

**FORMULATION AND EVALUATION OF *PUNICA GRANATUM* L.
PEEL EXTRACT AND *CURCUMA LONGA* L. EXTRACT CO-LOADED
MUCOADHESIVE GINGIVAL PATCH FOR LOCALIZED
PERIODONTITIS THERAPY**

***¹Gowthamraj S., ²Manivannan R., ³Nagarjun S., ⁴Naveenkumar V., ⁵Rajesh R.,
⁶Rameshkanna M., ⁷Ranjith M.**

India.

Article Received on 03 Sept. 2026,
Article Revised on 23 Sept. 2026,
Article Published on 01 October 2026,

<https://doi.org/10.5281/zenodo.23037959>

***Corresponding Author**

Gowthamraj S.

India.



How to cite this Article: *¹Gowthamraj S.,
²Manivannan R., ³Nagarjun S., ⁴Naveenkumar
V., ⁵Rajesh R., ⁶Rameshkanna M., ⁷Ranjith M.
(2026). Formulation and evaluation of punica
granatum l. Peel Extract and Curcuma longa l.
Extract Co-Loaded Mucoadhesive Gingival
Patch For Localized Periodontitis Therapy.
World Journal of Pharmaceutical Research,
15(19), 449–465.

This work is licensed under Creative Commons
Attribution 4.0 International license.

ABSTRACT

Periodontitis is a chronic inflammatory disease associated with periodontal pathogens such as *Porphyromonas gingivalis*. The present study aimed to formulate and evaluate a mucoadhesive gingival patch containing *Punica granatum* L. peel extract and *Curcuma longa* L. extract for localized periodontal therapy. The herbal extracts were selected for their potential antimicrobial, antioxidant and anti-inflammatory properties. *Punica granatum* peel extract was prepared by Soxhlet extraction, while *Curcuma longa* extract was prepared by maceration. Three formulations (F1, F2 and F3) were prepared using the solvent-casting method with chitosan, HPMC K15M and PEG 400. The prepared patches were evaluated for physicochemical, mechanical, mucoadhesive and drug-release properties. Among the formulations, F3 showed the highest drug content of 98.53

± 0.73%. F3 also demonstrated a controlled and sustained in-vitro release profile. The optimized F3 formulation was evaluated for antibacterial activity against *P. gingivalis*. F3 showed a zone of inhibition of 20.6 ± 0.8 mm compared with 24.8 ± 0.6 mm for chlorhexidine. The antibacterial activity may be attributed to phenolics, flavonoids, tannins and curcuminoids present in the extracts.

Overall, the developed herbal gingival patch demonstrated promising localized and sustained delivery characteristics. Therefore, F3 may serve as a promising herbal mucoadhesive system for localized periodontal therapy.

KEYWORDS: Periodontitis; *Punica granatum*; *Curcuma longa*; Pomegranate peel extract.

INTRODUCTION

Herbal medicine (HM) is an important component of complementary and alternative medicine, which in recent times has gained widespread popularity worldwide and is gradually moving toward integration into mainstream healthcare systems. Herbal medicine include preparations of biologically active natural products that consist largely of herbs or herbal materials. Herbal medicine, also known as phytotherapy or botanical medicine, is the use of plants and plant-derived products to prevent, manage, and treat diseases. It is one of the oldest forms of healthcare and has been practiced for thousands of years in civilizations such as India, China, Egypt, and Greece. According to the World Health Organization (WHO). Herbal medicine is defined as the use of medicinal plants or plant-derived materials for therapeutic purposes to prevent, diagnose, or treat diseases.

The term "periodontal disease" refers to a collection of long-term inflammatory disorders that gradually erode the gingiva, periodontal ligaments, root cementum, and alveolar bone that support teeth. Anaerobic gram-negative bacteria that cause localized infections are the main cause of these diseases. Gingivitis and periodontitis are the two primary classifications made by the American Association of Periodontology. Inflammatory periodontitis is an infected tissue disease. The hallmark of periodontitis is host-mediated, microbially-associated inflammation that causes loss of periodontal attachment. Gum, alveolar process mucosa, alveolar bone, periodontium, and root cementum are examples of the tissues that surround teeth.

The periodontium facilitates the connection to the bone, maintains the tooth, and guards against oral microbiota. The inflammatory process causes alveolar bone and connective tissue to disappear, which results in pathological tooth movement and a loss of bone support. Periodontal disease is the leading cause of tooth loss worldwide and a significant public health concern. The phrase "periodontal disease" refers to a broad range of pathological diseases that impact the tissues that support the teeth. Eliminating or reducing the pathogenic

microorganisms that cause periodontal disease and addressing the detrimental environmental and behavioral factors are essential to the success of periodontal therapy.

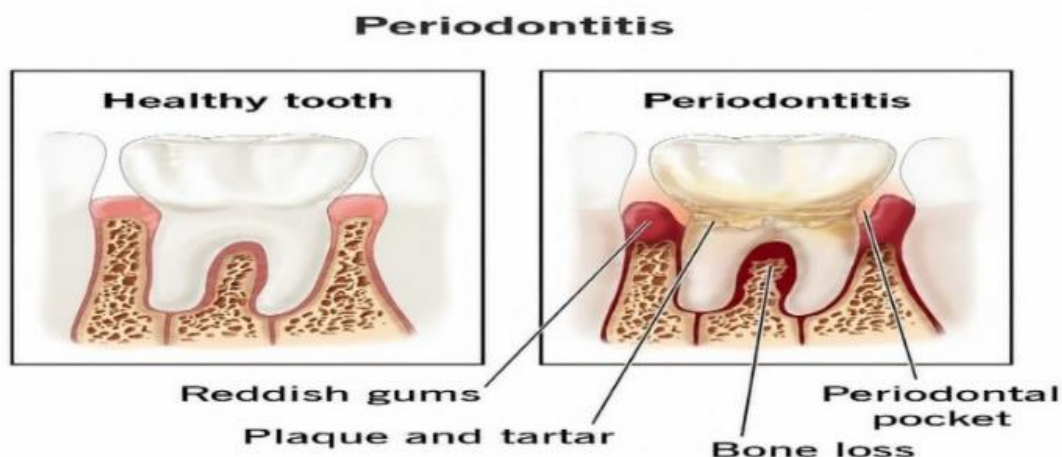


Fig. 1: Periodontitis.

CLASSIFICATION OF PERIODONTITIS

There are three types of periodontitis:

1. Necrotizing periodontitis
 - a. Necrotizing gingivitis
 - b. Necrotizing periodontitis
 - c. Necrotizing stomatitis
2. Periodontitis as a manifestation of Systemic Disease
3. Periodontitis.

PORPHYROMONAS GINGIVALIS (*P. gingivalis*)

A gram-negative anaerobic bacterium found in the oral cavity, *Porphyromonas gingivalis* is a member of the black-pigment *Bacteroides* group. On the blood agar plate, these bacteria grow into dark brown colonies. One major contributor to periodontal disease is *P. gingivalis*. Numerous extracellular virulence factors and proteases, such as lipopolysaccharides (LPS), pili, collagenase, homolysing, endotoxins, fatty acids, ammonia, hydrogen sulfide, and indol, are produced by these bacteria and cause gingival tissue to be destroyed. The different elements on *P. gingivalis*'s surface facilitate the bacteria's easy interaction with external media and aid in its growth, colonization, absorption of nutrients, and development of a biofilm that shields it from the immune system. The pathogenesis of *P. gingivalis* has been seen in a

number of animal models, including cellular models, mice, rabbits, and *Drosophila*, indicating a complicated process of host interaction with *P. gingivalis* at the level of periodontal disease. Genetic and environmental variables also affect the pathogenic process.

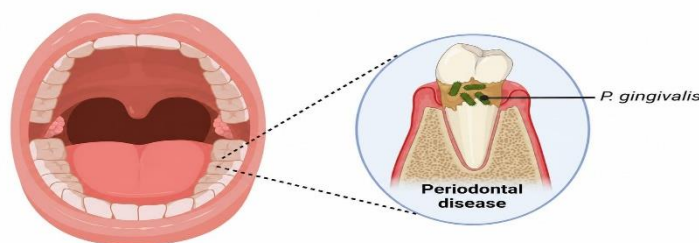


Fig. 2: Schematic representation of periodontal disease.

AIM

The main aim of the present study is to formulate, characterize, and evaluate a *Punica granatum* L peel extract and curcumin co-loaded mucoadhesive gingival patch for the localized treatment of periodontitis. The study aims to develop a safe, effective, and sustained drug delivery system capable of delivering herbal bioactive compounds directly to the periodontal pocket, thereby enhancing anti-inflammatory, antimicrobial, antioxidant, and wound-healing effects while minimizing systemic side effects and improving patient compliance.

OBJECTIVES

1. To prepare the peel extract of *Punica granatum* L. using a suitable extraction method and perform preliminary phytochemical screening.
2. To formulate *Punica granatum* L. peel extract and *Curcuma longa* L. co-loaded mucoadhesive gingival patches using suitable biocompatible polymers.
3. To optimize the formulation for suitable physical and mucoadhesive properties.
4. To evaluate the prepared patches for appearance, thickness, weight variation, folding endurance, tensile strength and percentage elongation.
5. To evaluate the surface pH, moisture content, moisture uptake and swelling index of the prepared patches.

The mucoadhesive patch was prepared using pomegranate peel extract and turmeric extract as herbal active ingredients. HPMC K15 and chitosan were used as film-forming and

mucoadhesive polymers, while PEG 400 was added as a plasticizer to improve flexibility and mechanical strength. The herbal extracts provide antibacterial, antioxidant and anti-inflammatory properties beneficial for periodontal therapy.

EXTRACTION

The extraction is a scientific method of separation, isolation, and recovery of valuable chemical compounds or active principles from plant materials or any other source through the utilization of an appropriate solvent. It is a method of breaking down the cell structure of the plant material in such a way that valuable chemical compounds such as oil, pigments, alkaloids, flavonoids, tannins, and other active principles can be extracted using a solvent.

EXTRACTION OF *PUNICA GRANATUM* L:

Fresh *Punica granatum* L. fruits were collected, and the peels were separated, washed with distilled water, and shade-dried at room temperature for 7–10 days. The dried peels were powdered using a mechanical grinder and sieved to obtain uniform particle size. About 75 g of the powder was packed into a cellulose thimble and subjected to Soxhlet extraction using 750 mL of 70% ethanol at 70–80°C for 6–8 hours. Extraction was continued until the siphon solvent became nearly colourless, indicating complete extraction.



Fig 3: *Punica granatum* L Extraction.

EXTRACTION OF *CURCUMA LONGA* L

Fresh *Curcuma longa* L. rhizomes were collected, washed thoroughly with distilled water, cut into small pieces, and shade-dried at room temperature for 7–10 days. The dried rhizomes were coarsely powdered and passed through a suitable sieve to obtain uniform particle size. About 30 g of the powdered material was transferred into a clean, dry container and macerated with 300

mL of 70% ethanol for 72 hours at room temperature, with occasional stirring to facilitate extraction. After maceration, the mixture was filtered through suitable filter paper to separate the marc from the extract. The filtrate was collected and concentrated under reduced pressure using a rotary evaporator at a controlled temperature to obtain the *Curcuma longa* L. extract.



Fig. 4: *Curcuma longa* L Extraction.

PREPARATION OF MUCOADHESIVE GINGIVAL PATCH: FORMULATION TABLE

The mucoadhesive gingival patches containing *Punica granatum* L. peel extract and *Curcuma longa* L. extract were prepared by the solvent casting method using chitosan and HPMC K15M as mucoadhesive polymers. PEG 400 was incorporated as a plasticizer. Three different formulations, namely F1, F2 and F3, were prepared by varying the concentrations of the herbal extracts and HPMC K15M while maintaining the concentration of chitosan and PEG 400 constant.

TABLE 1: FORMULATION TABLE OF MUCOADHESIVE GINGIVAL PATCH.

S.NO	INGREDIENTS	F1	F2	F3
1	<i>Punica granatum</i> L Peel Extract	600mg	800mg	1g
2	<i>Curcuma longa</i> L Extract	200mg	300mg	400mg
3	Chitosan	800mg	800mg	800mg
4	HPMC K15M	1.2g	1.5g	1.8g
5	PEG 400	400mg	400mg	400mg
6	Acetic Acid	4ml	4ml	4ml
7	Distilled Water	q.s. to 40ml	q.s. to 40ml	q.s. to 40ml

PREPARATION OF POLYMER SOLUTION

The required quantity of HPMC K15M was dispersed in distilled water with continuous stirring until a uniform solution was obtained. Chitosan (800 mg) was dissolved in 4 mL acetic acid solution and stirred until homogeneous. Both polymer solutions were then mixed thoroughly.



Fig. 5: *Preparation of polymer solution with using magnetic stirrer.*

PREPARATION OF DRUG SOLUTION

The required quantities of Punica granatum L. peel extract and Curcuma longa L. extract were accurately weighed and separately dissolved or dispersed in a suitable solvent. Both preparations were mixed to obtain a uniform drug mixture.

ADDITION OF PLASTICIZER

PEG 400 was added slowly to the polymeric solution with continuous stirring to improve the flexibility and elasticity of the patch.



Fig. 6: *Addition of plasticizer solution with using magnetic stirrer.*

INCORPORATION OF DRUG

The prepared herbal drug mixture was slowly added to the polymer-plasticizer solution and stirred continuously until a homogeneous mixture was obtained.



Fig. 7: Addition of drug solution with plasticizer.

HOMOGENIZATION OF FORMULATION

The formulation was continuously stirred to obtain a uniform casting solution and visually checked for lumps and air bubbles.

REMOVAL OF ENTRAPPED AIR

The casting solution was kept undisturbed to allow entrapped air bubbles to escape and obtain a smooth patch.

CASTING OF MUCOADHESIVE GINGIVAL PATCH

The homogeneous solution was poured into a clean, dry and levelled Petri plate and spread uniformly to obtain a patch of uniform thickness.



Fig. 8: Casting of Mucoadhesive Gingival Patch.

DRYING

The cast patch was dried under controlled conditions until a uniform, flexible and non-sticky film was obtained. The dried film was then carefully removed from the Petri plate.

CUTTING AND STORAGE

The dried film was cut into uniformly sized gingival patches. The patches were individually wrapped in aluminium foil and stored in a dry, protected condition until further evaluation.

EVALUATION OF MUCOADHESIVE GINGIVAL PATCH**PHYSICAL APPEARANCE**

The prepared patches were visually examined for colour, smoothness, flexibility, uniformity, cracks, air bubbles and other physical defects.

THICKNESS

The thickness of the patches was measured at different points using a digital micrometer, and the mean value was calculated.

WEIGHT VARIATION

Three patches were individually weighed using a digital balance, and the mean weight and standard deviation were determined.

FOLDING ENDURANCE

The patch was repeatedly folded at the same point until cracking or breaking occurred. The number of folds was recorded as folding endurance.

TENSILE STRENGTH

A patch strip was fixed between the clamps of a tensile strength apparatus and subjected to increasing force until breakage. Tensile strength was calculated from the breaking force and cross-sectional area.

PERCENTAGE ELONGATION

The initial and final lengths of the patch were measured during the tensile strength test. Percentage elongation was calculated using the change in length relative to the initial length.

SURFACE pH

The patch was moistened with a small quantity of distilled water and equilibrated. The surface pH was measured using a calibrated pH meter to assess its suitability for gingival application.

MOISTURE CONTENT

The patches were weighed before and after drying in a desiccator to constant weight. Percentage moisture content was calculated from the weight difference.

IN-VITRO DRUG RELEASE

The in-vitro release of *Punica granatum* L. peel extract and *Curcuma longa* L. extract was studied using a Franz diffusion cell at $37 \pm 0.5^\circ\text{C}$. Samples were withdrawn at predetermined intervals and analysed to determine cumulative drug release.

ANTIBACTERIAL ACTIVITY

The antibacterial activity of the optimized patch was evaluated against *Porphyromonas gingivalis* by the agar diffusion method. A blank patch was used as negative control and chlorhexidine as standard. The zone of inhibition was measured in mm.

RESULT AND DISCUSSION

EXTRACTION OF *PUNICA GRANATUM* L. PEEL:

The ethanolic extract of *Punica granatum* L. peel was prepared by Soxhlet extraction using 70% ethanol. From 75 g of powdered peel, 7.8 g of extract was obtained with a percentage yield of 10.4% w/w.

TABLE 2: PERCENTAGE YIELD OF *PUNICA GRANATUM* L PEEL EXTRACT.

S.NO	Weight of powdered <i>Punica granatum</i> L peel (g)	Weight of dried extract obtained(g)	Percentage yield
1	75g	7.8g	10.4%w/w

EXTRACTION OF *CURCUMA LONGA* L.

The ethanolic extract of *Curcuma longa* L. was prepared by maceration using 70% ethanol. From 30 g of powdered material, 1.4 g of extract was obtained with a percentage yield of 4.67% w/w.

TABLE 3: PERCENTAGE YIELD OF *CURCUMA LONGA* L PEEL EXTRACT.

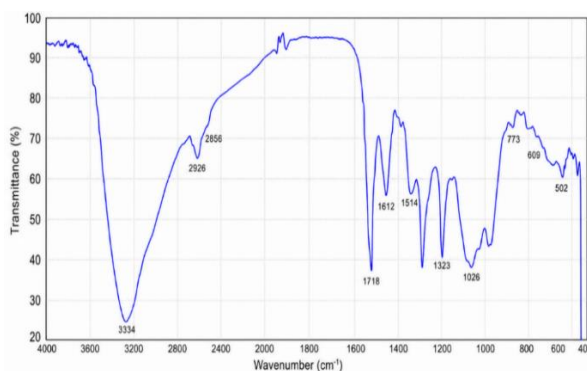
S.NO	Weight of powdered <i>Curcuma longa</i> L (g)	Weight of dried extract obtained(g)	Percentage yield
1	30g	1.4g	4.67%w/w

PRE-FORMULATION STUDIES

Punica granatum L. peel extract was dark reddish-brown, semisolid and slightly astringent in odour. It was soluble in ethanol and methanol and slightly soluble in water, with a melting point of 110°C. *Curcuma longa* L. extract was yellowish-orange, semisolid and slightly characteristic in odour. It was soluble in ethanol and methanol and slightly soluble in water, with a melting point of 96°C.

FTIR COMPATIBILITY STUDY

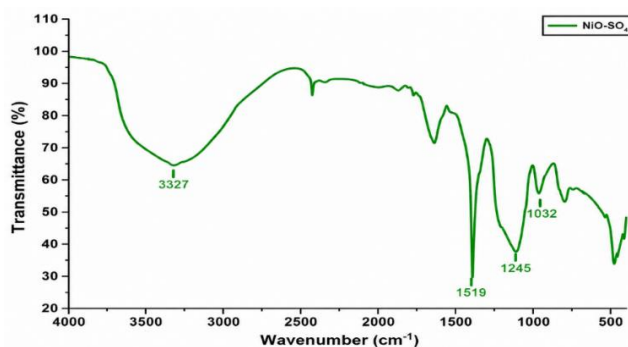
FTIR studies were conducted in order to confirm compatibility between the extract and excipients. Incompatibility can be detected by finding the shift or alteration of peaks. Hence extract, excipient and their mixture were subjected to FTIR studies. The obtained peaks were interpreted as shown in figure.

**Fig. 9: FTIR spectrum of *Punica granatum* L peel extract Table.****TABLE 4: FTIR INTERPRETATION OF *PUNICA GRANATUM* L PEEL EXTRACT.**

Observed Peak (cm ⁻¹)	Functional Group
3334	O–H stretching
2926	C–H stretching
1718	C=O stretching
1612	C=C aromatic stretching
1323	O–H deformation / C–O stretching
1026	C–O–C / C–O stretching

TABLE 5: FTIR INTERPRETATION OF *CURCUMA LONGA* L PEEL EXTRACT.

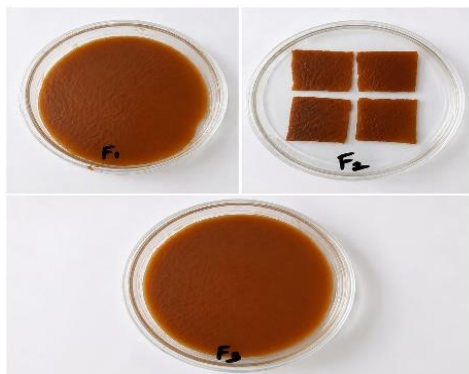
Observed Peak (cm ⁻¹)	Functional Group
3327	O–H stretching
1519	C=C aromatic skeletal vibration
1245	C–O stretching
1032	C–O–C / C–O stretching

**Fig 10: FTIR spectrum of *Curcuma longa* L extract Table.**

PRELIMINARY PHYTOCHEMICAL SCREENING

The phytochemical screening of *Punica granatum* L. peel extract showed the presence of phenols, flavonoids, tannins, saponins and terpenoids. *Curcuma longa* L. extract showed tannins, phenols, flavonoids, saponins and alkaloids.

FORMULATION AND EVALUATION OF MUCOADHESIVE GINGIVAL PATCH

**Fig 11: Mucoadhesive gingival patches.**

Three formulations (F1–F3) were successfully prepared by the solvent-casting method. The patches showed smooth and uniform surfaces without visible cracks or air bubbles. The patches were brown to dark brown due to incorporation of the herbal extracts. The formulations showed acceptable weight, thickness, moisture content, surface pH, folding endurance, tensile strength and percentage elongation. Overall, the patches demonstrated satisfactory physical and mechanical properties.

TABLE 6: EVALUATION OF MUCOADHESIVE GINGIVAL PATCHES.

Formulation	Weight (mg)	Thickness (mm)	Moisture Content (%)	Surface pH	Folding Endurance (folds)	Tensile Strength (MPa)	Percentage Elongation (%)
F1	168.4 ± 2.6	0.22 ± 0.01	5.12 ± 0.18	6.48 ± 0.04	214 ± 5	1.52 ± 0.05	25.6 ± 1.0
F2	172.6 ± 2.8	0.27 ± 0.01	4.68 ± 0.16	6.55 ± 0.03	236 ± 6	1.78 ± 0.04	28.9 ± 0.
F3	176.8 ± 2.4	0.31 ± 0.02	4.32 ± 0.14	6.61 ± 0.04	258 ± 7	2.05 ± 0.05	32.4 ± 1.1

DRUG CONTENT UNIFORMITY**TABLE 7: DRUG CONTENT UNIFORMITY OF MUCOADHESIVE GINGIVAL PATCHES.**

Formulation code	Drug content (%)
F1	96.12 ± 0.91
F2	97.46 ± 0.84
F3	98.53 ± 0.73

The drug content of F1, F2 and F3 was 96.12 ± 0.91%, 97.46 ± 0.84% and 98.53 ± 0.73%, respectively. F3 showed the highest drug content with good uniformity.

IN VITRO DRUG RELEASE

The formulations showed gradual and controlled release of the herbal extracts. F3 demonstrated a comparatively sustained release profile, reaching 98.5% release at 8 hours, indicating its potential for prolonged local drug availability.

**Fig. 12: Franz Diffusion Cell.****TABLE 8: IN-VITRO DRUG RELEASE OF MUCOADHESIVE PATCH.**

Time (hr)	F1 (%)	F2 (%)	F3 (%)
0.5	14.8	12.6	10.9
1	27.5	24.3	21.6
2	42.8	39.1	35.7

3	57.6	53.4	49.2
4	57.6	66.5	61.8
5	81.9	82.6	72.9
6	89.7	88.4	85.6
7	94.6	92.8	93.7
8	96.1	97.4	98.5

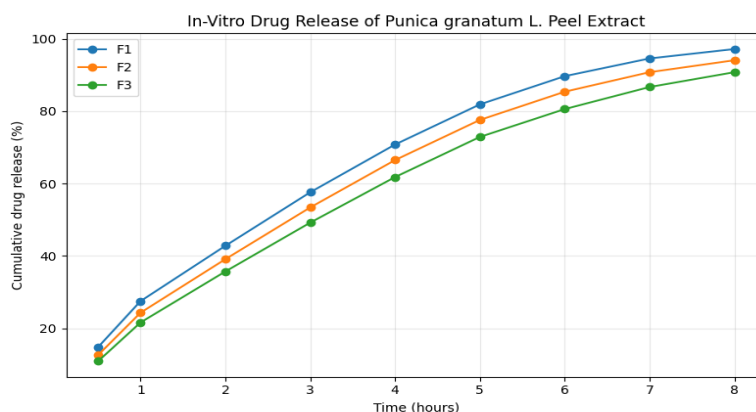


Fig 13: *in-vitro* drug release of mucoadhesive patch.

IN-VITRO ANTIBACTERIAL ACTIVITY

The *In-vitro* Antibacterial activity of the optimized F3 *Punica granatum* L. peel extract and *Curcuma longa* L. rhizome extract co-loaded mucoadhesive gingival patch was evaluated against *Porphyromonas gingivalis* by the agar diffusion method. A blank gingival patch was used as the negative control, while chlorhexidine was used as the standard antibacterial agent. The diameter of the zone of inhibition was measured in millimetres after incubation.

The optimized F3 formulation was evaluated against *Porphyromonas gingivalis*. F3 produced a zone of inhibition of 20.6 ± 0.8 mm, compared with 24.8 ± 0.6 mm for chlorhexidine. The blank patch showed no inhibition, confirming that the antibacterial activity was mainly due to the incorporated herbal extracts.



Fig. 14: In-vitro Antibacterial activity of optimized F3 mucoadhesive gingival patch against *Porphyromonas gingivalis*.

CONCLUSION

The present study successfully demonstrated the development of a mucoadhesive gingival patch containing *Punica granatum* L. peel extract and *Curcuma longa* L. extract for potential localized treatment of periodontitis. The prepared formulations showed satisfactory physical, physicochemical and mechanical properties with good drug content uniformity. Among F1, F2 and F3, the F3 formulation was selected as the optimized formulation due to its highest drug content of $98.53 \pm 0.73\%$ and comparatively controlled and sustained drug release. The optimized F3 formulation also exhibited promising antibacterial activity against *Porphyromonas gingivalis*. The developed herbal mucoadhesive patch may provide prolonged residence at the gingival site and localized delivery of the herbal bioactive constituents. Thus, the formulation shows potential as a promising herbal approach for localized periodontal therapy. Further stability and in-vivo studies are required to establish its long-term safety and therapeutic effectiveness.

BIBLIOGRAPHY

1. Murai H, Kuboniwa M, Kakiuchi M, Matsumura R, Hirata Y, Amano A. Curcumin inhibits growth of *Porphyromonas gingivalis* by arrest of bacterial dipeptidyl peptidase activity. *Journal of oral microbiology*, 2024 Dec 31; 16(1): 2373040.
2. Muhammad GM. ANTIBACTERIAL EFFECTS OF POMEGRANATE EXTRACT (ELLAGIC ACID) ON SOME CLINICALLY ISOLATED PERIODONTAL PATHOGENS IN VITRO STUDY (Doctoral dissertation, Baghdad University).

3. Gościński A, Paczkowska-Walendowska M, Skotnicka A, Ruchała MA, Cielecka-Piontek J. Can plant materials be valuable in the treatment of periodontal diseases? Practical review. *Pharmaceutics*, 2021 Dec 17; 13(12): 2185.
4. Bhutkar KG. Formulation and evaluation of Mucoadhesive herbal buccal patch of *Psidium guajava* L.
5. Shaikh R, Singh TR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. *Journal of pharmacy and Bioallied Sciences*, 2011 Jan; 3(1): 89.
6. Builders PF. Introductory chapter: Introduction to herbal medicine. *Herbal medicine*, 2018 Nov 5: 1-9.
7. Adhikari SN, Nayak BS, Nayak AK, Mohanty B. Formulation and evaluation of buccal patches for delivery of atenolol. *Aaps Pharmscitech*, 2010 Sep; 11(3): 1038-44.
8. Mussa FH. Development and evaluation of muco-adhesive buccal films containing metronidazole for the treatment of periodontal diseases. *Mediterranean Journal of Pharmacy and Pharmaceutical Sciences*, 2025 Nov 7; 5(4): 47-57.
9. Ramadhani Y, Rahmasari RR, Prajnasari KN, Alhakim MM, Aljunaid M, Al-Sharani HM, Tantiana T, Juliastuti WS, Ridwan RD, Diyatri I. A mucoadhesive gingival patch with Epigallocatechin-3-gallate green tea (*Camellia sinensis*) as an alternative adjunct therapy for periodontal disease: A narrative review. *Dent J.*, 2022 Jun; 55(2): 114-9.
10. Pasupuleti MK, Nagate RR, Alqahtani SM, Penmetsa GS, Gottumukkala SN, Ramesh KS. Role of medicinal herbs in periodontal therapy: a systematic review. *Journal of International Society of Preventive & Community Dentistry*, 2023 Feb 27; 13(1): 9.
11. Komal A, Ahmed N, Usman Khan M, Hilal F, Ijaz Khan M, Rehman AU. Novel elastic nanovesicular hydrogel system: advancing metronidazole delivery for effective periodontitis management. *Drug Development and Industrial Pharmacy*, 2026 Apr 3; 52(4): 667-83.
12. Gunupati S, Biradavolu S, Nitin P, Kalyani T. *Punica granatum* (Pomegranate) A Potential Herbal Medicine in Treating Periodontal Disease in the Modern World of Dentistry. *Pharmacological Studies in Natural Oral Care*, 2023 Oct 3: 435-51.
13. Kaur N, Nirmala SL, Kumar H. A review on study of buccal patches: current status of formulation and evaluation methods. *Journal of Drug Delivery & Therapeutics*, 2014 May 15; 4(3): 69-79.
14. Alnasrawy A, AL-khafaji Y, Altmimy F, Alnasrawy M. Isolation, characterization and estimation of ellagic acid activity against *Porphyromonas gingivalis* isolated from adult

- periodontitis patients in Kerbala City. *Karbala Journal of Pharmaceutical Sciences*, 2015; 6: 16-29.
15. Schwach-Abdellaoui K, Vivien-Castoni N, Gurny R. Local delivery of antimicrobial agents for the treatment of periodontal diseases. *Eur J Pharm Biopharm* 2000; 50: 83-99.
 16. Marc Quirynen, Win Teughels, Marc De Soete, Daniel Van Steenberghe. Topical antiseptics and antibiotics in the initial therapy of chronic adult periodontitis: Microbiological aspects. *Periodontology*, 2002; 28: 7-90.
 17. Daneshmand, Jorgensen MG, Nowzari H, Morrison JL, Slots J. Initial effect of controlled release Chlorhexidine of subgingival microorganisms. *J Periodontal Res.*, 2002; 37: 375-379.
 18. Nayak Aarati, Ranganath, Soumya B, Bhat Kishore, Mithun. Evaluation of anti bacterial and anticandidal efficacy of aqueous and alcoholic extract of Neem- An Invitro study. *Int J Res Ayur Pharm.*, 2011; 2(1): 230-235.
 19. Stover, E. and Mercure, E.W., The pomegranate: A new look at the fruit of paradise. *Hortscience*, 2007; 42: 1088–1092.
 20. 2. Bhowmik, D., Gopinath, H., Kumar, B.P., Duraivel, S., Aravind, G., Sampath Kumar, K.P., Medicinal uses of *Punica granatum* and its health benefits. *J. Pharmacogn. Phytother.*, 2013; 1: 28–35.
 21. 3. Viuda-Martos, M., Fernández-López, J., Pérez-Álvarez, J.A., Pomegranate and its many functional components as related to human health: A review. *Compr. Rev. Food Sci. Food Saf.*, 2010; 9: 635–654.
 22. 4. Costantini, S., Rusolo, F., De Vito, V., Moccia, S., Picariello, G., Capone, F., Guerriero, E., Castello, G., Volpe, M.G., Potential anti-inflammatory effects of the hydrophilic fraction of pomegranate (*punica granatum* L.) seed oil on breast cancer cell lines. *Molecules*, 2014; 19: 8644–8660.
 23. Colombo, E., Sangiovanni, E., Dell'Agli, M., A review on the anti-inflammatory activity of pomegranate in the gastrointestinal tract. *Evid. Based Complement. Alternat. Med.*, 2013; 247145.
 24. Forouzanfar, F., Afkhami Goli, A., Asadpour, E., Ghorbani, A., Sadeghnia, H.R., Protective effect of *Punica granatum* L. against serum/glucose deprivation-induced PC12 cells injury. *Evid. Based Complement. Alternat. Med.*, 2013; 716730.
 25. Beard, J.R.; Bloom, D.E. Towards a comprehensive public health response to population ageing. *Lancet.*, 2015; 385: 658–661.