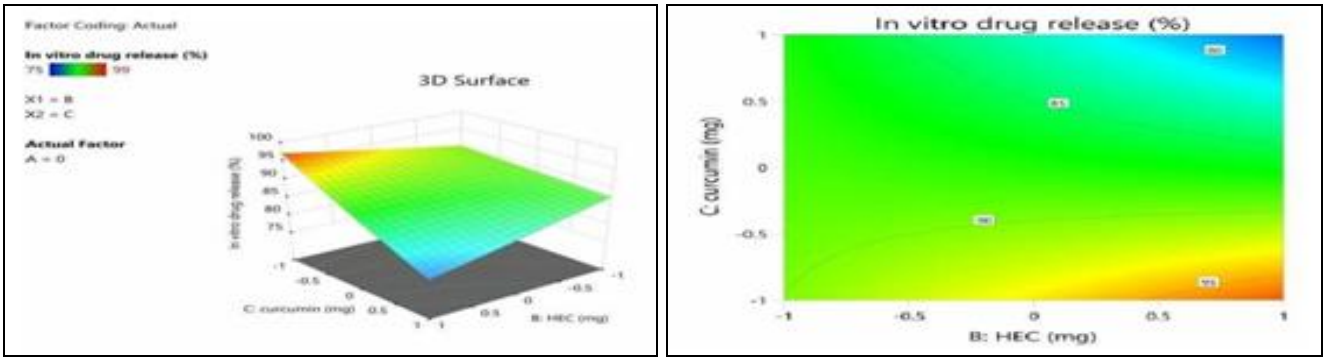


FIG. 3: CONTOUR AND 3D PLOT OF *IN-VITRO* DRUG RELEASE

Effect of Independent Variables on Drug Content (Y2): ANOVA test for the observed data of *in-vitro* drug release indicated that the 2-level factorial model was significant with an F value of 7.38 and P value <0.0500 are fitting for the data.

The resulting equation with coded values is as follows:

Drug Content = 93.63+2.87A

From the equation, it was observed that the PVA is mainly responsible for the drug content of the buccal PATCHES. From the contour plot, we can observe that 96% is the highest drug content in the F7 Formulation. The model suggests that the polymer PVA is essential for the drug content and its therapeutic activity. The Model F-value of 7.38 implies the model is significant. There is only a 3.48% chance that an F-value this large could occur due to noise. P-values less than 0.0500 indicate model terms are significant. In this case, A is a significant model term. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve our model. The following **Table 4** and **Fig. 4** depict the optimized value for the *in-vitro* drug release.

TABLE 4: ANOVA TABLE FOR RESPONSE 2

ANOVA for selected factorial model

Response 2: Drug content

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	66.12	1	66.12	7.38	0.0348	significant
A-PVA	66.12	1	66.12	7.38	0.0348	
Residual	53.75	6	8.96			
Cor Total	119.88	7				

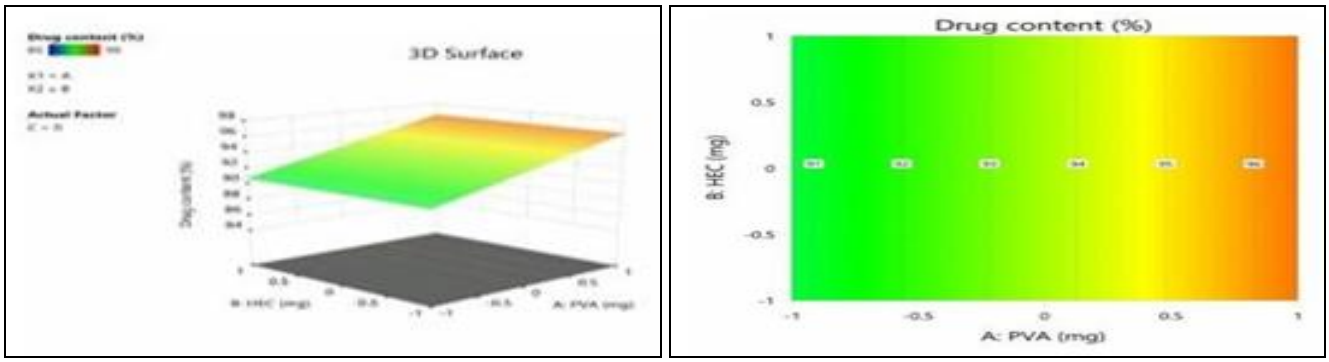


FIG. 4: CONTOUR AND 3D PLOT OF DRUG CONTENT

Evaluation Parameters for Buccal Patches:

Weight Uniformity Test [12]: The weight uniformity test was conducted by weighing 10 patches of the same formulation that were cut from various places, and their weights were calculated using a digital balance.

Thickness of Film [13]: The film thickness of 10 strips was measured with the help of a screw gauge. The strip was placed between the two jaws and the thickness was measured. Then the mean value was calculated.

Content Uniformity: The prepared patch's drug content was estimated using the technique below. The prepared clindamycin HCl patch was taken in a 100 ml standard volumetric flask. A phosphate buffer solution with a pH of 7.4 was added and made up to volume and was kept overnight in the flask. The solution was filtered, and 5 ml of this filtrate was pipetted out into a 100 ml standard volumetric flask and made up to the volume with pH 7.4 phosphate buffer solution and the absorbance was determined at 210 nm in UV Spectrophotometer.

Percentage Moisture Loss [14]: The integrity of the film under dry conditions was evaluated by measuring the percentage of moisture loss. The patch was weighed and stored in a desiccator with anhydrous calcium chloride. The patches were removed after three days, weighed again, and the percentage of moisture loss was calculated by utilizing the formula.

Moisture loss = Initial weight- Final weight / Initial weight ×100

Surface pH: The patch was allowed to swell for 1 hour on the surface of the agar plate, prepared by dissolving 2% w/v agar in warmed distilled water under stirring and then pouring the solution into the Petri dish to gel/solidify at room temperature. The surface pH was measured using pH paper placed on the surface of the swollen film. The mean of 3 readings was recorded.

Disintegration time: The film was cut into 1x1 cm^2 pieces and placed on a Petri plate containing 10ml distilled water. The total time taken by the film to disintegrate was noted using a digital stopwatch. The procedure was performed in triplicate.

Folding Endurance [15]: The folding endurance of the film was determined by repeatedly folding the film at the same place up to 300 times till it broke or folded, which is considered satisfactory to reveal good film properties this test was carried out on all the films.

Swelling Studies [16]: For swelling studies, each film 1x1 cm^2 was weighed and then placed in the phosphate buffer saline solution (pH 7.4). At predetermined periods (0.25,0.5,1,2,3,4,6,8,24, and 48 hours) each film was removed from the phosphate buffers, blotted dry with tissue paper, and weighed again. The degree of swelling was calculated by using the equation.

$$\text{Swelling ratio \%} = Wt- Wo / Wo \times 100$$

Wt – Weight of film at time t W0 – weight of film at time 0.

This test was performed in triplicate and results were recorded as mean ± SD.

***In-vitro* Drug Release Studies [17]:** The *in-vitro* release of Clindamycin HCl from the patch was carried out in small test tubes containing 10 ml of pH 7.4 phosphate buffer. The test tubes were sealed with aluminum foil and kept at 37ºC. The sample was withdrawn and replaced with the fresh pH 7.4 phosphate buffer solution for every 1 hour up to the 8th hour. Again, the sample was withdrawn at the 24th hour. The concentration of the drug in the withdrawn solution was measured at 210 nm using a UV-spectrophotometer.

***In-vitro* Drug Release Kinetic Studies:** The outcomes of the *in-vitro* release profiles obtained for each formulation were plotted using the following modalities of data treatment:

1. Zero order kinetic model Cumulative % drug released versus time.
2. First order kinetic model Log cumulative % drug remaining versus time.
3. Higuchi plot Cumulative % drug release versus square root of time.
4. Koresmeyer-peppas model Log cumulative % drug release versus log T.
5. Hixson-Crowell model Cube root of drug % remaining versus time.

Determination of Tensile Strength (TS) [18]: The tensile strength of the patch was evaluated by using the tensiometer. It consists of two load cell grips. The lower one was fixed and the upper one was movable. Film strips with dimensions of 2*2 cm were fixed between these cell grips, and force was gradually applied till the film broke. The tensile strength was taken directly from the dial reading in g or kg.

Antibacterial Activity:

Quantitative Suspension test for the Evaluation of Bactericidal Activity: EN 1276 Method: EN 1276 is a phase 2 step 1 suspension test for disinfectants intended for use in food, industrial, domestic, and institutional areas. The test evaluates the efficacy of the product against bacteria.

Test Method: In phase 2 step 1 suspension test, 8 parts of the test product are added to 1-part test microorganism and 1-part interfering substance. The mixture is allowed to interact for the duration of the contact time. One part of the mixture is added to 8 parts of neutralizer and 1 part of water for 5 minutes to halt bactericidal activity. The final mixture is then acquired and incubated for 2 days to allow surviving bacteria (if any) to proliferate. The bacterial colony is counted and compared against the original culture size.

FT-IR Spectrum [19]: By making pellets with anhydrous KBr, the drug's FTIR spectra for drugs, polymers, and physical mixture were obtained between 4000 cm^{-1} and 500 cm^{-1}.

Pure drugs Clindamycin and Curcumin and polymers PVA and HEC were subjected to FTIR studies. About 2 mg of pure drug, a combination of drug-polymer was triturated with KBr (Potassium bromide) to form a pellet. The mixture was placed in the sample holder and was analyzed by infrared to study the interference of polymers with the drug.

DSC Analysis [20]: DSC analysis was done to ascertain the compatibility of the drug with the excipients. It was performed on a DSC Q10 V 9.0, differential scanning calorimeter with a thermal analyzer. About 2.3 mg of the powdered sample was placed in a sealed aluminum pan, before heating under nitrogen flow (20ml/min) at a scanning rate of 10ºC min^{-1}. An empty aluminum pan was used as a reference.

Stability Studies of the Optimized Formulation: The stability study of the formulation was done at 40 °C±2 °C/75% RH±5%RH. As per ICH guidelines, the samples for stability analysis must be exposed to an environment of 40˚C±2˚C/75% RH±5 % RH for 6 months. As per the standard protocol, the samples must be analyzed at 0, 1, 2, 3- and 6- month time points. Accelerated stability studies were performed for the final optimized buccal mucoadhesive patches formulation F7 for 1 month. Samples were analyzed and reported.

RESULTS AND DISCUSSION: The present work aimed to achieve optimized formulations for Clindamycin hydrochloride and curcumin-loaded buccal patches by determining the effects of some important factors and their interactions during the process of preparation of buccal patches.

Weight Uniformity Test:

TABLE 5: WEIGHT UNIFORMITY OF THE CLINDAMYCIN HCL PATCHES

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8
Weight of patches [mg]	0.020 ±0.002	0.017 ±0.001	0.022 ±0.003	0.025 ±0.001	0.029 ±0.002	0.031 ±0.001	0.035 ±0.001	0.029 ±0.002

n=10

The prepared drug-loaded patches were tested for weight uniformity. The weight was found to be uniform in the prepared batches.

Thickness of the Patches:

TABLE 6: THICKNESS OF THE CLINDAMYCIN HCL PATCHES

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8
Thickness [mm]	0.127± 0.002	0.118± 0.012	0.129± 0.023	0.142± 0.001	0.163± 0.004	0.175± 0.013	0.184± 0.023	0.165± 0.063

n = 3

Drug-loaded mucoadhesive patches were tested for thickness. From the result, it was inferred that F2 has the least thickness whereas F7 has the highest thickness since it contains the highest concentration of polymer in the ratio 90:10 of Clindamycin and Curcumin respectively.

Content Uniformity:

TABLE 7: CONTENT UNIFORMITY OF THE CLINDAMYCIN HCL

Formulationcode	F1	F2	F3	F4	F5	F6	F7	F8
Average of IIItrials (mg)	11.48 ±0.23	11.82± 0.35	12.02± 0.16	11.93± 0.01	11.90± 0.52	11.82± 0.27	11.79± 0.38	11.60± 0.17

n=3

The test for content uniformity was performed, to assure that the drug was equally distributed throughout the formulation.

Percentage Moisture Loss:

TABLE 8: PERCENTAGE MOISTURE LOSS OF THE CLINDAMYCIN HCL PATCHES

Formulationcode	F1	F2	F3	F4	F5	F6	F7	F8
Average of IIITrials (%)	29.33	47.33	36.67	31.67	24.67	22.33	20.00	22.67

n=3

As per the results, F2 has the highest moisture loss while F7 has the lowest moisture loss. As the concentration of polymer increases the loss of moisture decreases.

Surface pH:

TABLE 9: SURFACE PH OF THE CLINDAMYCIN HCL PATCHES

Formulationcode	F1	F2	F3	F4	F5	F6	F7	F8
Average of IIITrials (%)	6.33	6.33	6	6	6	6	6.33	6

n=3

Since all formulations' surface pH fell between 6-7, or close to neutral pH, no irritation was anticipated.

Folding Endurance:

TABLE 10: FOLDING ENDURANCE OF THE CLINDAMYCIN HCL PATCHES

Formulationcode	F1	F2	F3	F4	F5	F6	F7	F8
Average of IIITrials	107.33	105.67	115	125.33	133.33	161.33	181.33	149.67

n=3

Drug-loaded mucoadhesive patches were tested for folding endurance. From the result, it was inferred that the F2 formulation has the least folding endurance whereas the F7 formulation has the highest folding endurance since it contains the highest concentration of polymer.

Determination of Tensile Strength (TS):

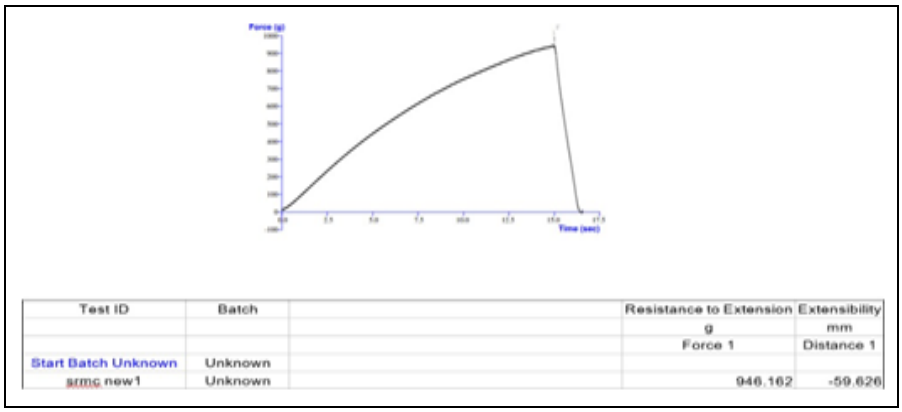


FIG. 5: TENSILE STRENGTH OF CLINDAMYCIN HCL OF F7 FORMULATION

The optimized formulation F7 which has the highest polymer concentration was tested for Tensile strength, and it was found to have a good tensile strength of 946.162g/mm [0.9461 kg/mm^2]

FTIR Spectrum: The obtained IR spectrum of the sample shows all the prominent and primary peaks and confirms the Clindamycin, Curcumin, Hydroxy Ethyl Cellulose, and Polyvinyl Alcohol.

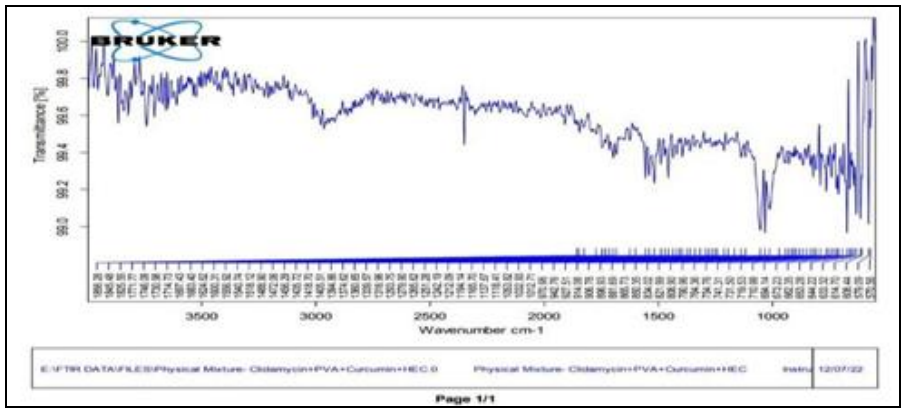


FIG. 6: IR SPECTRUM OF PHYSICAL MIXTURE

Clindamycin HCl and formulation were subjected to IR spectroscopic analysis, to ascertain whether there was any interaction between the drug and polymers used. The IR spectra obtained are given

in the **Fig. 6**. It appears that there is no chemical interaction between the drug and the polymer.

DSC Analysis: To investigate the possible interactions between the drug and polymers used, a differential scanning calorimetric study was carried out. DSC thermogram of the formulation was compared with the pure drug. The DSC thermogram is represented in **Fig. 7**. The pure Clindamycin HCl displayed a sharp endothermic peak at 81.6°C to the melting point of the drug and a similar peak was also observed in the formulation. From the DSC thermograms, it was observed that the decomposition temperature of the pure drug and the formulation remained the same. Hence it can be concluded that there was no significant interaction between the drug and the polymers used.

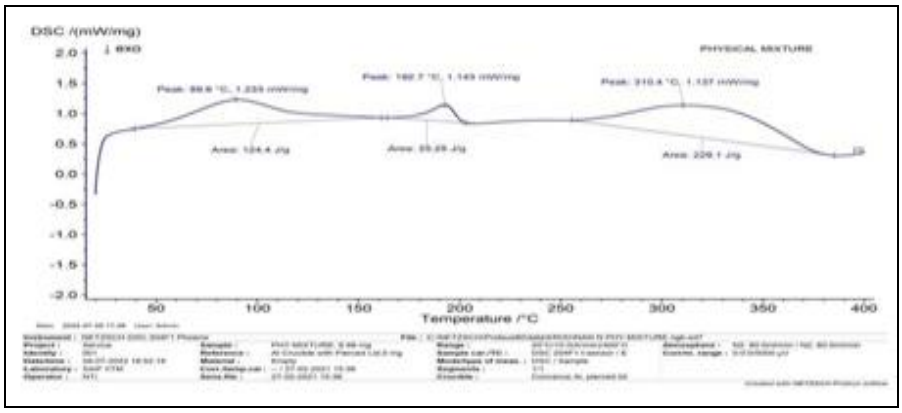
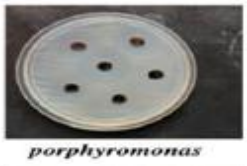
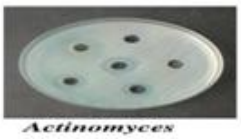


FIG. 7: DSC ANALYSIS OF PHYSICAL MIXTURE

Anti-Bacterial Study:

TABLE 11: ANTI-BACTERIAL STUDY

Si. no.	Test Organism	Initial Microbial Count (CFU/ml)	Initial Count Log 10	Final Count (cfu/ml)	Final Count Log Reduction	Limit	Bacterial Efficacy %
1.	 *porphyromonas*	2132981	6.329	2014	3.02	>4	99.906
2.	 *Streptococcus*	2138611	6.330	2341	2.96	>4	99.891
3.	 *Actinomyces*	2031783	6.308	2241	2.96	>4	99.890
4.	 *Candida albicans*	2368735	6.375	54100	1.64	>4	97.716

From the result obtained from the anti-bacterial study of F7 formulation, it was found that the drugs Clindamycin and Curcumin have the highest Efficacy in the inhibition of oral microorganism species like Porphyromonas, Streptococcus, Actinomyces, Candida albicans and it was found to be an optimized formulation for the buccal route of administration.

***In-vitro* Drug Release Studies:** All formulations were studied *in-vitro* using phosphate buffer pH 7.4.

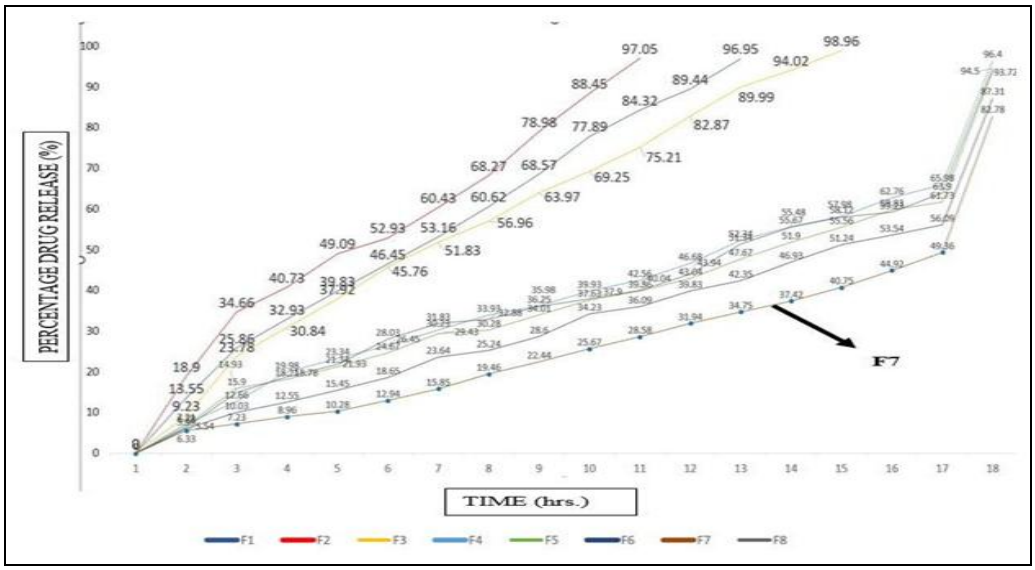


FIG. 8: *IN-VITRO* DRUG RELEASE OF THE FORMULATION F1, F2, F3, F4, F5, F6, F7, F8

From the obtained results, the F1 formulation releases the drug 96.95 at the 6th hour, the F2 formulation releases the drug 97.05 at the 5th hour, and the F3 formulation releases the drug 98.96 at the 7th hour respectively due to the presence of low polymer (PVA and HEC) concentration. In the F4, F5, F6, F7, and F8 formulations the release of the drug was 96.40, 93.72, 87.31, 82.78, 94.50 respectively at the 24th hour because the polymer concentration is increased when compared with the F1-F3 formulations. In the F4 -F8 formulation the F6 and F7 have sustained drug release of drug, as it has the highest concentration of polymer. By increasing the polymer concentration, the drug release was found to be sustained.

***In-vitro* Drug Release Kinetics:**

Formulation No. 7

TABLE 12: KINETICS DATA OF *IN-VITRO* DRUG RELEASE FOR F7

Time in hrs.	log T	The square root of T	Cumulative %drugrelease	Log cumulative %drugrelease	%Drug remaining	Log %drug remaining	Cube rootof drug % remaining
0 min	0	0	0	0	0	0	0
15 min	0.6020	0.3624	3.96	0.5976	96.04	1.9824	4.5794
30 min	0.3010	0.0906	5.54	0.7435	94.46	1.9752	4.5542
45 min	0.1249	0.0156	6.87	0.8369	93.13	1.9690	4.5327
1	0	0	7.23	0.8591	92.77	1.9674	4.5269
1.5	0.1760	0.0309	8.96	0.9523	91.04	1.9592	4.4986
2	0.3010	0.0906	10.28	1.0119	89.72	1.9528	4.4767
2.5	0.3979	0.1583	12.94	1.1119	87.06	1.9398	4.4320
3	0.4771	0.2276	15.85	1.2000	84.15	1.9250	4.3821
3.5	0.5440	0.2959	19.46	1.2891	80.54	1.9060	4.3185
4	0.6020	0.3624	22.44	1.3510	77.56	1.8896	4.2646
4.5	0.6532	0.4266	25.67	1.4094	74.33	1.8711	4.2045
5	0.6989	0.4884	28.58	1.4560	71.42	1.8538	4.1489
5.5	0.7403	0.5480	31.94	1.5043	68.06	1.8328	4.0828
6	0.7781	0.6054	34.75	1.5409	65.25	1.8145	4.0258
6.5	0.8129	0.6608	37.42	1.5731	62.58	1.7964	3.9701
7	0.8450	0.7140	40.75	1.6101	59.25	1.7726	3.8984
7.5	0.8750	0.7656	44.92	1.6524	55.08	1.7409	3.8047
8	0.9030	0.8154	49.36	1.6933	50.64	1.7044	3.6996
24	1.3802	1.9049	82.78	1.9179	17.22	1.2360	2.5823

From the various mathematical models, *in-vitro* kinetics studies were performed for all the formulations. The prepared patches undergo a diffusion mechanism because they follow non-fiction or anomalous transport.

Comparative Kinetics of All the Formulations: The comparative kinetics value for zero-order, first-order, Higuchi, Koresmeyer-peppas, and Hixson-Crowell are shown in the following **Table 11.**

TABLE 13: KINETIC RELEASE STUDY DATA FOR THE FORMULATIONS

Kinetics Model	Parameters	F 7
Zero-order drug release	R^2	0.9937
	K0	0.9035
First-order drug release	R^2	0.9778
	K1	0.9922
Higuchi drug release	R^2	0.0783
	KH	0.3087
Koresmeyer- Peppas drug release	R^2	0.9577
	Kkp	0.7757
Hixson-Crowell drug release	R^2	0.9837
	KHC	0.9837

From the various mathematical models, in-vitro kinetics studies were performed for all the formulations. They were subjected to various release kinetics such as Zero order, first order, Higuchi, Koresmeyer-Peppas, and Hixson-Crowell.

Here the R^2 value was found to be highest in First order, hence it follows First order kinetics type of drug release mechanism.

Stability Studies:
Test Results for Accelerated Stability Study:

Storage Condition: Room Temperature

Organoleptic Properties: For 4 weeks

TABLE 14: ORGANOLEPTIC PROPERTIES

1.	Color of Patch	Yellow color and Transparent
2.	Visual Appearance	No visual change
3.	Microbial growth	None
4.	Odor	Odorless

Stability studies were carried out on optimized formulation F7 for 1 month. The comparison of the parameters before and after stability studies is represented in **Table 15.**

TABLE 15: COMPARISON OF PARAMETERS BEFORE AND AFTER STABILITY STUDIES

Parameters	Before stability studies	After stability studies
Appearance	Yellow-colored Buccal Mucoadhesive Patch	Buccal Mucoadhesive Patch
Drug Content	94.5	93.8

CONCLUSION: The Muco-adhesive buccal patch is a unique technology for the controlled release of drugs in the buccal cavity for the treatment of periodontitis, which produces maximum therapeutic efficacy with potential reduction in the side effects.

The buccal patch was developed with the aim of Clindamycin and the curcumin-loaded patch would provide sustained drug release with improved therapeutic activity it is believed to reduce the side effects, improve stability, and produce a flexible formulation. Many studies have concluded that the muco-adhesive patch drug delivery system is non-irritating for application. Hence the muco-adhesive patch loaded with Clindamycin and Curcumin may lead to a better treatment when compared to the conventional therapy, so, the developed muco-adhesive patch would be a potential formulation for the treatment of Periodontitis.

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