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Original Article

Green Therapeutic Evaluation of *Symplocos racemosa* and Vitamin E: Antimicrobial, Cytotoxic, Anti-inflammatory and Antioxidant Activities-An *in vitro* Study

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ABSTRACT

Background: Natural therapeutic gels are gaining prominence in periodontal therapy due to their biocompatibility, ease of application, and ability to deliver sustained, localized therapeutic effects with minimal systemic side effects. *Symplocos racemosa* (Lodhra), famous for its astringent and anti-inflammatory properties, and Vitamin E, a potent antioxidant, offer potential benefits in managing periodontal diseases through their synergistic action. **Aim:** To formulate and evaluate a novel Local Drug Delivery (LDD) hydrogel incorporating *Symplocos racemosa* extract and Vitamin E, and to assess its *in vitro* antimicrobial, antioxidant, anti-inflammatory, and cytotoxic properties for periodontal applications. **Materials and Methods:** A Local Drug Delivery (LDD) hydrogel was formulated using an aqueous extract of *Symplocos racemosa* and Vitamin E. The extract was obtained by soaking 15 g of *Symplocos* powder in 150 mL of distilled water (1:10 w/v) for 48 hr, followed by filtration and concentration. The gel base was prepared using 2.5% Carbopol 940 and 0.1% sodium alginate, to which 1% Vitamin E was incorporated. The pH was adjusted to 6.0-6.5 using triethanolamine to ensure mucosal compatibility. The formulated hydrogel was evaluated for further *in vitro* properties. **Results:** The hydrogel exhibited broad-spectrum antimicrobial activity, displaying zones of inhibition comparable to those of standard antibiotics. Antioxidant assays revealed a concentration-dependent radical scavenging effect, with moderate efficacy relative to ascorbic acid. Anti-inflammatory tests showed consistent protein stabilization and inhibition of denaturation, with increasing efficacy at higher concentrations, though slightly lower than standard drugs. Cytotoxicity analysis confirmed good cell viability at lower concentrations and only mild effects at higher doses, indicating a favorable biocompatibility profile. **Conclusion:** The *Symplocos racemosa*-Vitamin E hydrogel demonstrated effective antimicrobial, antioxidant, and anti-inflammatory properties with good *in vitro* biocompatibility. These findings suggest its potential as a safe and natural adjunct for localized periodontal therapy, supporting healing while minimizing systemic exposure.

Keywords: Antioxidants, Drug Delivery Systems, Periodontitis, Phytotherapy.

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INTRODUCTION

Natural therapeutic gels are gaining prominence in oral care due to their biocompatibility, ease of application, and multifunctional therapeutic benefits (Karale *et al*., 2024). These gels effectively deliver active compounds directly to oral tissues, enabling localized and sustained action with minimal systemic side effects (Rangrej *et al*., 2017). They are especially useful in managing periodontal conditions such as gingivitis, periodontitis, oral ulcers, and mucosal irritations, offering anti-inflammatory, antimicrobial, antioxidant, and wound-healing properties derived from natural sources (Balch *et al*., 2008). As a result, such plant-based formulations are increasingly favored for their safety and patient acceptability.

Periodontitis is a chronic inflammatory disease that progressively destroys the supporting structures of teeth, potentially leading to tooth loss if untreated (Jain *et al*., 2008). Although mechanical debridement is central to treatment, it may be insufficient in eliminating pathogens in deep or inaccessible areas. In such cases, Local Drug Delivery (LDD) systems offer targeted therapy with high local concentrations and minimal systemic involvement (Rajeshwari *et al*., 2019). Among LDD options, natural gels are especially attractive due to their mucoadhesive properties, sustained-release profiles, and bioactivity. Their gel-based nature facilitates retention in periodontal pockets, supporting healing

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and microbial control, making them a promising adjunct to both non-surgical and surgical periodontal therapies (Da Rocha *et al*., 2015).

Symplocos racemosa (Lodhra) is a key medicinal plant in Ayurveda, known for its astringent, anti-inflammatory, and wound-healing properties (Sunil & Ignacimuthu, 2011). Rich in flavonoids, glycosides, and alkaloids, it has been traditionally used to manage inflammation, bleeding, and infections. Recent studies highlight its potential in oral care, particularly for reducing gingival inflammation and supporting tissue repair (Acharya *et al*., 2016). Its antimicrobial and regenerative effects make it suitable for incorporation into natural oral formulations such as gels and LDD systems (Kar *et al*., 2018).

Vitamin E, particularly alpha-tocopherol, is a potent fat-soluble antioxidant that protects tissues from oxidative stress and promotes healing (Banu *et al*., 2017). It plays a valuable role in oral health by reducing oxidative damage, enhancing epithelial regeneration, and alleviating inflammation (Divyadharsini & Maheswari, 2023). These effects are beneficial in managing gingivitis, oral ulcers, and post-procedural healing. Its inclusion in oral gels and LDD systems enhances their therapeutic potential (Brigelius-Flohé *et al*., 2002).

Based on these properties, a multifunctional hydrogel combining *Symplocos racemosa* and Vitamin E was formulated for periodontal applications. This innovative system leverages the anti-inflammatory and antimicrobial efficacy of Lodhra with the antioxidant benefits of Vitamin E to support localized healing. The hydrogel's biocompatibility, therapeutic synergy, and sustained-release capability make it a promising candidate for periodontal therapy. The present study was therefore undertaken to formulate this natural hydrogel and evaluate its *in vitro* properties for potential use in local drug delivery for periodontal management.

MATERIALS AND METHODS

The study was conducted in Saveetha Dental College and Hospitals between August 2024 and September 2024. The institutional scientific research board [SRB/ SDC/UG-2103/25/PERIO/075] was obtained before the start of the study.

Formulation of the LDD hydrogel

Preparation of Symplocos racemosa extract

To obtain the extract, 15 grams of *Symplocos racemosa* powder [Natural Herbals Pvt. Ltd., India, Bangalore] was weighed and soaked in 150 mL of double-distilled water, maintaining a 1:10 (w/v) ratio. The mixture was left undisturbed at room temperature for 24 to 48 hr, with occasional stirring to enhance the extraction of active phytoconstituents. After the soaking period, the mixture was filtered using Whatman filter paper to separate the plant residue from the liquid extract. The resulting filtrate was then concentrated by gently evaporating the excess water in a water bath maintained below 50°C, to avoid thermal degradation of heat-sensitive compounds. The final extract was stored in an amber-colored airtight container under refrigeration until further use.

Gel Base Preparation

For the preparation of the gel, 1.25 g of Carbopol 940 (2.5% w/v) and 0.05 g of sodium alginate (0.1% w/v) were accurately weighed. These gelling agents were chosen for their excellent viscosity, film-forming ability, and biocompatibility.

The previously prepared 50 mL of *Symplocos racemosa* extract was used as the solvent base. Carbopol 940 was slowly incorporated into the extract, followed by the gradual addition of sodium alginate while stirring continuously to ensure uniform dispersion. The mixture was allowed to hydrate for 1-2 hr at room temperature, during which a preliminary gel-like consistency began to form.

Incorporation of Vitamin E

Once the base gel was formed, 0.5 mL of commercially available Vitamin E (equivalent to 1% of the total formulation volume) was added to the hydrated gel. The mixture was stirred thoroughly to ensure uniform distribution of Vitamin E throughout the gel matrix, enhancing the antioxidant capacity of the formulation.

pH Adjustment and Gel Finalization

To activate the gelling property of Carbopol and to achieve a skin- and mucosa-compatible formulation, the pH of the gel was carefully adjusted to 6.0-6.5 using Triethanolamine (TEA) as a neutralizing agent. Gentle mixing was continued until a clear, homogeneous, and smooth gel was obtained, and the final hydrogel was formed. Further *in vitro* evaluations were done. Characterization of the Formulated LDD Hydrogel.

Antimicrobial activity

For assessing antimicrobial activity, the agar well diffusion method was employed (Bharath & Priyangha, 2025). The prepared LDD hydrogel incorporated with *Symplocos racemosa* and Vitamin E was tested against *Klebsiella pneumonia*e, *Escherichia coli, Streptococcus mutans*, and *Staphylococcus aureus*. A placebo hydrogel without the active ingredients (*Symplocos* and Vitamin E) was used alongside the test sample for better comparison of efficacy. Cotrimoxazole was used as the antibiotic control for *Klebsiella pneumonia*e, Chloramphenicol for *E. coli*, Amikacin for *S. mutans*, and Levofloxacin for *S. aureus*, respectively. The fresh microbial suspension was dispersed on Mueller-Hinton agar plates, and solutions were added to wells before incubation at 37°C for 24 hr. The zone of inhibition was measured, and the results were interpreted accordingly.

Antioxidant Activity Assay-2,2-Dipheny l-1-Picrylhydrazyl (DPPH) Assay

The antioxidant activity of the formulated LDD hydrogel containing *Symplocos racemosa* and vitamin E was evaluated using the 2,2-Diphenyl-1-Picrylhydrazyl (DPPH) radical scavenging assay (Malaiappan *et al*., 2024). This method is based on the ability of antioxidants to donate hydrogen atoms to neutralize DPPH, resulting in a color change from deep violet to pale yellow. In the assay, different concentrations (10, 20, 40, 80 and 160 µL/mL) of the LDD hydrogel were prepared. Each reaction mixture contained the test sample, 2 mL of methanol, and 0.1 mM DPPH solution, and ascorbic acid was used as the reference standard. The prepared mixtures were incubated in the dark at room temperature for 30 min, and after incubation, the absorbance of each solution was recorded spectrophotometrically at 517 nm. The percentage of radical scavenging activity was calculated, and the antioxidant efficiency of the sample was compared to that of ascorbic acid across all tested concentrations.

H_2O_2 (Hydrogen Peroxide) Assay

To assess the antioxidant activity of the formulated LDD hydrogel containing *Symplocos racemosa* and Vitamin E, the Hydrogen Peroxide Assay method was employed (Malaiappan *et al*., 2024). A reaction mixture was prepared using 0.5 mL of 0.018% iron-EDTA solution, 1.0 mL of Dimethyl Sulfoxide (DMSO; 0.85% in 0.1 mol/L phosphate buffer, pH 7.4), and 0.5 mL of 0.22% ascorbic acid. These pre-prepared hydrogel solutions in various concentrations (10, 20, 40, 80, and 160 µL/mL) were separately added to 0.6 mL of the H_2O_2 solution in clean test tubes and incubated in a water bath at 80-90°C for 15 min. To terminate the reaction, 1.0 mL of ice-cold 17.5% Trichloroacetic Acid (TCA) was added promptly. Following this, 3.0 mL of Nash reagent and distilled water were added to the reaction mixture. The solution was then incubated at room temperature for 15 min. The formation of a yellow color indicated a positive reaction, and the absorbance was measured at 412 nm using a spectrophotometer. Ascorbic acid served as the standard for calculating the percentage of inhibition.

Anti-Inflammatory Activity-Bovine Serum Albumin (BSA) Denaturation Assay

The anti-inflammatory activity of the LDD hydrogel containing *Symplocos racemosa* and vitamin E was evaluated using the BSA denaturation assay (Hemamalini *et al*., 2025). The hydrogel (5 mL) was incubated with 2 mL of 1% BSA solution (pH 6.5) at room temperature for 20 min, followed by heat-induced denaturation in a water bath at 55°C for another 20 min. After cooling to room temperature, the mixtures were centrifuged, and the absorbance of the supernatant was recorded at 570 nm using a UV-vis spectrophotometer.

Test concentrations of the LDD hydrogel were prepared at 10, 20, 40, 80, and 160 µL/mL. Salicylic acid was used as the reference standard. The percentage inhibition of protein denaturation was calculated by comparing the absorbance of each test sample with that of the control (salicylic acid).

Egg Albumin (EA) Denaturation Assay

To assess the anti-inflammatory activity of the formulated gel containing *Symplocos racemosa* and Vitamin E, the egg albumin denaturation method was employed (Natarajan & Jeevanandan, 2025). A reaction mixture was prepared by combining 0.2 mL of fresh egg albumin with 2.8 mL of Phosphate-Buffered Saline (PBS) to make a 5 mL solution. Varying concentrations of the test gel (10, 20, 40, 80 and 160 µL/mL) were separately added to the mixtures. Diclofenac sodium was used as the standard reference for comparison.

All samples were incubated at 37°C for 15 min, followed by cooling to room temperature. The degree of protein denaturation was measured by recording the absorbance at 660 nm using a UV-vis spectrophotometer. The percentage inhibition of protein denaturation was calculated to evaluate the anti-inflammatory potential of the test formulation.

Cytotoxicity analysis-MTT Assay

The cytotoxicity of the formulation was assessed using the MTT assay, a colorimetric method that evaluates cellular metabolic activity (Elanthendral, 2024). The experiment included a test group and a control group. The test group consisted of MG63 cells treated with the prepared formulation containing *Symplocos racemosa* and Vitamin E at concentrations of 5 (low concentration) and 100 µg/mL (high concentration). The control group received 0.1% DMSO in culture medium without any active compounds to account for potential solvent-induced effects. To each well, 20 µL of MTT solution (5 mg/mL in phosphate-buffered saline) was added, and the plates were incubated for 4 hr at 37°C in a humidified CO_2 incubator. During this time, viable cells reduced the yellow tetrazolium salt to insoluble purple formazan crystals. After incubation, the supernatant containing residual MTT was carefully aspirated to avoid disturbing the formazan. Subsequently, 100 µL of Dimethyl Sulfoxide (DMSO) was added to each well to dissolve the crystals, and the plates were gently agitated on a shaker for 10 min to ensure complete solubilization. Absorbance was recorded at 570 nm using a spectrophotometer, and the cytotoxicity was calculated.

Statistical Analysis

The present study was designed as an exploratory *in vitro* investigation. All experimental outcomes, including antioxidant, anti-inflammatory, and antimicrobial assays, were evaluated descriptively based on the observed values. As the experiments

were performed without replicates, no inferential statistical analysis was carried out.

RESULTS

Antimicrobial activity

The antimicrobial efficacy of the test sample containing *Symplocos racemosa* and Vitamin E was assessed, and the treatment group showed notable antibacterial activity, with the largest zone of inhibition (22 mm) observed against both *Klebsiella pneumoniae* and *Escherichia coli*, closely matching the standard antibiotics Co-trimoxazole (24 mm) and Chloramphenicol (19 mm), respectively. *Staphylococcus aureus* also exhibited a notable inhibition zone of 21 mm, which was only slightly lower than that produced by the positive control, Levofloxacin (23 mm). *Streptococcus mutans* was the least sensitive among the tested strains, with the test sample producing a 17 mm inhibition zone compared to 22 mm by the antibiotic Amikacin (Table 1). The control group in all cases showed no inhibition (0 mm), further confirming the specificity of the test compound's antimicrobial activity. These findings suggest that the test sample possesses broad-spectrum antibacterial potential, especially against Gram-negative bacteria such as *K. pneumoniae* and *E. coli*).

Antioxidant Activity Assay-2,2-Dipheny l-1-Picrylhydrazyl (DPPH) Assay

The antioxidant potential of the LDD hydrogel formulated with *Symplocos racemosa* and Vitamin E was evaluated using the DPPH radical scavenging assay at various concentrations ranging from 10 to 160 µL/mL. The results revealed a concentration-dependent increase in radical scavenging activity for the test sample. At 10 µL/mL, the hydrogel exhibited approximately 21.5% inhibition, which gradually rose to around 25% at the highest tested concentration of 160 µL/mL. In comparison, the reference antioxidant, ascorbic acid, consistently demonstrated a higher percentage of inhibition across all concentrations, ranging from approximately 42% to 46%.

Despite the test sample displaying moderate antioxidant activity, it remained lower than that of ascorbic acid at every concentration tested. Nonetheless, the steady upward trend in inhibition suggests that the hydrogel possesses inherent free radical scavenging potential, likely attributable to the combined antioxidant properties of *Symplocos racemosa* and Vitamin E (Figure 1).

H_2O_2 (Hydrogen Peroxide) Assay

The H_2O_2 scavenging activity of the LDD hydrogel containing *Symplocos racemosa* and Vitamin E was evaluated across concentrations of 10 to 160 µL/mL. The results demonstrated a concentration-dependent increase in inhibition, starting from approximately 19% at 10 µL/mL and reaching nearly 25% at 160 µL/mL. Ascorbic acid, used as the reference standard, exhibited superior inhibition at all concentrations, ranging from 24% to 35%. Despite being lower than the standard, the test formulation still showed progressive hydrogen peroxide scavenging ability, indicating moderate antioxidant potential (Figure 1).

Anti-Inflammatory Activity - Bovine Serum Albumin (BSA) Denaturation Assay

The anti-inflammatory potential of the LDD hydrogel formulated with *Symplocos racemosa* and Vitamin E was evaluated using the BSA protein denaturation inhibition assay. The test sample demonstrated a progressive increase in inhibition percentage across concentrations ranging from 10 to 160 µL/mL. At 10 µL/mL, the hydrogel showed approximately 49% inhibition, which increased to a maximum of around 53% at 80 µL/mL and remained consistent at 160 µL/mL. In comparison, the reference standard salicylic acid exhibited superior activity at all tested concentrations, with inhibition values ranging from approximately 57% to 65%. Despite being slightly lower than the standard, the hydrogel consistently demonstrated substantial inhibition, indicating effective anti-inflammatory properties (Figure 2).

Egg Albumin (EA) Denaturation Assay

The anti-inflammatory efficacy of the LDD hydrogel containing *Symplocos racemosa* and Vitamin E was assessed using the Egg Albumin (EA) protein denaturation assay. The results showed a concentration-dependent increase in the percentage of inhibition of protein denaturation by the sample. At 10 and 20 µL/mL, the sample exhibited relatively modest inhibition values of approximately 37% and 38%, respectively. This activity improved with increasing concentrations, reaching around 41% at 40 µL/mL, 48% at 80 µL/mL, and peaking at approximately 55% at 160 µL/mL. In comparison, the reference standard Diclofenac sodium showed consistently higher inhibition at all concentrations, ranging from approximately 56% at 10 µL/mL to around 70% at 160 µL/mL. Although the test sample was less

Table 1: Zone of Inhibition (ZOI) of Standard Antibiotics, Placebo Hydrogel, and Treatment Hydrogel Against Selected Microorganisms.

Microorganisms	Antibiotic	Control	Treatment
Klebsiella pneumoniae	Co-trimoxazole = 24 mm	0 mm	22 mm
Escherichia coli	Chloramphenicol = 19 mm	0 mm	22 mm
Streptococcus mutans	Amikacin = 22 mm	0 mm	17 mm
Staphylococcus aureus	Levofloxacin = 23 mm	0 mm	21 mm

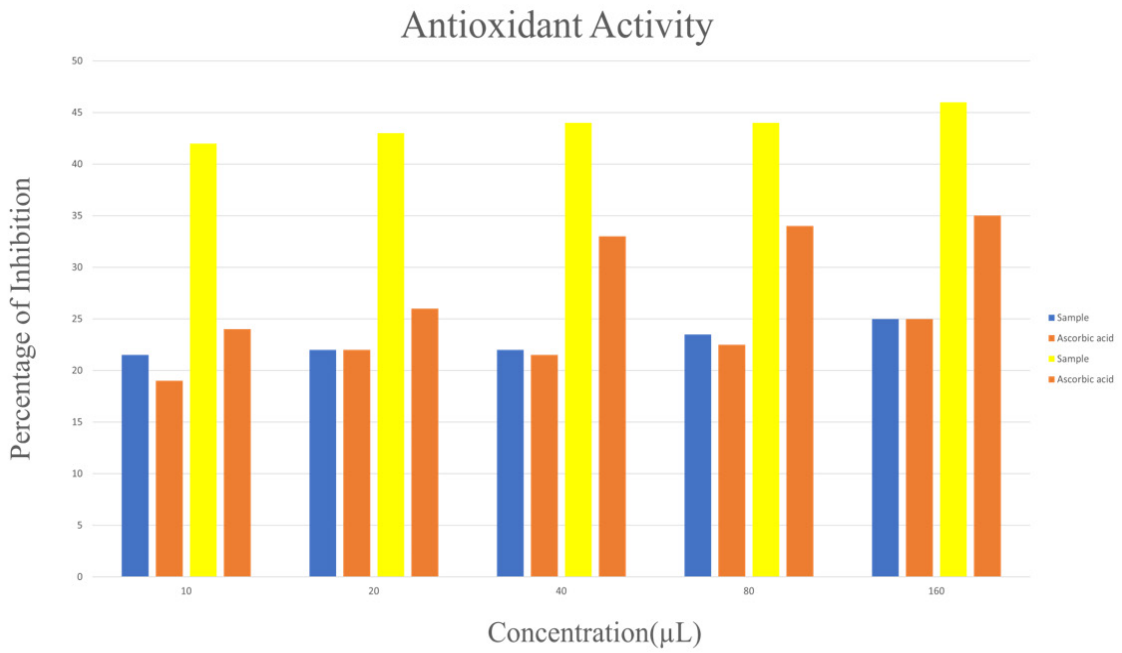

Figure 1: Antioxidant activity of the samples measured using DPPH and H_2O_2 assays. The first two bars represent the DPPH assay, and the next two bars represent the H_2O_2 assay. Ascorbic acid was used as the control for both assays. X-axis: Concentrations of the sample and ascorbic acid (µL/mL). Y-axis: Percentage of Inhibition (%).

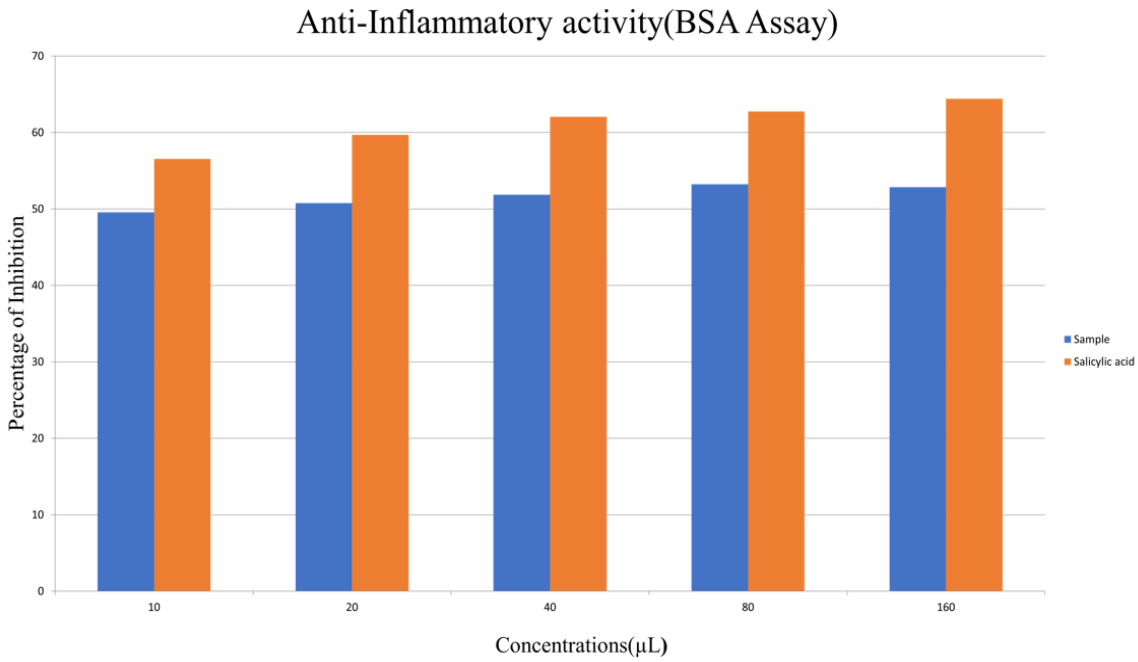

Figure 2: Anti-Inflammatory Activity of Sample Compared to Salicylic Acid Using BSA Assay at Different Concentrations X-axis: Concentrations of the sample and salicylic acid (µL/mL) Y-axis: Percentage of Inhibition (%).

potent than Diclofenac, its steadily increasing inhibition values confirm its potential anti-inflammatory property, likely due to the combined effect of phytoconstituents in *Symplocos racemosa* and the antioxidant activity of Vitamin E (Figure 3).

Cytotoxicity analysis -MTT Assay - Microscopic Evaluation

Following 24 hr of incubation, the control group (treated with 0.1% DMSO) displayed healthy, well-spread MG63 cells with no signs of cytotoxicity. The cells formed a dense, confluent monolayer and maintained normal morphology. At 5 µg/mL, the cells appeared similar to the control, showing no changes in density or morphology, indicating that the formulation did not exert cytotoxic effects at this concentration. However, at 100 µg/mL, a slight reduction in cell density was observed along with minor morphological changes. While most cells remained attached and viable, the subtle decrease in confluency suggested mild cytotoxicity at higher concentrations. Overall, the

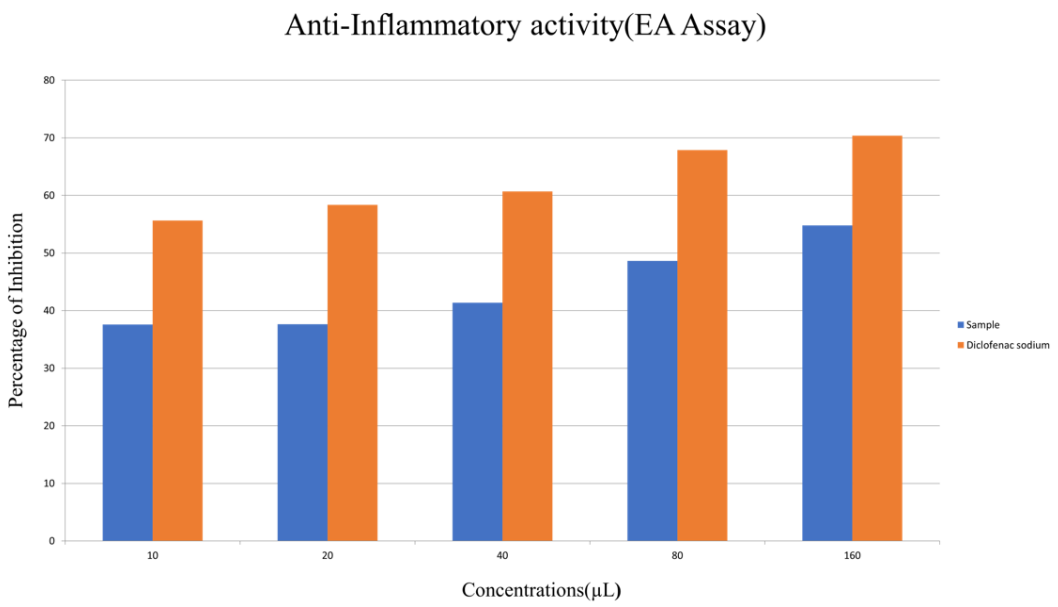

Figure 3: Anti-Inflammatory Activity of Sample Compared to Diclofenac Sodium Using Egg Albumin (EA) Assay at Different Concentrations X-axis: Concentrations of the sample and diclofenac sodium (µL/mL) Y-axis: Percentage of Inhibition (%).

formulation demonstrated good cellular compatibility across the tested doses, particularly at lower concentrations (Figure 4).

DISCUSSION

Localized periodontal therapy is integral to the successful management of periodontitis, serving an important role during both the initial treatment phase and in long-term maintenance. Its main objective is to eradicate or markedly reduce the bacterial load within specific diseased periodontal sites while safeguarding adjacent healthy tissues (Rizzo & Kehr, 2021). Central to this approach is mechanical debridement via Scaling and Root Planing (SRP), which entails the thorough removal of plaque deposits, calculus, and bacterial endotoxins from tooth and root surfaces beneath the gingival margin (Budală *et al*., 2023). Alongside SRP, locally administered antimicrobial agents-such as chlorhexidine chips, doxycycline gels, or minocycline microspheres-can be placed directly into periodontal pockets to inhibit pathogenic bacterial proliferation and extend the duration of therapeutic benefit (Amato *et al*., 2023).

Subgingival irrigation with antiseptic solutions helps further flush out debris and reduce inflammation. These localized approaches are particularly advantageous as they minimize systemic exposure and potential side effects associated with systemic antibiotics. Moreover, localized periodontal therapy is highly beneficial in managing early or site-specific periodontal lesions, and it often complements surgical procedures or systemic medications in more advanced cases. Overall, it forms an essential component of comprehensive periodontal care by helping to halt disease progression and promote regeneration and stability of the periodontium.

The management of periodontal diseases has evolved from purely mechanical approaches to a more holistic model that incorporates antimicrobial, anti-inflammatory, and regenerative strategies. With growing concerns over antibiotic resistance and adverse reactions to synthetic drugs, there has been a renewed interest in plant-based therapeutics as adjuncts to conventional periodontal treatment (Abu Tamam *et al*., 2024). One such promising agent is *Symplocos racemosa*, a traditional medicinal plant renowned for its astringent, anti-inflammatory, and antimicrobial effects (Verma *et al*., 2025). From a periodontal standpoint, *Symplocos* offers several benefits: it helps control gingival inflammation, reduces microbial colonization in periodontal pockets, and promotes healing of the gingival tissues. Its phytoconstituents contribute to the inhibition of collagenase activity, which is crucial in preventing periodontal tissue breakdown.

Similarly, Vitamin E is a powerful antioxidant that helps protect periodontal tissues from oxidative stress. It reduces inflammation and supports healing in gum tissues affected by periodontitis (Mi *et al*., 2024). Neutralizing free radicals prevents further tissue and bone destruction. Vitamin E also enhances immune response and promotes post-surgical recovery. When used with conventional therapy, it can improve clinical outcomes in periodontal care.

Therefore, the incorporation of *Symplocos* extract and Vitamin E into a Local Drug Delivery (LDD) gel provides a synergistic strategy for periodontal therapy. Their combined antioxidant, anti-inflammatory, and antimicrobial properties enhance healing and tissue regeneration. Both preclinical and emerging clinical findings support their integration, highlighting the potential of this novel formulation to improve periodontal treatment outcomes.

Our study aimed to evaluate the *in vitro* characteristics of the formulated LDD hydrogel. The antimicrobial assay revealed that the *Symplocos*-Vitamin E LDD gel exhibited broad-spectrum antimicrobial activity, effectively targeting both Gram-negative and Gram-positive periodontal pathogens. Its performance was comparable to standard antibiotics, with no activity observed in the control, confirming its specificity. These findings support its potential use as a localized therapeutic agent in periodontal treatment.

The antioxidant assays demonstrated that the *Symplocos*-Vitamin E LDD hydrogel exhibits a clear concentration-dependent radical scavenging effect, confirming the presence of active antioxidant constituents. Although the activity was moderate compared to ascorbic acid, the consistent upward trend in both DPPH and hydrogen peroxide assays suggests cumulative free radical neutralization. This intrinsic antioxidant property is advantageous for periodontal use, as oxidative stress is a major contributor to tissue degradation. By scavenging reactive species, the gel may promote better healing and attenuate inflammation at the affected site, thereby adding therapeutic benefits that extend beyond its antimicrobial effects.

The LDD hydrogel containing *Symplocos racemosa* and Vitamin E exhibited consistent anti-inflammatory activity, as evidenced by both BSA and EA protein denaturation assays. The concentration-dependent increase in inhibition across both models reflects the hydrogel's potential to stabilize proteins under inflammatory conditions, a desirable characteristic in periodontal therapy. While the inhibition levels were slightly lower than those of standard drugs, the formulation demonstrated substantial and reliable efficacy. This suggests that the synergistic action

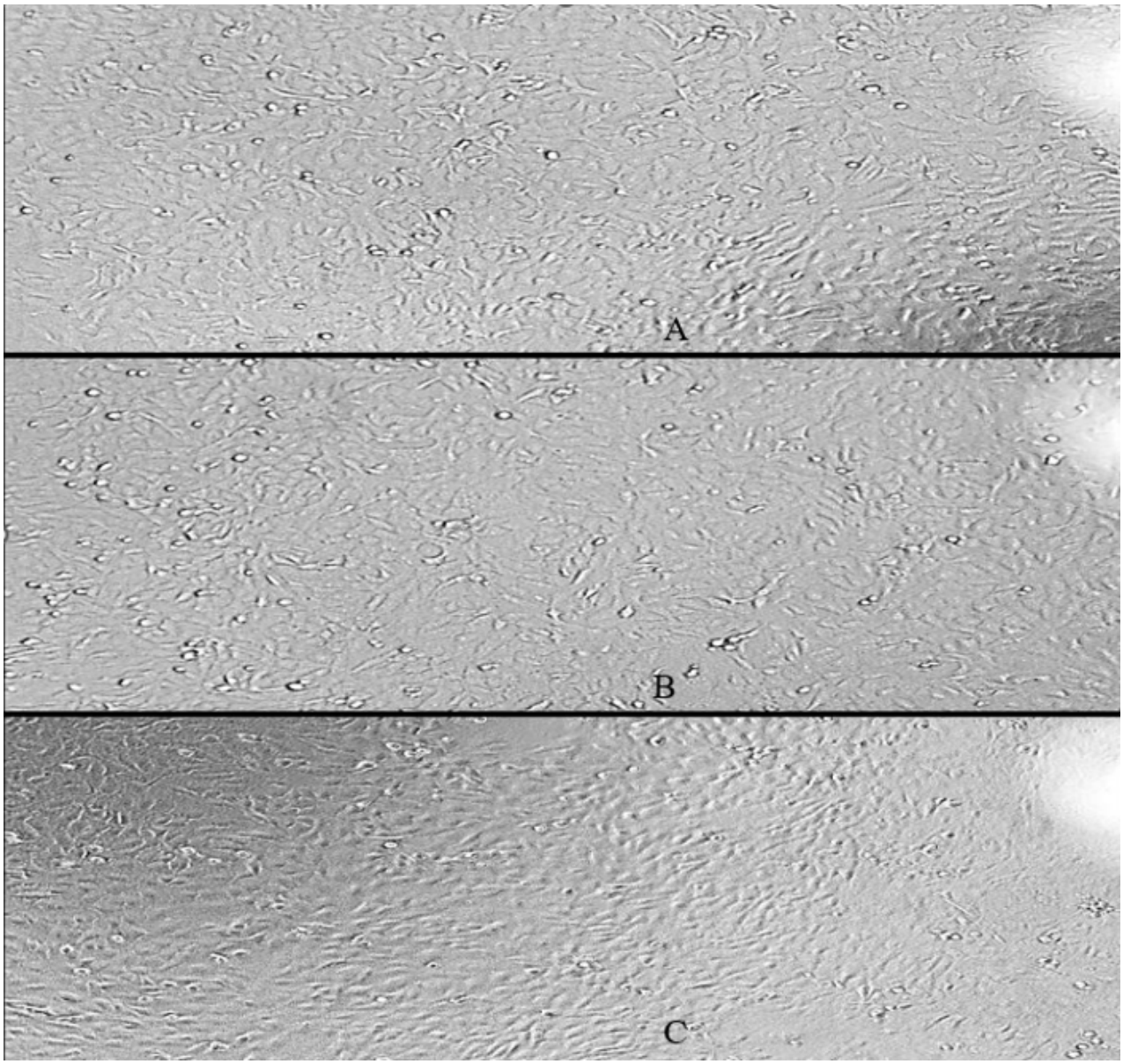

Figure 4: Morphological Assessment of Cell Viability by MTT Assay at Varying Concentrations of Sample (Control, 5 µg/mL, and 100 µg/mL).

of polyphenols from *Symplocos* and the antioxidant effect of Vitamin E contribute effectively to inflammation control. The steady response across both assays reinforces the gel's potential as a supportive agent in managing periodontal inflammation.

The cytotoxicity evaluation of the *Symplocos*-Vitamin E LDD hydrogel indicated a favorable safety profile, supporting its potential for intraoral use. The formulation maintained cellular integrity and supported cell attachment and viability, especially at lower concentrations, which is crucial for any material intended for periodontal application. The minimal cytotoxic response observed at higher concentrations suggests that the formulation remains within an acceptable safety margin. These observations align with the expected biocompatibility of natural phytochemicals and antioxidants, reinforcing the gel's potential for promoting tissue healing without adversely affecting surrounding cells.

Local Drug Delivery (LDD) offers a targeted approach in periodontal therapy by delivering therapeutic agents directly to the site of infection, and enables sustained drug release, ensuring prolonged contact with periodontal tissues and reducing the need for frequent application (Mombelli & Zekeridou, 2025). Herbal-based LDD systems further enhance this benefit by incorporating natural compounds with proven antimicrobial, anti-inflammatory, and antioxidant properties. These formulations are generally biocompatible, cost-effective, and pose a lower risk of resistance compared to synthetic agents (Pasupuleti *et al*., 2023). Overall, herbal LDDs provide a safe, efficient, and patient-friendly option for managing periodontal diseases.

Various natural agents, such as *Aloe vera* gel, pine gel, nutmeg gel, and green tea-based gels, have been explored in previous studies for their therapeutic potential in the Local Drug Delivery (LDD) systems targeting periodontal diseases (Keerthana *et al*., 2025; Rengaraj *et al*., 2025; Syed *et al*., 2025). In line with this, the present study introduces a novel formulation combining *Symplocos racemosa* extract and Vitamin E, aiming to synergistically enhance anti-inflammatory and antioxidant effects within a localized delivery platform.

Several studies have highlighted the therapeutic potential of *Symplocos racemosa* in various systemic conditions; however, only limited research has focused on its applications in oral and periodontal health. This makes our study particularly relevant and novel. One study on the bark phytoconstituents of *Symplocos racemosa* demonstrated increased antimicrobial, antibiofilm, and antiproliferative properties, supporting its role in managing infections. Additionally, the plant has been reported to exhibit antidiabetic, antiulcer, and mild analgesic activities, further emphasizing its broad pharmacological profile and potential integration into oral care formulations (Krishna *et al*., 2013).

Vitamin E, on the other hand, has been effectively used in the treatment of chronic periodontitis and in managing oral mucositis (Behfarnia *et al*., 2021). It is known to reduce oxidative stress by lowering superoxide dismutase levels, thereby minimizing tissue damage and promoting healing in inflamed oral tissues (Singh *et al*., 2014).

Thus, the formulated LDD gel, enriched with naturally derived components, presents a biocompatible and eco-friendly therapeutic option for periodontal care. Its herbal composition promotes localized healing, effectively reduces inflammation and microbial load, and minimizes the risk of adverse effects. This makes it a promising adjunct in the non-surgical management of periodontal diseases.

The present study highlights the potential of a hydrogel formulation incorporating *Symplocos racemosa* and Vitamin E as a natural, biocompatible, and cost-effective approach for periodontal therapy. The findings suggest promising antimicrobial and therapeutic effects with minimal systemic side effects. However, as the results are based on in vitro analysis, further in vivo and clinical studies with large sample size are required to confirm its efficacy and safety.

CONCLUSION

The formulated Local Drug Delivery (LDD) hydrogel containing *Symplocos racemosa* and Vitamin E exhibited promising *in vitro* results relevant to periodontal therapy. It demonstrated effective antimicrobial, antioxidant, and anti-inflammatory activity *in vitro*, along with good biocompatibility. These findings support its potential as a safe and natural adjunct for localized periodontal therapy, promoting healing while minimizing systemic effects. Overall, the hydrogel presents a safe and effective natural alternative for localized periodontal treatment, supporting healing while minimizing systemic exposure.

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ABBREVIATIONS

LDD: Local Drug Delivery; **TEA:** Triethanolamine; **DPPH:** 2,2-Diphenyl-1-picrylhydrazyl; **DMSO:** Dimethyl Sulfoxide; **TCA:** Trichloroacetic Acid; **H_2O_2:** Hydrogen Peroxide Assay; **BSA:** Bovine Serum Albumin Denaturation Assay; **EA:** Egg Albumin Denaturation Assay; **PBS:** Phosphate-Buffered Saline; **MTT:** [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay; **SRP:** Scaling and Root Planing.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FINANCIAL SUPPORT/SPONSORSHIP

The authors received no financial support or grants for this research.

AUTHORS' CONTRIBUTION

Dr. Priyangha P.T. contributed to conceptualization, data curation, manuscript writing, editing, review, and final editing. Dr. Darshine Devi. T was responsible for concepts, design, and literature search.

SUMMARY

A novel Local Drug Delivery (LDD) hydrogel incorporating *Symplocos racemosa* (Lodhra) extract and Vitamin E was formulated to evaluate its therapeutic potential in periodontal therapy. The hydrogel exhibited broad-spectrum antimicrobial activity, with inhibition zones comparable to standard antibiotics. Antioxidant assays demonstrated dose-dependent radical scavenging, while anti-inflammatory tests revealed consistent protein stabilization and inhibition of denaturation, indicating strong protective effects. Cytotoxicity analysis confirmed good cell viability at lower concentrations, with only mild effects at higher doses. These findings highlight the hydrogel's potential as a safe, biocompatible adjunct for localized periodontal therapy, offering antimicrobial, antioxidant, and anti-inflammatory benefits with minimal systemic impact.

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