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FORMULATION AND EVALUATION OF PERIODONTAL FILMS CONTAINING LEAF EXTRACT OF *PSIDIUM GUAJAVA* FOR TREATING PERIODONTITIS

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Keywords:

Periodontal film, Periodontitis, Chitosan, HPMC, Methanolic extract, *Psidium guajava* leaf

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ABSTRACT: The aim of this study was to investigate the antibacterial activity of *Psidium guajava* leaf extract in periodontal film for inserting in periodontal pockets. The study was performed by formulating bioerodible periodontal film containing *Psidium guajava* leaf extract by simple solvent casting method using two different polymers namely natural chitosan and semi synthetic HPMC. The formulated periodontal films were then cross linked with 2 % v/v glutaraldehyde for 3 hours for extending the release of drug. The periodontal films were evaluated for various physico-chemical parameters. The cumulative percentage drug release was found to be higher for periodontal film prepared with chitosan polymer. The results from the *in-vitro* release studies of *Psidium guajava* leaf extract from different batches of periodontal film have shown that the release followed zero order release kinetics for the batch F_4. The results of release data for batch F_4 fits well in Higuchi model, suggesting diffusion mechanism of drug release. The research findings have concluded that both chitosan and HPMC could be used for preparing periodontal film for extending the release of drugs.

INTRODUCTION: The Periodontal diseases are due to localization of inflammatory response to infection of periodontal pockets due to the accumulation of sub gingival plaque. These inflammatory responsesen compass several pathological conditions that affect the structures supporting thetooth. Periodontitis is a disease caused by specific groups of microorganismslike *Streptococcus mutans, Lactobacilli, Porphyromonas gingivalis, Enterococcus feacalis, Actinomycetes* and *Candida albicans*, which adheres to the tooth surface.

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The local delivery of antimicrobials to periodontal pockets can be initiated by using fibers, films, microparticles and gels prepared with biodegradable or non-biodegradable polymers [1]. Medicinal plants are used for maintaining oral hygiene for more than thousands of years.

The advantage of using medicinal plants is to reduce allergies and side effects, which otherwise can occur from synthetic chemicals. Most of the herbal drugs used in oral cavity are alkaline in nature having high antibacterial activity. These herbs help to maintain the acid-alkaline balance of saliva and there by decrease the formation of plaque/calculus, which help in preventing periodontal diseases [2]. In the present study we have tried to formulate a dental implants using natural antibacterial agent derived from the dried leaves extract of *Psidium guajava* belonging to family

Myrtaceae [3]. Many scientific article have reported that leaves, stems, and fruits of the plant *Psidium guajava* have a variety of pharmacological action such as antibacterial, antioxidant, hepatoprotective, antigenotoxic, antiplasmodial, anti-allergy, antispasmodic, antimicrobial, cardioactive, cytotoxic, antidiabetic, antitussive, anti inflammatory activity [4]. Soxhlet extraction method was adopted for preparing the *Psidum guajava* leaf extract [5].

The antimicrobial activity shown by plants belonging to family Myrtaceae are due to its high content of essential oils and phenolic compounds. Four antibacterial compounds have been isolated from the leaves of guava (*Psidium guajava* L.). Two new flavonoid glycosides namely morin-3-O - alpha-L-lyxopyranoside, morin – 3 – O – alpha - L-arabopyranoside, and two known flavonoids namely guaijavarin and quercetin were identified from this plant [6]. The methanolic extracts of *Psidium guajava* have shown *in-vitro* antibacterial effects on the growth of microorganism. The *Psidium guajava* leaf extract dose required in periodontal film was based on their minimum inhibitory concentration (MIC). The MIC value of *Psidium guajava* leaf extract against *S. mutans* was found to be 70 µg/ml.

MATERIALS AND METHODS: *Psidium guajava* leaf was collected from local area of Mukkam, Kerala, India; Chitosan was obtained as a gift sample from Central Institute of Fisheries Technology, Cochin, India; Hydroxy propy methyl cellulose K4M purchased from Yarrow chem product, Mumbai, India; Poly ethylene glycol 400 purchased from Nice Chemicals, Cochin, India; Gluteraldehyde biological grade from Sigma Chemical Company, USA and Glycerol purchased from Spectrum Reagent and Chemical Pvt, Ltd Edayar, India; Methanol was procured from E-Merck Limited, Mumbai, India.

Collection and Authentification of the Plant: The plant *Psidium guajava* (Family: Myrtaceae) was selected for the study and was collected from local area of Mukkam, Kozhikode District, Kerala State, India. The collected plant was authenticated from Calicut University, Herbarium and a voucher specimen (No: 88473) was deposited at the University of Calicut herbarium.

Preparation of Extract by Soxhlation: Dried leaf powder (25g) was packed in Whatmaan filter paper and Soxhleted in 150ml Petrolium ether at 55^{o}C for 2 hrs for defatting. The dried defatted leaf powder was again packed in Whatmaan filter paper and placed in flask and Soxhleted in 150 ml methanol at 65^{o}C for 12 hrs. The above processes were repeated for remaining quantity of dried leaf powder. The methanolic extract obtained for each batch were mixed and left for evaporation and stored in airtight container until use [8].

Preformulation Studies:

Determination of λ_{max}: The *Psidium guajava* leaf extract was dissolved in 5 ml of methanol and further diluted withphosphate buffer of p^{H} 6.6. Maximum absorbance for the extractwas measured in UV double beam spectrophotometer (Parkin Elmer λ 25) in wavelength ranging from 200 to 600 nm by using phosphate buffer pH 6.6 as blank [9].

MIC Determination: The MIC determine of the leaf extract against different organism was carried out in duplicate. To a microtitre plates, 100µl of Nutrient Broth (NB), Brain Heart Infusion Broth (BHIB) containing 0.5% serum was added respectively for *E. coli* and *S. mutan.* Test solution containing 2000 µg of extract was diluted in double quantity and 100 µl of the diluted extract was added to each well. Microtitre plates were then wrapped with aluminum foil. Microtitre plate inoculated with *E. coli* was incubated at 37°C for 24 hours and microtitre plate inoculated with *S. mutans* was incubated at 37°C for 48 hours. Experiments were repeated with standard drug ciprofloxacin 15 µg/0.1ml concentration. Positive control for *E. coli* and *S. mutan* were prepared by inoculating the organisms in 100 µl in nutrient broth and brain heart infusion broth respectively. Sterile broths were maintained as negative controls.

After 48 hours of incubation, 50µl resazurin dye was added to all wells in microtitre plates followed by incubation at 37°C for 60 minutes. The plates were then observed for color change from blue to pink or colorless. The lowest concentration of the extract, which inhibits the growth of microorganism, was indicated by no color change and the value was taken as MIC for the study [10].

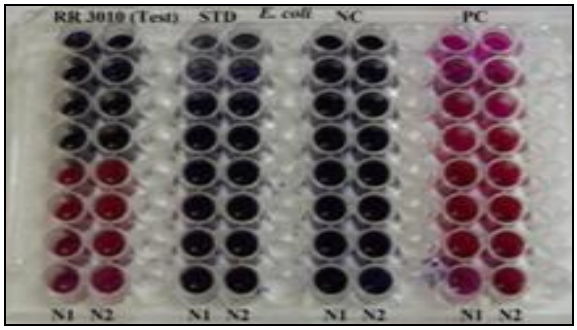

FIG. 1: IMAGE OF MICRO WELL PLATE FOR DETERMINATION OF MIC USING *E. COLI*

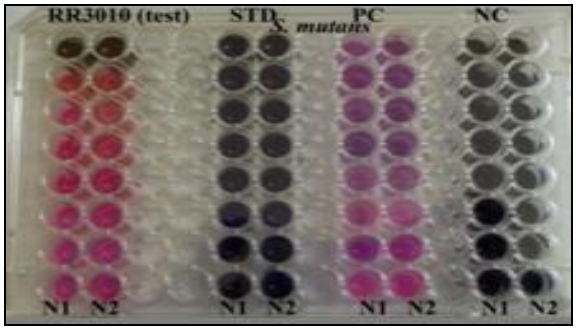

FIG. 2: IMAGE OF MICRO WELL PLATE FOR DETERMINATION OF MIC USING *S. MUTANS*

Drug - Excipient Compatibility Study: The drug (*Psidium guajava* leaf extract) - polymer interaction study was carried out in FT-IR (Shimadzu Japan IR Affinity - 1) spectroscopy. The IR spectrum for combined drug and polymer was taken in FTIR spectrophotometer and the spectrum was compared with the individual spectra for drug and checked for any possible interactions [11].

Formulation of *Psidium guajava* Leaf Extract Loaded Cross-linked Periodontal Films [12]: The periodontal films were prepared with two different polymers namely chitosan and Hydroxy Propyl Methyl Cellulose (HPMC) and with two types of plasticizers namely poly ethylene glycol and glycerol. The polymeric solutions were prepared by dispersing 1.5 g and 2 g of chitosanin 100 ml of 1% v/v acetic acid and 5ml water was used for dispersing 400 mg & 500 mg of HPMC. To the polymer solution corresponding plasticizers (PEG 600/glycerol) were added and mixed on a magnetic stirrer using a beaker. The solution was poured on to a clean labeled glass mould of 7 cm diameter and the solvent was made to evaporate slowly by inverting a glass funnel at room temperature (30°C) for 48 hrs. After drying the films were cut into strip of 7×2 mm^2 wrapped in aluminum foil and stored in a desiccator at room temperature in a dark place for further evaluation studies. Different periodontal films were prepared as per the ingredients mentioned in **Table 1** for getting different batches named as F_1 to F_8.

The periodontal film batches (F1 to F8) were cross-linked by 2% v/v glutaraldehyde solution. The film formed were exposed to vapors of 2 %v/v glutaraldehyde solution on a chromatographic chamber for 3 hours and then dried. After drying the film were wrapped in aluminum foil and stored in desiccators.

TABLE 1: COMPOSITION OF PERIODONTAL FILM CONTAINING *PSIDIUM GUAJAVA* LEAF EXTRACT

Formulation code	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Guava leaf extract (mg)	280	280	280	280	280	280	280	280
Chitosan (% w/v)	1.5	1.5	2	2	-	-	-	-
HPMC K_4M (mg)	-	-	-	-	400	400	500	500
PEG 600 (ml)	0.1	0.05	0.1	0.05	0.1	-	0.1	-
Glycerol (ml)	0.05	-	0.05	-	-	0.1	-	0.1
Alcohol (ml)	7	7	7	7	7	7	7	7
Gluteraldehye (%v/v)	2	2	2	2	2	2	2	2

Evaluation of Periodontal Film of *Psidium guajava* Leaf Extract [11, 13-15]:

Thickness Uniformity: The Uniformity of film thickness were measured by using digital screw gauge (Mitutoyo) at different areas of film and the average was calculated.

Uniformity in Weight of Films: The weight variation test for each periodontal film batches F_1 to F_8were carried out by weighing 3 films (each film having dimensions of 7 × 2 mm^2) which was cut from different places for the same formulation and their individual weight was determined by using the digital balance. The mean value was calculated.

Estimation of Percentage Moisture Loss: The Percentage moisture loss was determined by keeping the films (7 x 2 mm^2) on a desiccator containing anhydrous calcium chloride. After 3 days, the films were taken out and re-weighed.

The percentage moisture loss was calculated by using the following formula,

$$\% \text{ Moisture loss} = (IW - FW) / IW \times 100$$

IW = Initial weight, FW = Final weight.

Estimation of Percentage Moisture Absorption: The percentage moisture absorption was carried out by keeping the film of size (7 x 2 mm^2) on adesiccator containing 100ml of saturated solution of aluminum chloride which was maintained at 79.5%. The films were taken out after three days and weight was noted. The percentage moisture absorption was calculated by using the formula.

$$\% \text{ Moisture Absorption} = (FW - IW) / IW \times 100$$

IW = Initial weight, FW = Final weight.

Folding Endurance Studies: The folding endurance for the periodontal films was determined by repeatedly folding the film at the same place until it breaks, and the test is considered satisfactory to reveal good film properties. This test was repeated for all the batches for six times.

Surface pH: The surface pH of periodontal film was determined for investigating the possible side effects due to change in pH at the site of application. The acidic or alkaline pH of the periodontal film may cause irritation to periodontal mucosa. The periodontal films to be tested are placed on a Petri dish and 0.5 ml of distilled water was added to moisten the film. The film was kept for 1 hour and the pH was measured using pH meter. The averages of three values for each formulation were taken.

Percentage Swelling: The Swelling Index for the films was performed in simulated salivary fluid of P^H 6.6. The periodontal film batches (7 x 2 mm^2) were weighed and placed on stainless steel wire sieve. The mesh containing the film was submerged into 15 ml of simulated salivary medium. The stainless-steel mesh containing the film were then removed at definite time intervals by carefully wiping with absorbent tissue and reweighed. Increase in weight of the film was determined at each time interval until a constant weight was obtained. The degree of swelling was calculated by using formula:

$$S.I = (W_T - W_0) / W_0 \times 100$$

S.I = Swelling Index, W_T= weight of film at time t

W_0= weight of the film at time 0.

Drug Content Uniformity: The drug loaded periodontal film (7×2mm^2) were cut from different areas of film & placed on a 10ml volumetric flask. The film portion were then dissolved in 5 ml of 1% (v/v) acetic acid for film prepared with chitosan polymer and for film prepared with HPMC was dissolved in 5 ml of ethanol-water mixture of 1:1 ratio.

The volumetric flasks containing dissolved film were made up to 10 ml with respective solvents (1% (v/v) acetic acid for the film prepared with chitosan polymer & ethanol-water mixture of 1:1 ratio for the film prepared with HPMC polymer). 1 ml was pipetted out from volumetric flask and diluted with 1 ml of phosphate buffer Ph 6.6. The resulting solution absorbances were measured at 380nm.

***In-vitro* Drug Release Studies:** The *in-vitro* drug release was carried out by placing periodontal film in a 1 ml of phosphate buffer pH 6.6 at room temperature for 24 hrs. A set of six batches of film of known weight and dimension was used for the study.1.0 ml of phosphate buffer pH 6.6 were removed and replaced with 1.0 ml of fresh phosphate buffer pH 6.6.

The concentration of drug was determined by UV/VIS spectrophotometer (Parkin Elmer) at 380 nm after diluting with 1.0 ml of phosphate buffer Ph 6.6. The procedure was repeated for 5 consecutive days for all the formulations.

***In-vitro* Antibacterial Studies:** The prepared periodontal films were tested for antibacterial activity using agar diffusion on Mueller Hinton Agar media. The media was sterilized by autoclave at 121°C at 15 lbs pressure for 15 minutes.

The molten agar was allowed to cool at 45°C and 20ml of Mueller Hinton agar and poured aseptically into Petri plates. The agar was allowed to set until it solidified. Agar test plates for each test organism were prepared. The test organism was spread by using sterile swabs onto the Mueller Hinton agar plates.

The wells were punctured in the centre by using a sterile cork borer. The wells were filled with *Psidium guajava* leaf extract. The plates were incubated at 37°C for 24 hrs. After incubation the plates were observed for the zone of inhibition. The zones were measured using zone measuring scale.

Stability Studies: The stability of the entire drug loaded polymer films were carried out at different temperatures. The films having size (7 × 2 mm^2) were weighed and grouped in to three sets (18 films in each set). The films were wrapped individually in butter paper and again wrapped on a aluminum foil and placed on petridishes. The petridish were stored at different temperatures like 25 ± 2°C (room temperature), 2–8 ±2°C (refrigerator temperature), 40±2°C (oven temperature) for a period of 30 days. The periodontal films were observed for changes in physical forms, like color, appearance, flexibility, or texture, and drug content at an interval of 10 days.

Kinetic Data Analysis: The data obtained from *in-vitro* release studies of best formulations chosen were fitted to various models such as zero order, first order, Higuchi and Korsmeyer Peppa's to obtain the kinetic modeling of drug release.

RESULTS & DISCUSSION:

Determination of λ_{max}: Theλ_{max} of the *Psidium guajava* leaf extract was found to be 370 nm.

Determination of MIC: The MIC values of *Psidium guajava* leaf extract against *E. coli* and *S. mutans* was found to be 25 µg/ml and 70 µg/ml respectively. That shows in **Fig. 1** & **2.**

FTIR Study: The FTIR spectra for the pure extract and the extract in combination with periodontal film were found to be similar indicating no interactions between leaf extract and polymer indicated in **Fig. 3-5.**

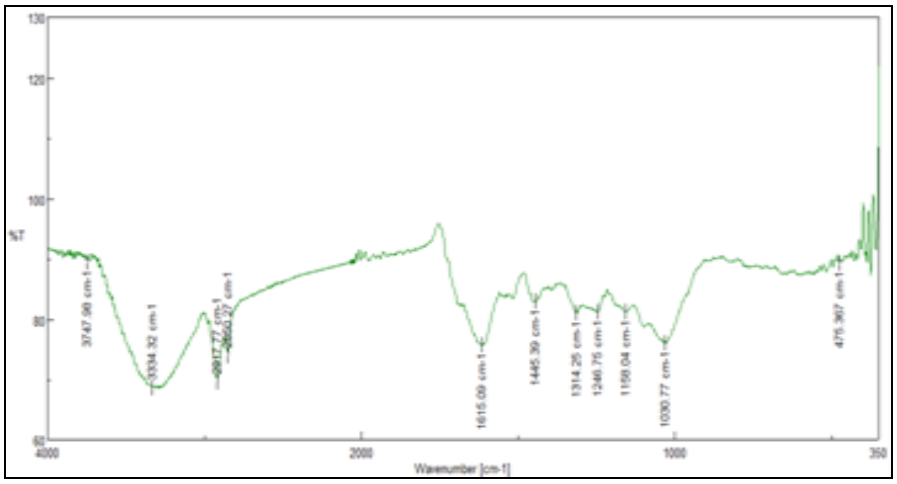

FIG. 3: FTIR OF *PSIDIUM GUAJAVA* LEAF EXTRACT

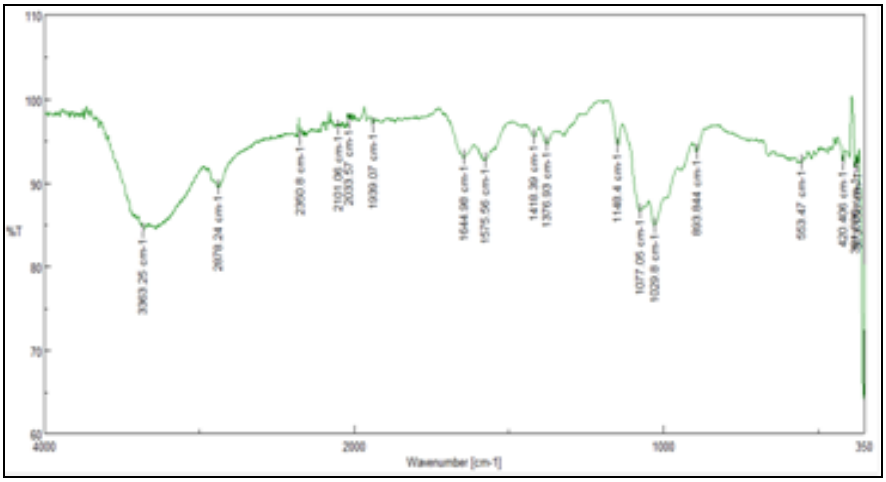

FIG. 4: FTIR OF *PSIDIUM GUAJAVA* LEAF EXTRACT IN PERIODONTAL FILM PREPARED WITH CHITOSAN POLYMER

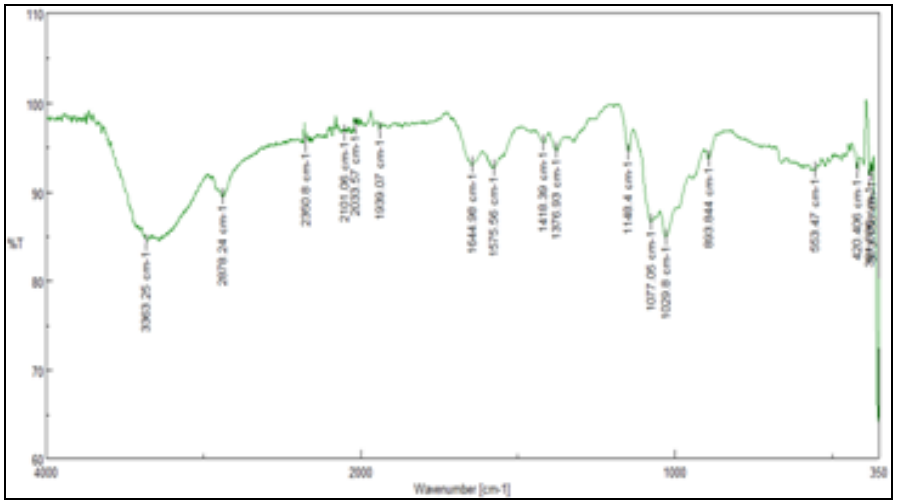

FIG. 5: FTIR OF *PSIDIUM GUAJAVA* LEAF EXTRACT IN PERIODONTAL FILM PREPARED WITH HPMC POLYMER

Evaluation of Periodontal Film:

Thickness: The thickness of the periodontal film were evaluated by using a screw gauge and found to be almost uniform for each formulation included in **Table 2**.

Uniformity of Weight: Drug loaded periodontal film ($7\times2mm^2$) was tested for uniformity in weight and the results have shown that the periodontal films have uniform weight, that mentioned in **Table 2.**

Percentage Moisture Loss: The percentage moisture loss for drug loaded periodontal films was found to decrease from 6.61 to 3.15 % for the batches F_1 to F_4 prepared with chitosan polymer and for the film prepared with HPMC polymer was found to be 10.3 to 7.33 % for the batches F_6-F_7. The percentage moisture loss from periodontal film was found to decrease with increase in polymer concentration shown in **Table 2**.

Percentage Moisture Absorption: The percentage moisture absorption for the periodontal films was carried out and the results have shown that percentage moisture absorption was in range from 1.78 to 2.06% for films prepared with chitosan polymer and 3.84% to 7.3% for film prepared with HPMC polymer. Percentage moisture absorption was found to increase with increase in polymer concentration shown in **Table 2**.

Folding Endurance of the Film: The folding endurance for the periodontal film was estimated and the result have shown that for all films folding endurance was found to have a value>100 folding, indicating that all batches of periodontal film have ideal film properties. The folding endurance was found to be greater for periodontal films prepared with chitosan, when compared with HPMC indicated in **Table 2.**

Surface pH: Surface pH for the periodontal film for batches F_1 to F_4 prepared with chitosan polymer was found to be in range 5.9 to 6.4 and for the film batches F_5 to F_8 prepared with HPMC polymer was 6.6 to 6.1. The surface PH for all the films was found to be neutral and does not cause any irritation when applied to periodontal pocket indicated in **Table 2**.

Percentage Swelling: The swelling index for all periodontal films was calculated and found to be 22.8, 21.3, 24.3,23.3 % for batches F_1, F_2, F_3, F_4 respectively and 29.3, 27.3, 32.3, 30.4% for F_5, F_6, F_7, F_8 respectively **Table 2**. The swelling percentage was found to increase with increase in concentration of polymer. The swelling behavior was found to be greater for film prepared with HPMC polymer shown in **Table 2**.

Drug Content Uniformity: The percentage drug content of periodontal films for all batch was determined. The result have shown that drug content was in range from 70.16%to 79.33% **Table 2.** The percentage drug content in periodontal films was found to be more in F_2 and F_4.

The periodontal film batches were ranked in order $F_4>F_2>F_1>F_3>F_5>F_6>F_7>F_8$. The periodontal film formulated was found to have uniform drug content

with minimum batch to batch variability included in **Table 2**.

***In -vitro* Drug Release:** The *in-vitro* release of drug from periodontal film was analysed, and the release of the drug from film was found to be better for the batch F_4 and poor release for batch F_7. The cumulative percentage drug release was higher for periodontal film made with chitosan polymer. This may be due to hydrophilic polymers, which get degraded easily from saliva and gingival crevicular fluid (GCF).

The current study has shown that the cross linked formulation F_4 & F_2 prepared with chitosan was found to be a better formulations for delivering the maximum drug release into the periodontal pockets in 5 days. The best formulation was found to be F_4 which showed the highest cumulative percentage drug release of 74.10% in 5 days shown in **Fig 6 & 7**.

***In-vitro* Antibacterial Study:** *In-vitro* antibacterial activity was carried out against *S. mutans* and *E. coli* organisms. The results have shown that the formulated periodontal film named batch F_4 containing *Psidium guajava* leaf extract have retained the antibacterial activity. The study also revealed that same antibacterial activity was observed for pure *Psidium guajava* leaf extract and the periodontal film containing *Psidium guajava* leaf extract shown in **Table 4**.

Stability Studies: The stability studies for periodontal film (F_4) containing *Psidium guajava* leaf extract was carried out and the results have shown that, no significant changes were observed with respect to physical and chemical characteristics of periodontal films. The results have shown that the formulated periodontal film was physically and chemically stable. The film could retain the pharmaceutical properties for different environmental conditions over a period of 1 month indicated in **Table 5**.

Release Kinetics: The release kinetics data have indicated that release of drug from periodontal films batch F_4- which follows zero order release kinetics, had the correlation coefficient values higher in zero order equation. The release rate was found to be independent of the concentration of the drug.

The selected formulation also best fit with Higuchi model release kinetics. The release mechanism was also studied by using Korsmeyer–Peppa's model and found that the release mechanism of drug from periodontal film followed anomalous transport or non-Fickian diffusion shown in **Table 6.**

TABLE 2: AVERAGE VALUES OF VARIOUS PHYSICO-CHEMICAL PROPERTIES OF PERIODONTAL FILMS

Film code	Mean ± SD							
	Thikness mm	Uniformity of Weight mg	Percentage Moisture Loss %	Percentage Moisture Absorption %	Folding Endurance of the Film	Surface pH	Swelling Percentage %	Drug Content Uniformity %
F_1	0.063 ± 0.0057	0.963 ± 0.0252	6.61 ± 0.0964	1.78 ± 0.0351	205 ± 4.041	5.9 ± 0.1528	22.8 ± 0.5568	74.17 ± 0.0557
F_2	0.063 ± 0.0153	0.813 ± 0.0252	5.12 ± 0.0586	1.30 ± 0.0451	215 ± 3.000	6.2 ± 0.100	21.3 ± 0.6028	76.50 ± 0.0600
F_3	0.063 ± 0.0100	1.960 ± 0.1730	4.37 ± 0.0493	2.32 ± 0.0379	224 ± 2.646	6.4 ± 0.1732	24.3 ± 0.2950	72.20 ± 0.7209
F_4	0.063 ± 0.0100	1.857 ± 0.1739	3.15 ± 0.0500	2.06 ± 0.0503	232 ± 0.578	6.4 ± 0.2646	23.3 ± 0.4509	79.33 ± 0.1905
F_5	0.100 ± 0.0100	0.967 ± 0.0513	9.29 ± 0.0200	3.84 ± 0.0379	145 ± 2.646	6.6 ± 0.1732	29.3 ± 0.2252	71.73 ± 0.0557
F_6	0.117 ± 0.0058	0.977 ± 0.047	10.3 ± 0.0800	5.02 ± 0.0361	114 ± 3.055	6.5 ± 0.1528	27.3 ± 0.1572	71.33 ± 0.1100
F_7	0.090 ± 0.0100	1.890 ± 0.0551	7.33 ± 0.0513	6.94 ± 0.0666	159 ± 1.527	6.4 ± 0.5196	32.3 ± 0.4509	70.95 ± 0.0557
F_8	0.103 ± 0.0153	2.090 ± 0.0608	8.16 ± 0.0568	7.30 ± 0.0200	154 ± 2.646	6.1 ± 0.2082	30.4 ± 0.3786	70.16 ± 0.0458

TABLE 3: CUMULATIVE % DRUG RELEASE OF *PSIDIUM GUAJAVA* LEAF EXTRACT FROM DIFFERENT FORMULATIONS

Time (Days)	% Cumulative Drug Release							
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	31.84	43.65	37.28	46.54	48.41	52.74	49.41	44.00
2	45.87	48.70	43.52	52.78	54.75	61.87	55.87	56.98
3	51.60	54.20	54.89	61.35	63.31	66.28	59.65	62.12
4	59.26	62.91	60.10	66.85	-	-	-	-
5	65.71	71.51	69.63	74.10	-	-	-	-

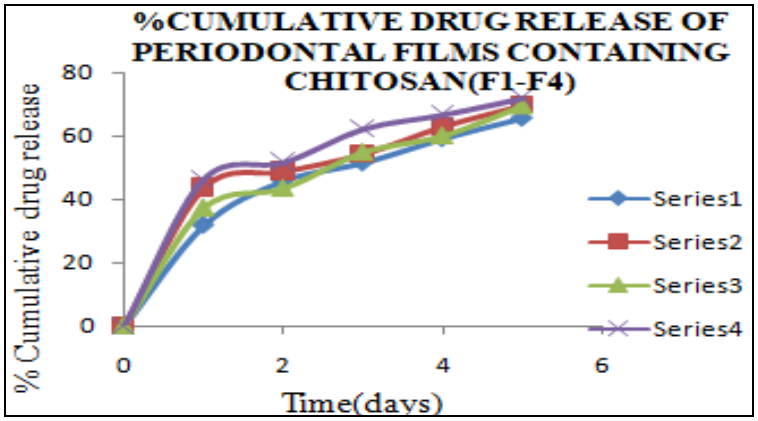

FIG. 6: COMPARISON OF *IN-VITRO* % CUMULATIVE RELEASE PROFILE OF PERIODONTAL FILMS BATCHES F_1-F_4

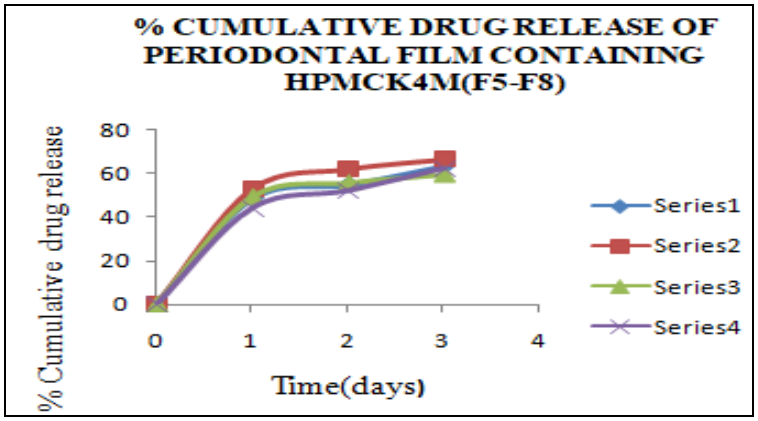

FIG. 7: COMPARISON OF *IN-VITRO* % CUMULATIVE RELEASE PROFILE OF PERIODONTAL FILMS BATCHES F_5-F_8

TABLE 4: MEASUREMENT OF ZONE OF INHIBITION USING *E. COLI* AND *S. MUTANS*

Organism	Sample	Zone of inhibition (mm)
E. coli	Methanolic extract of *Psidium guajava*	18
	Dental film F_4	14
S. mutans	Methanolic extract of *Psidium guajava*	15
	Dental filmF_4	12

TABLE 5: STABILITY STUDY DATA OF PERIODONTAL FILM

Temperature	Evaluation Parameters	Observation (Days)			
		0	10	20	30
25 ± 2°C	Physical appearance	Light yellowish brown colour	No change	No change	No change
	Drug content (%)	79.33	79.30	79.30	79.30
2–8 ±2°C	Physical appearance	Light yellowish brown colour	No change	No change	No change
	Drug content (%)	79.33	79.30	79.30	79.30
40±2°C	Physical appearance	Light yellowish brown colour	No change	No change	No change
	Drug content (%)	79.33	79.25	77.10	74.35

TABLE 6: REGRESSION CO-EFFICIENT (R^2) VALUES OF KINETIC MODELS FOR FORMULATION F

Formulation code	R^2 Values			
	Zero order	First order	Higuchi model	Hixson-Crowell model
F_4	0.996	0.916	0.985	0.954

CONCLUSION: In the present study we tried to load *Psidium guajava* leaf extract in two different biodegradable polymers namely natural Chitosan and semi synthetic HPMC for use in periodontal infections for enhancing the bioavailability of the drug. The periodontal films were further cross-linked with glutaraldehyde 2% and aimed to extent and control the drug release for a greater number of days. The FT-IR spectra have revealed that, there was no interaction between the polymer and the

drug. The polymer used was compatible with the drug. Evaluation parameters like thickness, percentage moisture loss, percentage moisture absorption, folding endurance have indicated that the films were mechanically stable. Weight variation and drug content uniformity was found to be uniform for all the films.

The *in-vitro* release studies of herbal extract from periodontal films was carried out in phosphate buffer solution, pH 6.6 and have shown that the extend of drug release was found to continue for 5 days from periodontal film prepared with chitosan polymer and 3 days for periodontal film prepared with HPMC polymer.

The average amount of drug released per day was found to be above the minimum inhibitory concentration of herbal extract (70 µg /ml). The *in-vitro* release studies have shown that the films remained intact without much degradation. The results of *in-vitro* drug release have suggested that the natural polymer chitosan was found to be better suited for treating periodontitis for extending the drug release from periodontal films.

The periodontal film batch F_4 showed satisfactory results. The Stability studies for all the periodontal batches were carried out and the results have shown that the periodontal film batch F_4 was found to be stable at different environmental condition. The kinetic studies were carried out for the selected batch $F_4$and the results have shown that the release followed zero order release kinetics.

The release kinetics for the selected batch best fit in Higuchi's model. The release of drug content from the film followed diffusion rate-controlled mechanism. The release mechanism using Korsmeyer-Peppa's model has revealed that release of drug from periodontal film follow non-Fickian diffusion. The study results have suggested the use of natural polymers for extending the drug release from periodontal films.

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