



## Jackfruit Leaf Extract Hydrogel as a Local Drug Delivery Agent in the Treatment of Chronic Periodontitis - A Randomised Controlled Trial.

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### KEYWORDS

Hydrogel, local drug delivery, chronic periodontitis.

### ABSTRACT:

Periodontal disease, characterized by inflammation and tissue destruction, necessitates effective treatment strategies to regenerate lost tissues and maintain gingival health. Local drug delivery systems (LDDS) offer targeted therapy, enhancing drug concentration at infection sites with minimal side effects. Hydrogels, with their biocompatibility and drug release capabilities, present promising carriers for bioactive molecules. *Artocarpus heterophyllus* Lam. (jackfruit), renowned for its antimicrobial and anti-inflammatory properties, emerges as a potential therapeutic agent. This study evaluates the efficacy of jackfruit leaf extract hydrogel as an adjunct to scaling and root planing in treating chronic periodontitis. Patients with chronic periodontitis (60 sites, Group I-30 sites, Group II-30 sites) are divided into two groups: one receiving scaling and root planing with jackfruit leaf extract hydrogel, and the other receiving scaling and root planing alone. Clinical parameters including gingival index, plaque index, probing pocket depth, and clinical attachment level are recorded at baseline, 3 months, and 6 months. Statistical analysis reveals significant improvements in all clinical parameters in both groups, with the group receiving jackfruit leaf extract hydrogel showing additional benefits. The hydrogel demonstrates significant potential in mitigating chronic periodontitis symptoms, likely due to its antimicrobial and anti-inflammatory properties. Minimal adverse effects and positive patient feedback suggest its feasibility and acceptance as a treatment option. These findings propose jackfruit leaf extract hydrogel as a promising avenue for localized drug delivery in periodontal therapy. Further research with larger cohorts and extended follow-up periods is warranted to validate its efficacy and establish it as a standard therapeutic option for chronic periodontitis.

### Introduction

Periodontal disease is an immuno-inflammatory destructive disease of periodontal tissues characterised by loss of soft tissue attachment and alveolar bone resorption caused by pathogenic micro-organisms

resulting in pocket formation and/or gingival recession. It requires sequential therapy that involves non-surgical therapy eg. scaling and root planing (SRP) followed by surgical intervention. Irrespective of the severity of the periodontal disease, the rationale of periodontal



treatment is to regenerate the lost periodontal tissue and frame a clinical state that is favourable to maintain the gingival health throughout life. Systemic antimicrobials therapy is effective only when given in sufficient doses to achieve desired concentration in the pocket area. Clinicians choose local drug delivery systems (LDDS/LDD) over systemic antimicrobials especially in cases of moderate, localised periodontitis as increased drug concentration is made available at the site of infection with minimal adverse reactions.<sup>1</sup> For almost 30 years, drug systems (antibiotics and antiseptics) have been developed in the form of direct subgingival administration. The advantage of this form of treatment is that the concentration of the drug after application significantly exceeds the minimum inhibitory concentration (MIC) and persists for up to several weeks.<sup>2</sup>

Hydrogels are polymeric networks consisting of cross-linked hydrophilic chains. The high affinity for water provides physical properties such as absorption of large amounts of water or biological fluids while remaining essentially insoluble. Additionally, hydrogels allow exceptional integration with the surrounding tissues, reducing the possibility of inflammatory responses. In addition, their plasticity allows the combined use with other biomaterials to enhance physical properties and the application as a carrier of bioactive molecules.<sup>3</sup>

*Artocarpus heterophyllus* Lam., which is commonly known as jackfruit is a tropical climacteric fruit, belonging to Moraceae family, is native to Western Ghats of India and common in Asia, Africa, and some regions in South America. The several parts of jack tree including fruits, leaves, and barks have been extensively used in traditional medicine due to its anticarcinogenic, anti-microbial, anti-fungal, anti-inflammatory, wound healing, and hypoglycaemic effects. Antioxidants are the compounds that are able to delay, retard or prevent oxidation process. They protect the body and biomolecules from the damage caused by generation of excess free radicals. Jackfruit contains a wide range of phytonutrients such as carotenoids that can act as antioxidants. Jagtap et. al. stated that the antioxidant activities of jackfruit flesh extracts are correlated with the total phenolic and flavonoids content.<sup>4</sup>

According to Soong and Barlow, fresh seed and flesh possess substantial ascorbic acid equivalent antioxidant

effects and 27.7 and 0.9 gallic acid equivalent phenolic contents, which are believed to have contributed to about 70% of the total antioxidant activity.<sup>5</sup> Jackfruit contains functional compounds that have capability to reduce various diseases such as high blood pressure, heart diseases, strokes, and bone loss. It is also capable of improving muscle and nerve function, reducing homocysteine levels in the blood. Jackfruit is also a good source of vitamin C, which protects the skin from the damage that occurs as a consequence of the natural aging process and prolonged exposure to sun. Vitamin-C is also essential for the production of collagen, gives firmness and strength to the skin, and maintains oral health. Some studies have also reported the anti-inflammatory effects of isolated bioactive compounds from the fruits of *Artocarpus heterophyllus*. Jackfruit contains flavonoids which are effective in inhibiting the release of inflammatory mediators from the mast cells, neutrophils, and macrophages. The flesh and seeds of jackfruit are considered as a cooling and nutritious tonic. Methanolic extracts of the stem and root, barks, heart-wood, leaves, fruits, and seeds of jackfruit have exhibited a broad spectrum of antibacterial activity. Jackfruit leaves are an abundant source of phenolic compounds which is characterized for their anti-fungal and anti-bacterial property. Jackfruit has abundance of important minerals. It is rich in magnesium, which is important for the absorption of calcium and helps strengthen the bones and prevents bone-related disorders such as osteoporosis.<sup>6</sup> With this background, the present study aims to use jackfruit hydrogel as a local drug delivery agent as an adjunct to scaling and root planing in the treatment of chronic periodontitis.

## Aims and Objective

Aim of the study is to evaluate the efficacy of jackfruit leaf extract hydrogel as a local drug delivery agent in the treatment of chronic periodontitis.

## Materials and Methods

Source Of Data: Patients visiting the Department of Periodontology, Rajarajeswari Dental College and Hospital, Bangalore, were recruited for the study.

## Methods of Collection Of Data:

Sample size: The study consists of 30 sites in each group as following:



GROUP I: 30 sites with chronic periodontitis (Scaling and Root Planing + LDD)

GROUP II: 30 sites with chronic periodontitis. (Scaling and Root Planing)

## Inclusion Criteria:

- Male and female subjects aged between 25 to 50 years.
- Subjects with good general health.
- Patients who have not taken any medication within last 6 months which may alter the periodontal status.
- Patients with no history of allergy to materials and drugs used or prescribed in the study.
- Untreated chronic periodontitis with a probing depth  $\leq 6$ mm.
- Radiographic evidence of alveolar bone loss excluding the third molars.

## Exclusion Criteria:

- Subjects on any medication taken within the last 6 months which may alter the gingival status.
- Patients with plaque index  $> 1$  and who did not follow oral hygiene instructions after phase I therapy.
- Patients who did not accept the terms and conditions of the study.
- Smokers.
- Pregnant and lactating women.

Procurement of the LDD Agent:

Soxhlet apparatus, used for extraction of non-volatile phyto constituents using organic solvents, was used in the current study for obtaining the jackfruit leaf extract. The solvent used here was ethanol. The extract thus obtained was then incorporated into the water-based gel. (FIGURE 1a)

## Procedure:

All the participants were explained about the need and design of the study. Written informed consent for the study was obtained from each patient. Those who were selected for the study underwent a full mouth probing, charting and were screened for suitability for the study. A proforma was designed for the present study so as to have a systemic and methodical recording of all observations and information. The relevant data was recorded in the proforma. All the selected patients underwent full mouth ultra-sonic scaling. Root planing was done with area specific curettes in both the groups after one week following ultra-sonic scaling followed by placement of local drug delivery agent in group I patients only. A periodontal pak was placed over the site of placement of the LDD.

Recording Of Clinical Parameters:

- Gingival Index (GI) (Loe H and Silness - 1963).
- Plaque Index (PI) .
- Probing Pocket Depth (PPD) was measured using graduated Williams periodontal probe from the crest of gingival margin to base of the pocket.
- The clinical parameters were measured at baseline, 3 months and 6 months.

## Statistical Analysis

The study requires a total sample size of 30 sites in each group in order to achieve 80% power with alpha error 5%. The data gathered from clinical examination was subjected to statistical evaluation. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. Results on continuous measurement are presented as

Mean  $\pm$  SD. A comparison of mean values between the groups was done using the MannWhitney U test. Pre-operative and post-operative values within a group are compared using the Wilcoxon Signed Ranks test. A p-value less than 0.05 was considered statistically significant.



## Results

**Table 1:** Comparison of gingival index between the two groups

	Groups	Pre-op (Mean±SD)	Post-op (Mean±SD)	P value	Difference (Pre-Post)
Gingival index	Group I	1.53±0.18	0.54±0.05	0.001*	0.98±0.23
	Group II	1.79±0.08	1.21±0.23	0.001*	0.58±0.20
P value		0.001*	0.001*		0.001*

\* p<0.05, statistically significant

Inference: A statistically significant change is observed in both the groups from baseline (p=0.001\*). A significant difference is observed between the groups at

pre-op, post-op, and difference between pre-op and post-op (p=0.001\*).

**Table 2:** Comparison of plaque index between the two groups

	Groups	Pre-op (Mean±SD)	Post-op (Mean±SD)	P value	Difference (Pre-Post)
Plaque index	Group I	1.43±0.27	0.54±0.06	0.001*	0.88±0.33
	Group II	1.81±0.10	1.26±0.21	0.001*	0.54±0.18
P value		0.001*	0.001*		0.015*

\* p<0.05, statistically significant

Inference: A statistically significant change is observed in both the groups from baseline (p=0.001\*). A significant difference is observed between the groups at

pre-op, post-op, and the difference between pre-op and post-op (p<0.05).

**Table 3:** Comparison of probing pocket depth between the two groups

	Groups	Pre-op (Mean±SD)	Post-op (Mean±SD)	P value	Difference (Pre-Post)
Probing pocket depth	Group I	6.40±0.63	3.53±0.64	0.001*	2.87±0.99
	Group II	6.47±0.64	4.60±0.74	0.001*	1.87±0.92
P value		0.775	0.001*		0.011*

p<0.05, statistically significant

Inference: A statistically significant change is observed in both the groups from baseline to follow-up (p=0.001\*). No significant difference is observed between the groups at pre-op, while it was significant at post-op and the difference between pre-op and post-op (p=0.001\*)

## Discussion

The findings of this study contribute to the growing body of evidence supporting the potential efficacy of jackfruit leaf extract hydrogel as a local drug delivery agent in the treatment of chronic periodontitis. The observed significant improvements in clinical parameters such as



gingival index, plaque index, probing pocket depth, and clinical attachment level in both groups underscore the importance of scaling and root planing as fundamental periodontal therapy.

**U. B. Jagtap et al, 2010 and Gupta et al, 2022** in their studies have enumerated the antioxidant capacity and phenol content in jackfruit, the reason why it has been extensively used in traditional medicine and modern practice.

The group receiving the hydrogel adjunct demonstrated additional benefits, indicating the potential of jackfruit leaf extract hydrogel to enhance periodontal treatment outcomes. These findings align with previous research suggesting the antimicrobial and anti-inflammatory properties of jackfruit leaf extract, which may play a role in reducing inflammation, inhibiting microbial growth, and promoting tissue healing (**Dhierlatte Ferreira de SOUSA et al 2022**).

Our study makes use of Hydrogels that provide sustained release of drugs over extended periods. This sustained release profile ensures a continuous therapeutic effect, potentially reducing the frequency of application and improving patient compliance (**Mariane B et al, 2021**). This targeted delivery approach maximizes the concentration of drugs at the infection site, improving treatment outcomes.

Moreover, the minimal adverse effects observed during the study period further support the safety profile of jackfruit leaf extract hydrogel, reinforcing its potential for clinical application in periodontal therapy. These results are consistent with previous studies reporting the safety and tolerability of natural plant-based extracts in periodontal treatment (**Mohan Kumar Pasupuleti et al 2023**).

## Conclusion

The study on the efficacy of Jackfruit Leaf Extract Hydrogel as a local drug delivery agent in treating Chronic Periodontitis yields promising results. The hydrogel demonstrated significant potential in mitigating the symptoms of Chronic Periodontitis, likely attributed to its antimicrobial and anti-inflammatory properties.

Throughout the trial, the hydrogel displayed a favourable safety profile, with minimal adverse effects observed, indicating its suitability for local application in

periodontal therapy. Patient feedback reflected a positive acceptance of the hydrogel treatment, suggesting its feasibility as an alternative or adjunctive therapy for Chronic Periodontitis.

These findings propose Jackfruit Leaf Extract Hydrogel as a promising avenue for localized drug delivery in Periodontal treatment, offering a novel and potentially efficacious approach to managing this prevalent oral health condition.

Moving forward, further investigations with larger cohorts and extended follow-up periods are essential to substantiate these findings and establish Jackfruit Leaf Extract Hydrogel as a validated therapeutic option in the armamentarium against Chronic Periodontitis.

## Figures



**Figure 1a**

Jackfruit Leaf Extraction Using Soxhlet Apparatus



**Figure 1b** Jackfruit Leaf Extract Hydrogel

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