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Original Research Article

Effect of leaf extract of *Carica papaya* gel as local drug delivery in periodontitis subjects

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ABSTRACT

Background: The destruction of tooth supporting structures as a result of an inflammatory host response is the characteristic of periodontitis. Mechanical plaque management techniques like non-surgical periodontal therapy (NSPT) is crucial for preventing these diseases. *Carica papaya* leaves are rich in nutrients and vitamins and possess antibacterial, anti-fungal, properties and can be used as a reasonably safe alternative to synthetic pharmaceuticals. Objectives were to evaluate, compare and correlate the clinical parameters at baseline and 21st day after non-surgical periodontal therapy alone and after placement of *Carica papaya* gel.
Methods: A total of 50 subjects with chronic periodontitis were selected and randomly divided into 2 groups - group A, non-surgical periodontal therapy alone (25), and group B, non-surgical periodontal therapy followed by local drug delivery with *Carica papaya* gel at selected sites (25). Gingival index, plaque index, bleeding on probing, pocket depth, and clinical attachment level were recorded at baseline and 21st day.
Results: A statistical reduction in the clinical parameters was seen in both the groups. But comparatively *Carica papaya* leaf extract gel showed more reduction in BOP, inflammation and probing depth when compared with group A.
Conclusions: *Carica papaya* gel in the form of LDD have demonstrated the efficacy and safety as adjunct products to non-surgical periodontal therapy, with notable improvements in the clinical outcomes which attributed to their anti-inflammatory property. Hence, *Carica papaya* gel can be used as a promising therapeutic agent.

Keywords: Periodontitis, Local drug delivery, Non-surgical periodontal therapy

INTRODUCTION

The conventional description of periodontal disease is the progressive degeneration of the periodontal complex's soft and hard tissues, which can be triggered by dysbiotic microbial populations and deviant immune responses in the gingival and periodontal tissues. When dental plaque builds up near the gingival margin, it triggers an inflammatory reaction that changes microbiology and may exert catastrophic impacts on the periodontium of those who are vulnerable. The harmful effects of periodontitis extend beyond the oral cavity and are linked to various systemic diseases.[1,2]

The key oral pathogens responsible for the onset and advancement of periodontitis, results in visible signs such as the formation of a periodontal pocket which act as perfect environment for bacterial colonization. Proper periodontal maintenance therapy, thorough root surface debridement, patient compliance, and commitment to oral hygiene are all necessary for achievement of long-term success.[3,4]

In addition to scaling and root planning (SRP), adjunctive systemic or local host-modulating agents like local drug delivery system (LDDS) can help in the treatment of periodontal disease with optimal results and lowest risk in pharmacological therapy. LDDs helps in controlling the release of medications that are delivered locally and are recommended as a supplement to periodontal therapy.[5]

The various drug delivery systems include irrigations, fibres, films, injectable, gels, strips, microparticles, and nanoparticle systems in the management of periodontal disease. Gels are cross-linked semisolid systems where the active drug molecules are evenly distributed in a steady-state. Broad port needle syringes are used to gently administer gels containing active therapeutic agents directly into the subgingival periodontal pocket, ensuring an even distribution of the medication.[6,7]

Carica papaya commonly known as papaya belongs to Caricaceae family has been used for a long time to treat a variety of illnesses, including inflammatory conditions. Its ripe fruits, unripe fruits, seeds, leaves, stem and bark possess antibacterial, anti-inflammatory, hypoglycemic, antifertility, hepatoprotective, anti-tumor, anti-hypertensive and wound healing property.[8] Its antibacterial properties are mainly due to the wide range of phytochemicals that are important for nutrition and medicine, such as polysaccharides, vitamins, minerals, enzymes, proteins, alkaloids, glycosides, lectins, and saponins. Natural antioxidants are abundant in its leaves, fruits, and seeds. Moreover, its chemical constituents, such as papain, benzyl isothiocyanate (BiTC), myricetin, rutin, quercetin, α-tocopherol, caffeic acid, and kaempferol, exhibit substantial antioxidant qualities.[9,10]

Several studies have highlighted the promising potential of *Carica papaya* as mouthwash against few Gram positive and Gram negative bacteria. Other than mouthwash form further clinical studies are needed to particularly show the efficacy of leaf extract of *Carica papaya* gel as local drug delivery in periodontitis subjects. Therefore, this study aimed to assess and compare the effect of *Carica papaya* leaf extract gel on various clinical parameters in periodontitis subjects, including plaque scores, gingival scores, periodontal pocket depth, and clinical attachment level.

METHODS

Type of study

It was an original research study.

Study design

A total of 50 subjects with chronic periodontitis aged between 25-60 years, was selected from the outpatient department of Periodontics, P.M.N.M. Dental College and Hospital, Bagalkot. The participants were divided into 2 groups as follows - group A: non-surgical periodontal therapy alone (25), and group B: non-surgical periodontal therapy followed by local drug delivery with *Carica papaya* gel at selected sites (25) (Figure 1).

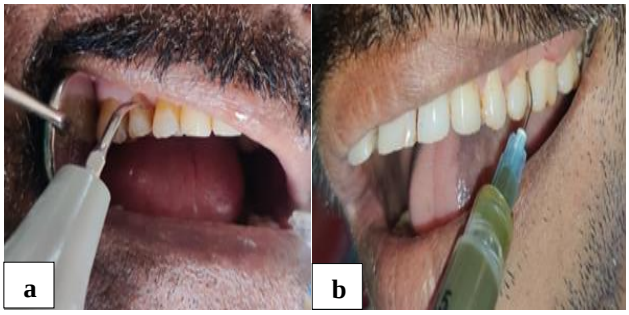

Figure 1 (a and b): Showing group A and B.

Sample size estimation

Keeping alpha error at 5%, power of the study at 90%, the sample size estimated was approximately 16 in each group. For follow-up study, to avoid loss due to attrition we took a total of 50 periodontitis subjects with 25 subjects in each group.

Inclusion criteria

Subject willing to participate in the study and given written consent for the same, patients aged 25-60 years, with periodontitis, patients diagnosed as periodontitis (according to 2017 World Workshop Classification), minimum number of 20 teeth present, patients who have not received any antimicrobial treatment for the past three months were included.

Exclusion criteria

The exclusion criteria of this study were patients with systemic diseases that could influence periodontal conditions, patients who have undergone periodontal therapy in the past 6 months, patients on any medications, subjects consuming tobacco in any form, pregnant and lactating females and subjects allergic to papaya.

Preparation of Carica papaya gel

Fresh papaya leaves were collected, washed, shade dried and then grinded into small particles by mechanical grinder. 100g of powder was mixed with 500ml of ethanol and kept for 7-8 days (cold maceration). Later it was filtered by Whatman filter paper and then kept inside hot air oven under 50^0C and the extract was prepared. The polymer (carbopol 934) was placed in water for 2 hours. Then the solvent which contains the plant extract was added to the polymer and mixed for twenty minutes. PH was adjusted with 98% triethanolamine and 0.03 gms of methyl paraben was added to this mixture as preservative. Then the mixture was allowed to equilibrate for twenty-four hours and the gel was prepared. The preparation of *Carica papaya* gel was carried out at Hanagal Shri

Kumareshwar college of Pharmacy, Bagalkot (Figure 2).[11,12]

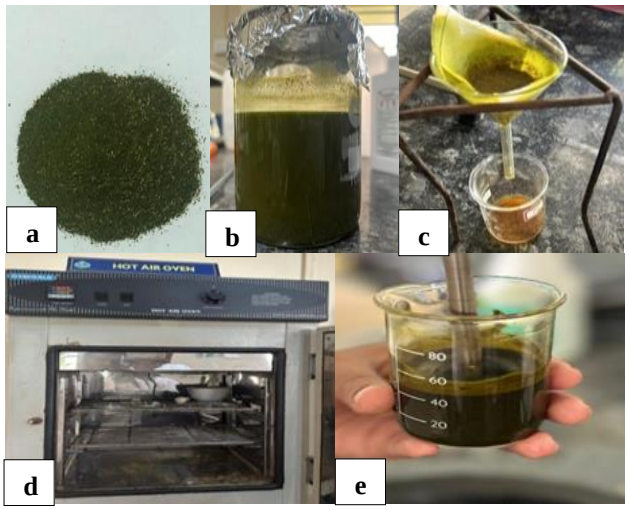

Figure 2: Preparation of carica papaya gel (a) powder, (b) maceration, (c) filtration, (d) evaporation, and € gel.

Clinical examination to assess the periodontal condition

Clinical examination was performed on all the subjects using gingival index, plaque index, bleeding on probing, pocket probing depth (PPD) and clinical attachment loss (CAL).

All the subjects undergone scaling on the day of examination. Gel prepared from *Carica papaya* leaf extract was placed subgingivally as local drug delivery agent into periodontal pocket in group B subjects by using 23-gauge blunt needle with 45-degree angulation. Clinical parameters were recorded on the day of examination and 21 days after gel placement.

The data collected was analysed using Chi-square test, independent t test or Mann-Whitney U test, dependent t test or Wilcoxon matched pairs, Karl Pearson's correlation or Spearman's rank correlation coefficient. All the participants were clearly explained regarding the need and design of the study. A duly signed written informed consent was obtained from all the subjects willing to participate in the study.

Duration of the study

The time duration taken to complete the study was 3 months from July 2024 to October 2024.

RESULTS

The results of our study showed that there was a statistical difference in the clinical parameters between both groups at day 21. The scores of changes in all parameters from baseline to 21 days in group A and Group B not follow normal distribution. Therefore, the non-parametric tests were applied (Table 1). Gingival index score showed a mean difference of 0.72 in group A, from base line to day 21 and group B showed a mean difference of 0.86 from base line to day 21 with p value of 0.0001 (Table 2). Plaque index score showed a mean difference of 0.77 in group A, from base line to day 21 and group B showed a mean difference of 0.94 from base line to day 21 (Table 3). Bleeding on probing score showed a mean difference of 0.73 in group A, from base line to day 21 and group B showed a mean difference of 0.92 from base line to day 21 (Table 4). Pocket probing depth score showed a mean difference of 0.64 in group A, from base line to day 21 and group B showed a mean difference of 1.00 from base line to day 21 (Table 5). Clinical attachment level score showed a mean difference of 0.70 in group A, from base line to day 21 and group B showed a mean difference of 1.07 from base line to day 21 (Table 6). Statistically significant difference in PI, GI, BOP, PPD, CAL was found at baseline, 21 days in both the groups. But intergroup comparison shows more significant difference in all the clinical parameters in group B compared to group A after the follow up of 21 days.

Table 1: Normality of changes in all parameters from baseline to 21 days in group A and group B.

Parameters	Groups	Kolmogorov-Smirnov	df	Sig.	Shapiro-Wilk	df	Sig.
PI	Group A	0.1670	25	0.0690	0.8780	25	0.0060*
	Group B	0.1150	25	0.2000	0.9680	25	0.5830
GI	Group A	0.2030	25	0.0100*	0.8010	25	0.0001*
	Group B	0.1770	25	0.0430*	0.9200	25	0.0500*
BOP	Group A	0.2320	25	0.0010*	0.8250	25	0.0010*
	Group B	0.1500	25	0.1520	0.9700	25	0.6400
PPD	Group A	0.2010	25	0.0110*	0.8750	25	0.0060*
	Group B	0.1800	25	0.0360*	0.9060	25	0.0250*
CAL	Group A	0.1460	25	0.1800	0.9560	25	0.3420
	Group B	0.1640	25	0.0830	0.9300	25	0.0500*

*Statistically significant.

Table 2: Comparison of group A and group B with GI scores at baseline and day 21 treatment.

Time points	Group A			Group B			U-value	Z-value	P value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	1.66	0.31	26.22	1.63	0.34	24.78	294.5	0.3395	0.7342
Day 21	0.94	0.32	29.70	0.76	0.15	21.30	207.5	2.0276	0.0426*
Difference	0.72	0.33	22.18	0.86	0.24	28.82	229.5	-1.6007	0.1094

*Statistically significant.

Table 3: Comparison of group A and group B with PI scores at baseline and day 21 treatment.

Time points	Group A			Group B			U-value	Z-value	P value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	1.69	0.32	25.34	1.67	0.26	25.66	308.5	-0.0679	0.9459
Day 21	0.92	0.29	31.32	0.73	0.12	19.68	167.0	2.8134	0.0049*
Difference	0.77	0.36	21.16	0.94	0.22	29.84	204.0	-2.0955	0.0361*

*Statistically significant.

Table 4: Comparison of group A and group B with BOP scores at baseline and day 21 treatment.

Time points	Group A			Group B			U-value	Z-value	P value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	1.65	0.25	26.08	1.65	0.27	24.92	298.0	0.2716	0.7859
Day 21	0.92	0.27	31.46	0.73	0.24	19.54	163.5	2.8813	0.0040*
Difference	0.73	0.34	20.34	0.92	0.23	30.66	183.5	-2.4933	0.0127*

*Statistically significant.

Table 5: Comparison of group A and group B with PPD scores at baseline and day 21 treatment.

Time points	Group A			Group B			U-value	Z-value	P value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	1.78	0.35	21.70	2.17	0.90	29.30	217.5	-1.8336	0.0667
Day 21	1.15	0.39	28.38	1.17	0.73	22.62	240.5	1.3873	0.1654
Difference	0.64	0.38	17.72	1.00	0.34	33.28	118.0	-3.7642	0.0002

Table 6: Comparison of group A and group B with CAL scores at baseline and day 21 treatment.

Time points	Group A			Group B			U-value	Z-value	P value
	Mean	SD	Mean rank	Mean	SD	Mean rank			
Baseline	2.05	0.42	21.76	2.37	0.92	29.24	219.0	-1.8045	0.0712
Day 21	1.35	0.36	29.98	1.30	0.82	21.02	200.5	2.1634	0.0305
Difference	0.70	0.30	18.20	1.07	0.37	32.80	130.0	-3.5313	0.0004

DISCUSSION

The antibacterial activities of leaf extract of *Carica papaya* gel on periodontitis was investigated in this study. Periodontitis, one of the most common chronic diseases in the world is highly infectious one which is triggered due to bacterial colonization. Its progression can lead to the destruction of periodontium with manifestations like gingival inflammation, clinical attachment loss, alveolar bone loss, periodontal pockets, tooth mobility, bleeding on probing and pathologic migration of tooth.[13]

Along with scaling and rootplaning, LDD with medications have been introduced in recent years, showing notable improvements in periodontal health. Systemic medication delivery problems, such as gastric disturbances can be reduced by the use of LDD. Chlorhexidine digluconate and tetracycline are typical synthetic drugs used as LDD but has some limitations including tooth

surface discoloration, taste changes, and mucosal allergies. As a safer substitute for synthetic medications, different herbal extracts have been employed for LDD in recent years.[14]

Several studies have provided evidence for the antimicrobial property of *Carica papaya* leaves in various forms in periodontitis as well as gingivitis subjects. Vivekananda et al in their study evaluated the clinical and microbiological efficacy of *Carica papaya* seed extract mouthwash on periodontitis subjects. The results showed that *Carica papaya* seed extract mouthwash provided more favorable approach in the treatment of plaque-induced gingivitis, periodontitis and also oral malodor.[15] In another study, Rao et al investigated the antibacterial efficacy of kidodent, probiotics, and *Carica papaya* leaf extract mouthwashes in reducing *Streptococcus mutans* count in school children. And they concluded that probiotics and *C. papaya* leaf extract mouthwashes were equally effective as Kidodent in reducing *S. mutans* count in saliva.[16]

Ravi et al conducted a study to evaluate the antimicrobial efficacy of papaya leaves and unriped papaya fruit extracts against periodontopathogens. And the results showed that MIC for *Porphyromonas gingivalis* with ethanolic fruit extract was 25 µg/ml and ethanolic leaf extract was 50 µg/ml. MIC for *Prevotella intermedia* with ethanolic fruit extract and ethanolic leaf extract was 75 µg/ml. MIC for *Fusobacterium nucleatum* with ethanolic fruit extract and ethanolic leaf extract was 10 µg/ml. MIC for *Aggregatibacter actinomycetemcomitans* with ethanolic fruit extract and leaf extract and aqueous leaf extract was 25 µg/ml. Hence they concluded that both the papaya fruit and leaves has antimicrobial effect against periodontopathogens.[9]

In our study, GI index score showed a mean difference of 0.72 in group A, from base line to day 21 with p value of 0.0001 and group B showed a mean difference of 0.86 from base line to day 21 with p value of 0.0001. Similarly, plaque index score showed a mean difference of 0.77 in group A, from base line to day 21 with p value of 0.0001 and group B showed a mean difference of 0.94 from base line to day 21 with p value of 0.0001. Bleeding on probing score showed a mean difference of 0.73 in group A, from base line to day 21 with p value of 0.0001 and group B showed a mean difference of 0.92 from base line to day 21 with p value of 0.0001. Pocket probing depth showed a mean difference of 0.64 in group A, from base line to day 21 with p value of 0.0001 and group B showed a mean difference of 1.0 from base line to day 21 with p value of 0.0001. Clinical attachment level showed a mean difference of 0.70 in group A, from base line to day 21 with p-value of 0.0001 and group B showed a mean difference of 1.07 from base line to day 21 with p value of 0.0001.

All the results indicate the statistical difference in the various clinical parameters among both the groups. After finishing the 21 days study *Carica papaya* leaf extract gel showed reduction in BOP, inflammation and probing depth when compared with group A.

Some of the limitations of this study includes short follow-up period, absence of histological analysis, absence of radiographic analysis and not employing advanced microbiological analysis. Apart from these limitations, *Carica papaya* gel can be prepared in a simple, easier and non-invasive method. Based on the findings of this study, *Carica papaya* leaf extract gel can be used a promising therapeutic agent in the form of local drug delivery following the scaling and root planning in periodontitis.

CONCLUSION

Local drug delivery has a promising role in dentistry by improving the clinical outcomes. This study has explained the role of leaf extract of *Carica papaya* gel in reducing various clinical parameters. Due to its anti-inflammatory properties, *Carica papaya* leaf extract gel in the form of LDD has shown considerable improvements in clinical outcomes and proven to be both safe and effective as a supporting product to nonsurgical periodontal therapy. But still, further clinical studies are not available to prove the antimicrobial properties of *Carica papaya* gel in periodontitis subjects. Hence more clinical trials of long term and large sample size need to be performed to evaluate the efficacy of *Carica papaya* gel.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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