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Preparation, Characterization and Qualitative Assessment of Electrospun Cranberry Loaded Nanofiber Membrane- In Vitro Study

Poulami Chakraborty[1], Sankari Malaiappan[2*]

[1]Postgraduate, Department of Periodontology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.

[2]Head of the Department, Department of Periodontology, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, India.

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KEYWORDS

Cranberry; Electrospin-ning; Local drug delivery; drug release pattern; Periodontitis

ABSTRACT:

Introduction: Periodontal disease is a long-term inflammatory condition that leads to the gradual deterioration of the tissues supporting the teeth, potentially leading to tooth loss. While mechanical debridement is standard, combining it with antimicrobial therapy improves outcomes. Cranberry's anti-inflammatory and antimicrobial properties show promise in periodontal care. Electrospinning creates nanofiber membranes for localized delivery, enabling controlled release.

Objectives: This study develops and analyzes cranberry-infused electrospun nanofiber membranes for periodontal therapy.

Methods: A nanofiber membrane was developed by blending 50 mg of cranberry powder with 15% polyvinyl alcohol (PVA) and 2% chitosan in a 4:1 ratio, followed by overnight stirring. The mixture was electrospun using an 18G blunt needle at 15.9 kV, with fibers collected 12 cm away at a 0.005 ml/min flow rate. Morphology of nanofiber was analysed through SEM, further characterization was done by analysing drug release pattern, degradation rate, antimicrobial activity.

Results: The cranberry-loaded nanofiber membrane exhibited uniform distribution, no bead formation, an average diameter of 466 ± 12 nm, and 75% degradation by day 15. It showed controlled drug release with an initial burst followed by sustained release and strong antimicrobial properties, inhibiting bacterial growth by over 99.9995%, making it a promising option for periodontal therapy.

Conclusions: In conclusion, the cranberry-loaded nanofiber membrane exhibited uniform distribution, controlled drug release, and antimicrobial activity, making it a promising option for periodontal therapy. Its properties suggest effectiveness in periodontitis treatment, providing sustained benefits and improved outcomes.

1. Introduction

Periodontitis is a multifactorial disease, making it a complex entity for complete therapeutic resolution [1]. Thus conventional treatments such as scaling and root planing, are big challenges in controlling bacterial growth and inflammation, and often encounter challenges in delivering therapeutic agents directly to periodontal pockets where they are most needed [2]. Therefore innovative therapeutic approaches are needed as supplement to Non surgical periodontal treatment. This critical need for innovative drug delivery systems emerged with the concept of a local drug delivery system that can improve the efficiency of therapeutic agents while minimizing systemic side effects [3-5].

Nanotechnology has gained recognition as a promising advancement solution to address these challenges by enabling targeted and controlled drug delivery [6]. Electrospun nanofiber membranes, in particular, have gained attention due to their high substantivity, Ratio of surface area to volume, tunable porosity, and capacity to

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encapsulate a variety of bioactive compounds [7-9]. These membranes offer a versatile platform for local drug delivery applications, providing sustained release and enhanced bioavailability of drugs at the site of application [10].

Cranberry (*Vaccinium macrocarpon*), rich in bioactive compounds ,proanthocyanidins, recognized as a potent antimicrobial and anti-inflammatory properties [11]. Incorporating cranberry extract into electrospun nanofiber membranes presents a promising strategy for developing novel therapeutic approaches towards periodontal disease management. The polyphenolic compounds in cranberries have demonstrated efficacy against periodontal pathogens such as *Porphyromonas gingivalis* are the key stone pathogen [12-13].

This study focuses on the preparation and characterization of electrospun cranberry-loaded nanofiber membranes as a localized drug delivery system as a supplement to non surgical periodontal treatment. It includes evaluating its substantial drug release pattern, biodegradability and also its antimicrobial potential.

2. Methods

2.1 Preparation

15 grams of polyvinyl alcohol (PVA) were dissolved in 100 milliliters of distilled water and agitated at 700 rpm until completely dissolved in order to create a 15% w/v PVA solution. To create a 2% chitosan solution, 1 g of chitosan was separately added to 50 ml of acetic acid. The mixture was then agitated overnight to ensure homogeneity. Then, a combination was created by mixing 2% chitosan, 15% PVA, and 50 mg of cranberry extract in a 4:1 ratio while stirring for a full day. At a flow rate of 0.005 ml/min, the fibers were collected on a plate 12 cm from the needle tip after the solution was put into a 10 ml syringe and electrospun using an 18 G blunt-end needle at 15.9 kV (figure-1A)

Fabricated cranberry loaded nanofiber membrane was carried for further analysis (figure-1B).

Figure-1A - Electrospinning process of cranberry loaded nanofiber membrane

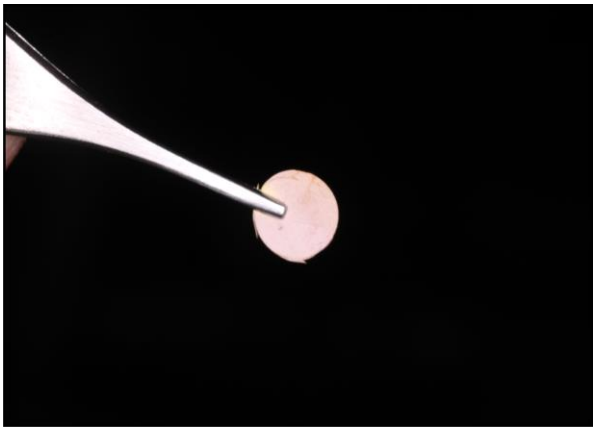

Figure 1B- Fabricated Cranberry loaded Electrospun nanofiber membrane

2.2 Characterization

2.2.1 Scanning electron microscopic analysis

SEM analysis was used to visualize and evaluate the nanofiber membrane's morphology and other characteristics. This technique makes it possible to evaluate the sample's surface composition both quantitatively and qualitatively. The size of pores can be measured using SEM and examined with imageJ software. Using a sputter coater, platinum was initially applied to the sample at ambient temperature. SEM was used to evaluate the general shape of the membrane samples after platinum plating on a stub (JEOL JSM-

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IT800). The procedure, which was conducted at a 5 kV acceleration voltage, involved taking pictures at various magnifications.

2.2.2 Drug release pattern

A 1 cm by 1 cm piece of the fabricated membrane was placed in 1 ml of phosphate buffer solution (PBS) to study the drug release behavior. The solution was sampled at 1, 3, 6, 12, 24, and 48-hour intervals and analyzed using a Jasco V-730 UV-Visible spectrophotometer. The absorption spectra of the samples were recorded within the 200–1100 nm wavelength range to assess the release profile of the drug and the interaction between the ligand and metal complex.

2.2.3 Degradation analysis

The membrane was cut into 1 cm × 1 cm sections and submerged in 4 ml of phosphate buffer solution in order to measure the membrane's rate of disintegration. At 24 hours, 3 days, 5 days, 7 days, 9 days, 11 days, 13 days, and 15 days, respectively, the samples were submerged. These samples were weighed at predetermined intervals before and after being submerged in PBS. The proportion of mass loss over time was later calculated using the formula below:

$$\frac{\text{Initial weight - final weight}}{\text{Final weight}} \times 100\%$$

2.2.4 Antimicrobial analysis

For antimicrobial analysis the electrospun nanofiber membrane was cut into standardized pieces 1cm x 1cm. Membrane sample was kept in anaerobic blood agar with 15 microlitre of *P. gingivalis* culture and incubated for 7 days. After 7 days the membrane has been washed and swabs collected from the sample surface. Lawn culture was done in anaerobic blood agar plate and incubated for 7 days at 37^{o} C. After 7 days colony forming units are observed under microscope.

3. Results

3.1 Scanning electronic microscopic analysis

The SEM images (Figure 2) show that the nanofiber membranes have a uniform and continuous fiber network with an average diameter of approximately 466 ± 12 nm. The fibers exhibit a smooth surface with minimal bead formation, indicating a successful electrospinning process. Cranberry particles are observed embedded within the nanofibers. The distribution of cranberry particles appears to be relatively homogeneous across the membrane. Some images show clusters of cranberry particles on the fiber surfaces and within the fiber matrix, suggesting effective incorporation of the cranberry extract into the nanofiber matrix. The fiber diameter was measured from multiple SEM images, and the distribution data indicate that the majority of fibers have diameters ranging from [1000 nm to 2000 nm]. These images are taken at various magnifications ranging from 200x, 500x, 1.00kx, 2.00kx, 5.00kx,10.00kx. The incorporation of cranberry particles into the nanofibers does not appear to significantly alter the fiber morphology. However, the presence of cranberry particles is evident and provides additional surface features that could influence the membrane's interaction with biological agents or its functionality in applications.

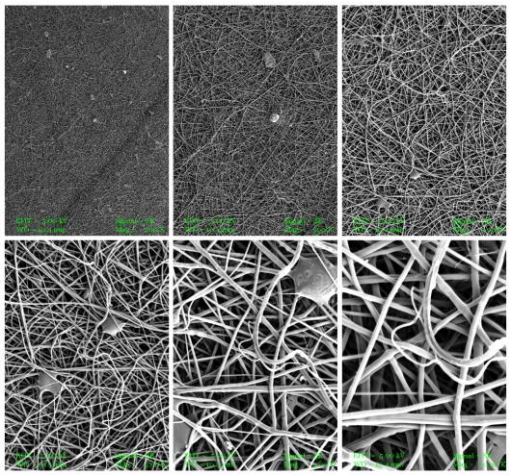

Figure 2- Scanning electron microscopic images of Cranberry loaded nanofiber membrane of various magnifications 200x, 500x, 1.00kx, 2.00kx, 5.00kx,10.00kx at 5.00kV

3.2 Drug release pattern

For cranberry-loaded electrospun nanofiber membranes, the drug release pattern often shows a combination of a persistent release phase after the first burst discharge. The initial burst is due to the fast drug disintegration on the surface, while the sustained release occurs as the drug is gradually released from within the nanofibers (figure 3).

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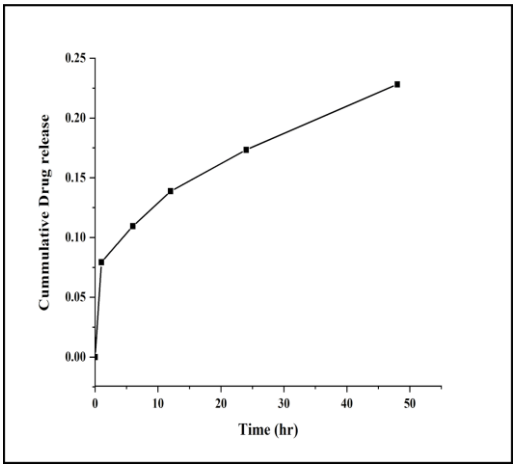

Figure 3- Drug release pattern at different time intervals of Cranberry loaded nanofiber membrane

3.3 Degradation analysis

The degradation of the nanofiber membranes was evaluated by monitoring changes in their mass and structural integrity over the 15-day period. During the first 2 days, the membranes showed a significant initial burst release of approximately 30% of the loaded cranberry. Following the initial burst, the release rate of cranberry from the nanofiber membranes tapered off and entered a sustained release phase. Over the next 13 days, the cumulative release rate gradually increased, reaching approximately 75% of the total cranberry load by day 15. This gradual degradation corresponds with the sustained release profile, suggesting that the nanofibers maintain their structural integrity while allowing controlled drug release (figure 4).

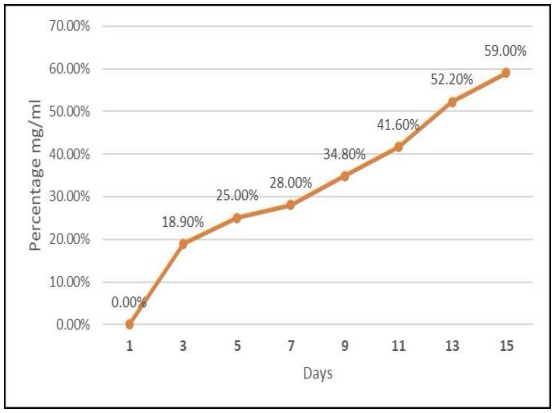

Figure 4- Degradation rate of Cranberry loaded nanofiber membrane

3.4 Antimicrobial analysis

The antimicrobial efficacy of the cranberry-loaded electrospun nanofiber membrane was assessed by evaluating its impact on the growth of *Porphyromonas gingivalis*. The analysis involved culturing *P. gingivalis* in the presence of the cranberry-loaded nanofiber membrane and measuring the reduction in colony-forming units (CFUs).Initial bacterial counts prior to treatment were approximately 200,000,000 CFUs. After incubation with the cranberry-loaded nanofiber membrane, the CFU count was significantly reduced to 981. This represents a dramatic decrease of over 99.9995% in bacterial growth (figure 5a and figure 5b).

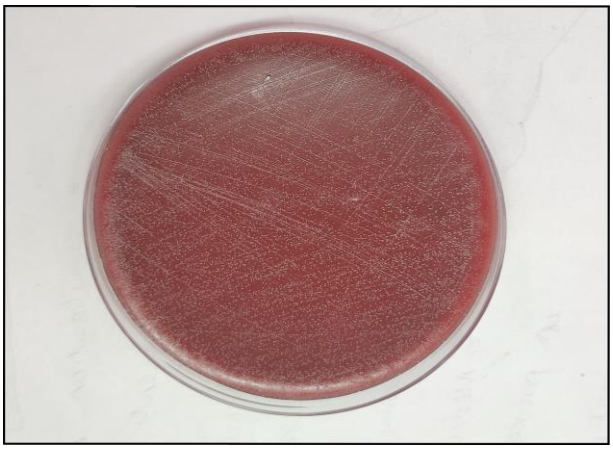

Figure 5a - CFU of *P.gingivalis* on nanofiber membrane of control group

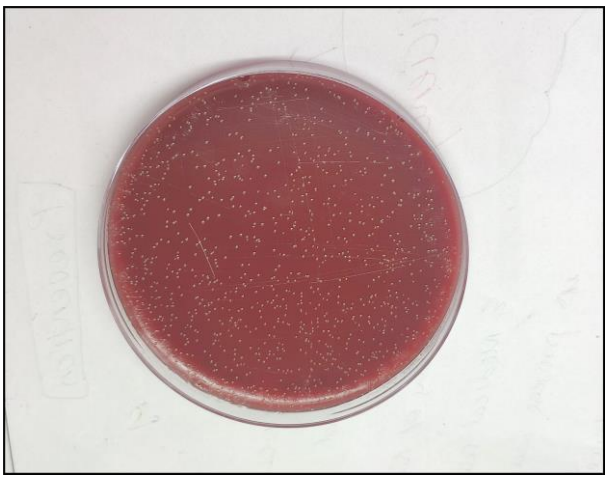

Figure 5b - CFU of *P.gingivalis* on Cranberry loaded nanofiber membrane

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4. Discussion

The integration of cranberry-loaded electrospun nanofiber membranes in the management of periodontitis offers a promising approach due to their dual benefits of antimicrobial and anti-inflammatory effects. The substantial reduction in colony-forming units (CFUs) of *Porphyromonas gingivalis* from 200,000,000 to 981 demonstrates the potent antimicrobial activity of the cranberry extract. This is consistent with previous research of Nandakumar M et al., highlighting cranberry's effectiveness against periodontal pathogens. Cranberry's bioactive compounds, such as proanthocyanidins, are known for their antimicrobial properties and ability to inhibit bacterial adhesion, which is crucial for managing periodontitis [14-15].

The use of electrospun nanofibers as a delivery system enhances the effectiveness of cranberry extracts by providing a high surface area for drug release. The sustained release profile observed in this study aligns with findings from other studies demonstrating that electrospun nanofibers can offer prolonged release of therapeutic agents, thus maintaining effective concentrations over time [16-17]. This continuous release is particularly beneficial in periodontal therapy, as it ensures persistent exposure of the antimicrobial agents to pathogenic bacteria, potentially leading to better clinical outcomes.

Moreover, cranberry's anti-inflammatory properties complement its antimicrobial effects. The extract has been shown to reduce inflammation by inhibiting pro-inflammatory cytokines, which can help alleviate the tissue damage associated with periodontitis [18-19]. The incorporation of these properties into the nanofiber membranes supports the healing of periodontal tissues and could reduce the reliance on systemic antibiotics, addressing concerns about antibiotic resistance [20].

The use of cranberry-loaded nanofiber membranes could reduce the frequency of applications compared to conventional treatments, improving patient compliance. Additionally, their ability to address both bacterial and inflammatory components of periodontitis offers a more comprehensive treatment approach. Future studies should focus on clinical trials to validate these findings in a real-world setting, assess long-term effects, and optimize the formulation for enhanced efficacy and patient comfort.

5. Conclusion

In conclusion, cranberry-loaded electrospun nanofiber membranes represent a significant advancement in periodontal treatment strategies. By combining the antimicrobial and anti-inflammatory properties of cranberry with the advanced delivery capabilities of electrospun nanofibers, this approach holds promise for improved management of periodontitis, potentially leading to better patient outcomes and reduced need for systemic interventions.

6. Conflict of interest

The authors declare that there is no conflict of interest among them.

7. Funding

No grant has been received by any funding organization in the public , commercial or not for profit sector for this research.

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