

Preparation, Characterization, and Antimicrobial Activity of Doxycycline-Loaded Selenium Nanoparticles as a Potential Local Nanodrug Delivery System Against Clinical Isolates of Periodontal Pathogens: An Ex Vivo Study

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ABSTRACT

Background: Nanotechnology-based drug delivery systems have emerged as a promising strategy for improving drug stability, targeted delivery, and sustained release.

Aim: To prepare, characterize, and evaluate the antimicrobial efficacy of doxycycline-loaded selenium nanoparticles against clinical isolates of red complex periodontal pathogens.

Materials and Methods: The prepared nanoparticles were characterized by particle size analysis, Polydispersity Index, and zeta potential measurements, SEM, TEM, FTIR. Antimicrobial efficacy against clinical isolates of red complex organisms was assessed using the agar well diffusion method, and MIC was assessed using the broth microdilution technique.

Results: Selenium nanoparticles exhibited particle size mean of 85 ± 12 nm, which increased to 102 ± 15 nm following doxycycline loading. SEM and TEM analyses demonstrated uniformly distributed, spherical nanoparticles, while FTIR spectra confirmed the interaction between doxycycline and selenium nanoparticles without altering the chemical integrity of the drug. The nanoparticles demonstrated a sustained drug release pattern, achieving complete drug release over 72 hours. Doxycycline-loaded selenium nanoparticles produced higher antimicrobial activity with largest zones of inhibition against *P. gingivalis* (20.7 ± 1.16 mm), *T. forsythia* (21.1 ± 1.20 mm), and *T. denticola* (19.5 ± 1.08 mm). Furthermore, doxycycline-loaded selenium nanoparticles exhibited the lowest MIC ($0.5 \mu\text{g/mL}$), indicating superior antibacterial efficacy.

Conclusion: Doxycycline-loaded selenium nanoparticles represent a promising nanocarrier-based local drug delivery system for periodontal therapy.

Keywords: Periodontitis, Selenium nanoparticles, Doxycycline, Local drug delivery; Nanotechnology, Antimicrobial activity, Red complex bacteria.

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INTRODUCTION

Periodontal disease process involves activation of inflammatory mediators and host-derived proteolytic enzymes, causing degradation of alveolar bone. Although dental plaque biofilm serves as the primary etiological factor, microbial ecosystem play crucial role in disease progression. Among the diverse microorganisms associated with periodontal disease, the red complex pathogens, including *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*, are considered the principal contributors to periodontal tissue destruction.¹ These microorganisms possess numerous virulence factors that facilitate biofilm formation, tissue invasion, persistence within periodontal tissues, and evasion of host defense mechanisms, making complete eradication difficult through conventional mechanical therapy alone. Complete elimination of periodontal pathogens is also difficult because of complex root anatomy, deep periodontal pockets, furcation involvement, developmental grooves, root concavities, and bacterial invasion into periodontal tissues. These limitations have encouraged the promotion of additional therapeutic modalities, including lasers, antimicrobial photodynamic therapy, host-modulation therapy, and local drug delivery (LDD) systems.²

Prolonged use of systemic antimicrobial therapy is associated with several disadvantages, including adverse drug reactions, bacterial resistance, and inadequate concentration of drug at localized site. LDD slowly releases drug into targeted sites and reduces associated adverse effects. Consequently, local drug delivery has become an effective adjunctive strategy for improving periodontal treatment outcomes.³

Several antimicrobial agents such as doxycycline, minocycline, chlorhexidine are incorporated as fibers, films, strips, chips, gels, microparticles, nanoparticles are used as LDD.⁴ Among these agents, doxycycline has attracted considerable attention. In addition to inhibiting bacterial protein synthesis, doxycycline suppresses matrix metalloproteinases, modulates inflammatory cytokine production, reduces oxidative stress, and supports periodontal bone regeneration.⁵

Nanoscale formulation exhibit superior biological activity compared with inorganic selenium compounds. Previous investigations have demonstrated that selenium nanoparticles inhibit periodontal pathogens, disrupt microbial biofilms, regulate inflammatory cytokines, reduce oxidative stress, promote angiogenesis, enhance osteoblastic differentiation, and support bone regeneration. Furthermore, SeNPs have shown promising application in local drug delivery systems, periodontal gels, regenerative biomaterials, and implant surface coatings, thereby improving periodontal and peri-implant tissue health.⁶

The incorporation of doxycycline into selenium nanoparticles may further enhance antimicrobial efficacy through synergistic mechanism. Selenium nanoparticles facilitate targeted drug delivery, improve drug stability, provide sustained drug release, and enhance penetration into microbial biofilms, while doxycycline exerts potent antimicrobial and host-modulatory effects.⁷ Nanocarrier-based drug delivery systems have demonstrated improved therapeutic efficacy, controlled drug release, and enhanced bioavailability compared with conventional formulations, suggesting that doxycycline-loaded selenium nanoparticles may overcome several limitations. The present **ex vivo** study was conducted to evaluate doxycycline-loaded selenium nanoparticles and to assess their antimicrobial action against clinically isolated periodontal pathogens, as a novel nanocarrier-based local drug delivery system for periodontal therapy.

MATERIALS AND METHODS

Design of the study:

The study was conducted as an **ex vivo laboratory-based experimental study** to synthesize doxycycline-loaded selenium nanoparticles (Doxy-SeNPs), characterize their physicochemical properties, and investigate their antimicrobial activity against periodontal pathogens isolated from clinical specimens. All laboratory procedures were performed following standardized experimental protocols. Ethical approval for the study was obtained from the Institutional Ethics Committee of CKS Theja Institute of Dental Sciences and Research, Tirupati (Approval No. CKS/PERIO/23-24/02).

Isolation and Identification of Periodontal Pathogens

Subgingival plaque samples were obtained from the deepest periodontal pockets of patients diagnosed with periodontitis after careful removal of supragingival deposits. Sterile paper points were inserted into the periodontal pocket for sample collection under aseptic conditions. Immediately after collection, the specimens were transferred into anaerobic transport medium and transported to the microbiology laboratory for further processing.

The samples were cultured on selective microbiological media and incubated anaerobically at **37°C for 48–72 hours**. The recovered isolates were identified using colony characteristics, Gram staining, and standard biochemical tests. Pure cultures of *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* were subsequently used for antimicrobial evaluation by agar well diffusion assay and minimum inhibitory concentration (MIC) analysis.⁸

Preparation of Doxycycline-Loaded Selenium Nanoparticles⁹

Analytical grade chemicals were used throughout the experimental procedures. Sodium selenite served as the selenium source, whereas doxycycline hyclate was

selected as the antimicrobial agent. Ascorbic acid was employed as the reducing agent for nanoparticle synthesis, and deionized water was used for the preparation of all solutions.

Selenium nanoparticles were synthesized by a chemical reduction technique with slight modifications to previously reported methods. Sodium selenite solution was stirred continuously, followed by the slow addition of freshly prepared ascorbic acid solution under controlled experimental conditions. Reduction of selenium ions was evidenced by the appearance of a brick-red colour, indicating nanoparticle formation. Continuous stirring was maintained for complete reduction and stabilization of the synthesized nanoparticles.

For drug loading, doxycycline hyclate was introduced into the selenium nanoparticle suspension under constant stirring. The mixture was maintained under continuous agitation for sufficient time to facilitate adsorption of the drug onto the nanoparticle surface. The resulting formulation was separated by centrifugation to remove unbound drug molecules, and the pellet was washed several times with deionized water. Finally, the purified nanoparticles were freeze-dried and stored in airtight containers until further characterization and antimicrobial testing.

Characterization of Doxycycline-Loaded Selenium Nanoparticles¹⁰

The hydrodynamic diameter and polydispersity index (PDI) of the synthesized nanoparticles were determined by dynamic light scattering (DLS). These measurements were performed to evaluate the average particle size and the uniformity of particle distribution within the formulation.

The surface electrical charge of the nanoparticles was measured using zeta potential analysis. This assessment was carried out to determine the colloidal stability of the prepared formulation, as surface charge particle aggregation and suspension stability during storage.

The external morphology of the synthesized nanoparticles was examined using scanning electron microscopy (SEM). Prior to imaging, dried nanoparticle samples were mounted onto aluminium stubs and coated with a thin layer of gold to improve electrical conductivity. The micrographs were evaluated for particle shape, surface characteristics, and the presence of any aggregation.

Transmission electron microscopy (TEM) was employed to obtain high-resolution images of the nanoparticles and to determine their morphology and particle size. A diluted nanoparticle suspension was placed on carbon-coated copper grids, air dried, and examined under the microscope. TEM analysis provided detailed information regarding the structural characteristics and size distribution of the prepared nanoparticles.

Fourier transform infrared spectroscopy (FTIR) was performed to identify the functional groups present in doxycycline, selenium nanoparticles, and doxycycline-

loaded selenium nanoparticles. Spectra were recorded over the range to evaluate possible interactions between the drug and the nanoparticle matrix following drug incorporation.

Drug loading and entrapment efficiency were determined after separating the nanoparticle-bound drug from the free drug by centrifugation. The amount of untrapped doxycycline remaining in the supernatant was quantified using UV-Visible spectrophotometry. Drug loading (%) was calculated as the amount of doxycycline incorporated relative to the total weight of the nanoparticle formulation, whereas entrapment efficiency (%) represented the proportion of the initial drug successfully incorporated into the nanoparticles. Both parameters were calculated using standard equations reported in the literature.

Evaluation of Antimicrobial Activity¹¹

The antimicrobial activity of elemental selenium, selenium nanoparticles (SeNPs), doxycycline, and doxycycline-loaded selenium nanoparticles (Doxy-SeNPs) were evaluated using the agar well diffusion technique. Bacterial suspensions were standardized to a turbidity equivalent to the **0.5 McFarland standards** and uniformly inoculated onto Mueller-Hinton agar plates. Circular wells measuring **5 mm** in diameter were prepared aseptically, and equal volumes of the respective test formulations were introduced into each well.

Following anaerobic incubation at **37°C**, the diameter of the clear inhibitory zones surrounding each well was measured using a HiMedia antibiotic zone scale. All experiments were carried out in triplicate, and the mean inhibition zone diameter was considered for analysis.

Determination of Minimum Inhibitory Concentration¹²

The minimum inhibitory concentration (MIC) of each test formulation was determined using the broth microdilution technique. Serial two-fold dilutions of selenium, selenium nanoparticles, doxycycline, and doxycycline-loaded selenium nanoparticles were prepared in Mueller-Hinton broth to obtain concentration ranging from **0.125 to 128 µg/mL**. Each dilution was inoculated with bacterial suspensions adjusted to the **0.5 McFarland standards** and incubated under anaerobic conditions at **37°C for 24–48 hours**.

Following incubation, the tubes were examined for visible bacterial growth. The MIC was defined as the lowest concentration of the formulation that completely inhibited microbial growth. Every experiment was performed three times independently to ensure the reproducibility of the findings.

Statistical Analysis

The experimental data obtained from all assays were analyzed using IBM SPSS Statistics version 26.0. Owing to the non-parametric distribution of the data, differences among the study groups were assessed using the Kruskal–Wallis test. When statistically significant differences were observed, pairwise comparisons were performed using the Mann–Whitney U test. Statistical significance was established at a probability value of $P < 0.05$.

RESULTS

Synthesis of Doxycycline-Loaded Selenium Nanoparticles

Table1: Particle size, poly dispersity index and zeta potential of nanoparticles

Parameter	Selenium nanoparticles	Doxycycline-loaded seleniumnanoparticles
ParticleSize (nm)	85 ± 12 nm	102 ± 15 nm
PolydispersityIndex	0.28 ± 0.04	0.31 ± 0.05
ZetaPotential(mV)	-28 ± 3 mV	-22 ± 2 mV

Scanning electron microscopy (SEM) demonstrated that the synthesized SeNPs were predominantly showing smooth surface spherical morphology and uniform

Dynamic light scattering analysis demonstrated that the mean particle size increased from 85 ± 12 nm for selenium nanoparticles to 102 ± 15 nm for doxycycline loading. Similarly, the polydispersity index increased slightly from 0.28 ± 0.04 to 0.31 ± 0.05 , indicating a homogeneous particle size distribution without significant aggregation. Zeta potential values changed from -28 ± 3 mV for selenium nanoparticles to -22 ± 2 mV after doxycycline loading, demonstrating satisfactory colloidal stability and successful drug adsorption onto the nanoparticle surface (Table 1).

distribution, exhibiting minimal aggregation, which indicated effective stabilization during synthesis (Fig. 1).

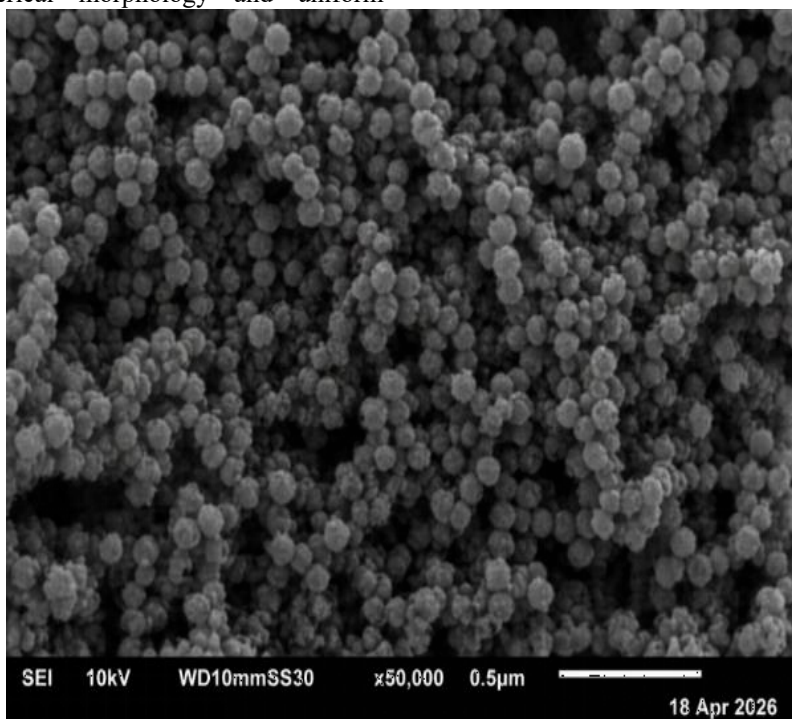


Figure1: SEM micrograph of SeNPs

Transmission electron microscopy (TEM) further confirmed that the doxycycline-loaded selenium nanoparticles were spherical, well-defined, and uniformly dispersed, with particle sizes ranging from approximately **70–90 nm**. A diffuse peripheral layer surrounding the

electron-dense selenium core suggested successful adsorption of doxycycline onto the nanoparticle surface, while minimal aggregation indicated good formulation stability (Fig. 2).

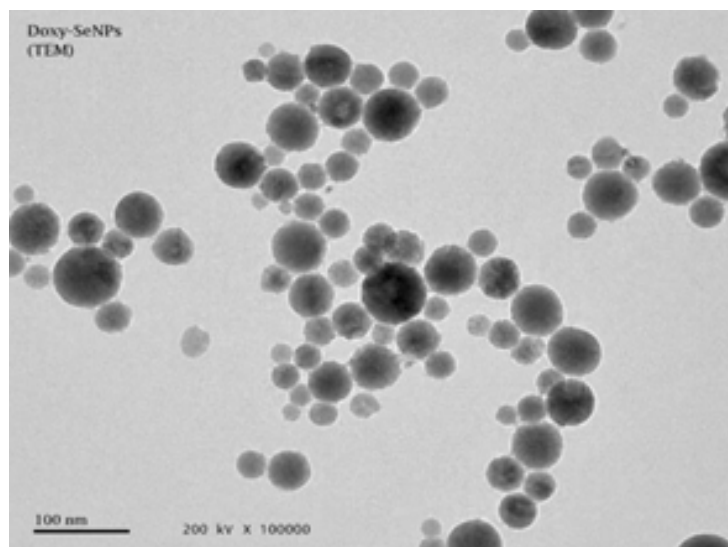


Figure 2. TEM image of doxycycline-loaded selenium nanoparticles

FTIR revealed the characteristic absorption peaks of both selenium nanoparticles and doxycycline. The spectra of doxycycline-loaded selenium nanoparticles exhibited slight peak shifts and band broadening compared with

pure doxycycline, confirming successful interaction between the drug and the selenium nanoparticle matrix without alteration of the chemical structure (Fig. 3)

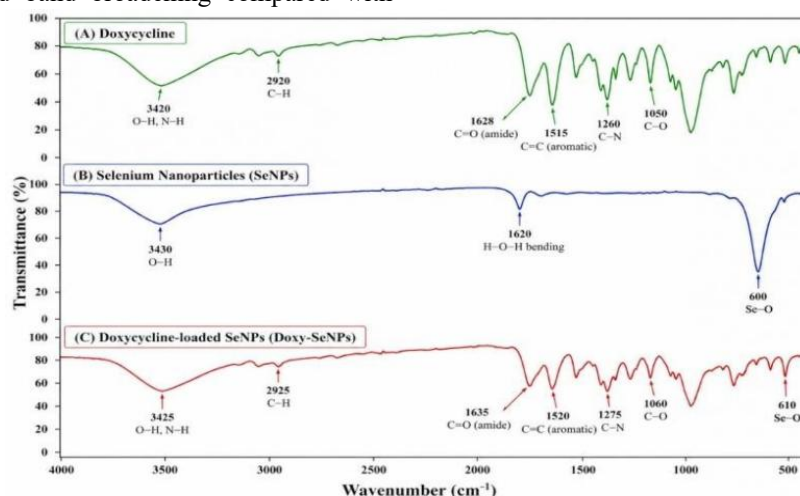


Figure 3: FTIR Spectra of doxycycline, SeNPs and doxycycline loaded SeNPs

The developed nanoparticle formulation exhibited a **drug loading efficiency of $68.5 \pm 3.2\%$** and an **entrapment efficiency of $82.3 \pm 2.8\%$** , indicating efficient incorporation of doxycycline into the selenium nanoparticle system.

Antibacterial Activity

The antibacterial activity of plain selenium, selenium nanoparticles (SeNPs), plain doxycycline, and doxycycline-loaded selenium nanoparticles (Doxy-SeNPs) was evaluated against *red complex microorganisms* using the agar well diffusion assay.

Among all the tested formulations, doxycycline-loaded selenium nanoparticles exhibited the greatest antibacterial activity against all three periodontal pathogens, producing mean zones of inhibition of **20.7 ± 1.16 mm**, **21.1 ± 1.20 mm**, and **19.5 ± 1.08 mm** against *P. gingivalis*, *T.*

forsythia, and *T. denticola*, respectively. In comparison, plain doxycycline produced inhibition zones of **15.3 ± 0.95 mm**, **15.3 ± 0.95 mm**, and **14.5 ± 1.08 mm**, while selenium nanoparticles produced inhibition zones of **10.2 ± 1.03 mm**, **10.3 ± 0.95 mm**, and **9.5 ± 1.08 mm**, respectively. Plain selenium demonstrated the lowest antibacterial activity, with inhibition zones of **6.0 ± 0.82 mm**, **6.1 ± 0.74 mm**, and **5.3 ± 0.95 mm** against the respective microorganisms.

The low standard deviation values observed across all groups indicated excellent reproducibility of the experimental procedure. Overall, incorporation of doxycycline into selenium nanoparticles significantly enhanced antibacterial efficacy compared with plain selenium, selenium nanoparticles alone, and plain doxycycline (Table 2).

Table 2: In Vitro Antibacterial Activity of Different Test Formulations Against Selected Periodontal Pathogens

Test Formulation	<i>Porphyromonas gingivalis</i> Mean $\pm$ SD (mm)	<i>Tannerella forsythia</i> Mean $\pm$ SD (mm)	<i>Treponema denticola</i> Mean $\pm$ SD (mm)
Plain Selenium	6.0 $\pm$ 0.82	6.1 $\pm$ 0.74	5.3 $\pm$ 0.95
Selenium Nanoparticles (SeNPs)	10.2 $\pm$ 1.03	10.3 $\pm$ 0.95	9.5 $\pm$ 1.08
Plain Doxycycline	15.3 $\pm$ 0.95	15.3 $\pm$ 0.95	14.5 $\pm$ 1.08
Doxycycline-Loaded SeNPs	20.7 $\pm$ 1.16	21.1 $\pm$ 1.20	19.5 $\pm$ 1.08
P value	<0.001*	<0.001*	<0.001*

Kruskal–Wallis test followed by Mann–Whitney U test was used for statistical analysis. A value of **P < 0.05** was considered statistically significant.

Minimum Inhibitory Concentration (MIC)

The minimum inhibitory concentration (MIC) values further confirmed the superior antibacterial efficacy of doxycycline-loaded selenium nanoparticles. Among the test formulations, Doxy-SeNPs demonstrated the lowest MIC (**0.5 μ g/mL**), followed by plain doxycycline (2

μ g/mL), selenium nanoparticles (**32 μ g/mL**), and plain selenium (**64 μ g/mL**) (Table 2.)

The markedly lower MIC of doxycycline-loaded selenium nanoparticle indicates enhanced antimicrobial potency, suggesting that incorporation of doxycycline into the selenium nanoparticle carrier with improved antibacterial activity, potentially through enhanced penetration into bacterial biofilms and sustained drug availability at lower concentrations.

Table 3 : Minimum inhibitory concentration of different test groups

Test group	MIC(μ g/mL)
Plain Selenium	64 μ g/mL
Selenium Nanoparticles(SeNPs)	32 μ g/mL
Plain Doxycycline	2 μ g/mL
Doxycycline-Loaded SeNPs(Doxy-SeNPs)	0.5 μ g/mL

DISCUSSION

The present **ex vivo** study investigated Doxy-SeNPs as a potential local drug delivery system for periodontal therapy. The findings demonstrated successful synthesis of the nanoparticle formulation, favorable physicochemical characteristics, and efficient drug loading against clinically isolated periodontal pathogens. Collectively selenium nanoparticles are efficient nanocarriers for the localized delivery of doxycycline in periodontal therapy.

Periodontitis is primarily associated with polymicrobial biofilms dominated by red complex organisms. Complete elimination of pathogenic microorganisms is often limited by complex root morphology, deep periodontal pockets, and bacterial invasion into periodontal tissues. Earlier studies by Goodson et al.¹³ and Salvi et al.¹⁴ demonstrated that locally delivered antimicrobial agents significantly improve periodontal treatment outcomes by maintaining effective antimicrobial concentrations at the diseased site.

In the present investigation, SeNPs were done by chemical reduction method in which sodium selenite served as precursor and ascorbic acid acted like reducing agent. Doxycycline hyclate was subsequently incorporated into the nanoparticle suspension through continuous magnetic stirring to facilitate adsorption onto the nanoparticle surface. Similar methods of selenium nanoparticle synthesis have been described by Ramamurthy et al.,¹⁵ Sharma et al.,¹⁶ Srivastava et al.¹⁷, Medina-Cruz et al.,¹⁸

and Altememy et al.,¹⁹ supporting the feasibility and reproducibility of the present formulation approach.

Nanoparticles within the nanoscale range possess unique physicochemical characteristics that enable effective interaction with bacterial biofilms and improved penetration into periodontal pockets. SeNPs exhibited a particle size mean of **85 $\pm$ 12 nm**, which increased to **102 $\pm$ 15 nm** following doxycycline loading. This increase in particle size provides indirect evidence of successful drug adsorption while maintaining particle dimensions within the optimal nanoscale range for biomedical applications. Similar particle sizes have been reported by Ramamurthy et al.,¹⁵ Srivastava et al.,¹⁷ Medina-Cruz et al.,¹⁸ who also demonstrated excellent physicochemical stability and biological performance of selenium nanoparticles within this size range.

Nanoparticle dispersions stability is largely dependent on surface charge. Analysis of Zeta potential demonstrated **–28 $\pm$ 3 mV** for selenium nanoparticles and **–22 $\pm$ 2 mV** following drug loading, indicating that the formulation remained colloidally stable after incorporation of doxycycline. Similar zeta potential values have been observed in Geoffrion et al.,²⁰ Wadhwani et al.,²¹ and Mourdikoudis et al.,²² studies suggesting that nanoparticles with zeta potentials between –20 and –30 mV possess adequate electrostatic stability and reduced aggregation.

Morphological evaluation using scanning electron microscope demonstrated that the synthesized nanoparticles were predominantly uniformly distributed spherical in shape and exhibited minimal aggregation. TEM images further revealed a diffuse peripheral layer surrounding the electron-dense selenium core, suggesting adsorption of doxycycline molecules onto the nanoparticle surface. These observations provide additional evidence supporting successful drug loading while confirming the structural integrity and stability of the nanoparticle formulation. Comparable spherical morphology and minimal aggregation have been reported in previous selenium nanoparticle studies.

Characteristic absorption peaks corresponding to doxycycline and selenium nanoparticles were retained in FTIR analysis while minor peak shifts and broadening were observed in the drug-loaded formulation. These spectral changes indicate molecular interactions between doxycycline and the nanoparticle surface without altering the fundamental chemical structure of the drug. Similar FTIR findings have been observed by Altememy et al.,²³ Vijayalakshmi et al.,²³ and Mekawy et al.,²⁴ confirming successful drug encapsulation and nanoparticle stability.

Efficient drug loading is an essential prerequisite for successful nanoparticle formulation and showed **68.5 ± 3.2% of drug efficacy with 82.3 ± 2.8%**, entrapment efficiency indicating efficient incorporation of doxycycline into the selenium nanoparticle matrix. High entrapment efficiency is advantageous because it minimizes drug loss, prolongs retention of drug in carrier system, and facilitates sustained drug release. Similar findings have been reported by Danhier et al.,²⁵ Cover et al.,²⁶ Altememy et al.,¹⁹ and Mekawy et al.,²⁴ who demonstrated that selenium- and polymer-based nanoparticles possess high drug loading and encapsulation efficiencies suitable for controlled drug delivery applications.

The **in vitro** drug release study showed a biphasic release profile, comprising an initial rapid release followed by sustained drug release over 72 hours. The early release was likely due to doxycycline present on the nanoparticle surface, whereas the prolonged release resulted from the gradual diffusion of the encapsulated drug. This controlled release pattern may enhance periodontal therapy by providing an immediate antimicrobial effect while maintaining therapeutic drug concentrations for an extended duration. Similar sustained-release profiles have been observed in Danhier et al.,²⁵ Cover et al.,²⁶ Vijayalakshmi et al.,²³ and Patra et al.²⁷

Antimicrobial evaluation demonstrated that doxycycline-loaded selenium nanoparticles produced significantly greater zones of inhibition against *red complex organisms* compared to plain selenium, selenium nanoparticles alone, and doxycycline alone. Furthermore, the drug-loaded nanoparticles exhibited the lowest minimum inhibitory concentration, indicating superior antibacterial potency. These findings suggest a synergistic interaction between

doxycycline and selenium nanoparticles, resulting in enhanced antimicrobial efficacy. Similar antimicrobial effects of selenium nanoparticles have been reported by Medina-Cruz et al.,¹⁸ Geoffrion et al.,²⁰ Altememy et al.,¹⁹ Hou et al.,²⁸ Hamman et al.,²⁹.

The improved antibacterial property may be attained due to multiple complementary mechanisms. Selenium nanoparticles possess intrinsic antimicrobial properties such as inhibition of biofilm formation, and microbial metabolic pathway disturbances. Simultaneously, doxycycline inhibits bacterial protein synthesis while exerting host-modulating effects through suppression of matrix metalloproteinase's and inflammatory cytokines. The nanoparticle carrier further enhances drug stability, facilitates penetration into periodontal biofilms, and promotes sustained drug release. Collectively, these mechanisms contribute to enhanced antibacterial activity and improved therapeutic potential.

The present findings are also consistent with clinical investigations evaluating locally delivered doxycycline for periodontal therapy. Garrett et al.,³⁰ Eickholz et al.,³¹ Akalin et al.,³² Preshaw et al.,³³ Tomasi et al.,³⁴ and Jorgensen et al.,³⁵ demonstrated that sustained local delivery of doxycycline improves periodontal outcomes by maintaining therapeutic drug concentrations within periodontal pockets for prolonged periods. More recently, Aimetti et al. further highlighted the advantages of site-specific doxycycline delivery for periodontal regeneration.

The present investigation was conducted under **ex vivo** conditions, and therefore the biological behavior of the nanoparticle formulation within the complex periodontal environment could not be fully assessed. Parameters such as biocompatibility, pharmacokinetics, biodegradation, tissue penetration, host immune response, and long-term therapeutic outcomes require evaluation under **in vivo** conditions. Furthermore, randomized clinical trials involving larger sample sizes and safety of doxycycline-loaded selenium nanoparticles before their routine application in periodontal therapy should be addressed.

CONCLUSION:

Doxycycline-loaded selenium nanoparticles in contrast to plain selenium, selenium nanoparticles, and plain doxycycline showed superior microbial inhibition against periodontal pathogens, enhancing their local drug delivery applications in periodontal therapy. Developed nanoparticle formulation can be considerable as a potential local drug delivery system for periodontal therapy.

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