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Silver Nanoparticle-Based Transdermal Patch from *Lippia Nodiflora*: A Promising Approach for Accelerating Wound Healing and Anti-Inflammatory Activity

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Abstract

The growing demand for safe and effective wound healing therapies has led to the exploration of nanotechnology-based transdermal systems. In this study, a transdermal patch incorporating silver nanoparticles (AgNPs) synthesized from the ethyl acetate extract of *Lippia nodiflora* was developed using the solvent casting method with HPMC as the polymer base. Phytochemical analysis confirmed the presence of flavonoids (60 mg QE/g), phenolics (7.5 mg GAE/g), and tannins (50 mg GAE/g), known for their antioxidant and wound-healing properties. The biosynthesized AgNPs (mean size 355.3 nm, zeta potential –28.4 mV) exhibited strong antioxidant activity of 95.69 µg/mL (DPPH) and 97.88 µg/mL (nitric oxide scavenging). Transdermal patches (F1–F5) were uniform in thickness (42–55 µm), folding endurance (100–150), and drug content (79–90%), with surface pH values close to skin compatibility (5.8–8.1). Among the formulations, F5 showed the highest cumulative drug release (95.82% in 24 h) and followed zero-order kinetics (R^2 = 0.9976), indicating sustained release through non-Fickian diffusion. These findings highlight the potential of *L. nodiflora*-mediated AgNP transdermal patches as multifunctional wound dressings offering antioxidant, anti-inflammatory, and controlled-release benefits. Future work should validate efficacy through *in vivo* and clinical studies.

Keywords: Transdermal patch, *Lippa nodiflora*, Wound healing, silvernanoparticles, Green synthesis.

Introduction

The research described in this study holds significant importance in the field of wound healing and anti-inflammatory therapy. By utilizing the ethyl acetate extract of Lippia nodiflora for the green synthesis of silver nanoparticles and incorporating them into a transdermal patch, the study aims to leverage the wound healing and anti-inflammatory properties of both Lippia nodiflora and silver nanoparticles.[1]This innovative approach has the potential to provide localized and targeted treatment options for wounds, minimizing the risk of infection, promoting faster healing, and reducing inflammation. By combining the therapeutic benefits of *Lippia nodiflora* and the antimicrobial, anti-inflammatory, and regenerative effects of silver nanoparticles, the transdermal patch developed in this study could offer an effective and efficient wound healing solution.[2]

Recent phytochemical investigations report that *Lippia nodiflora* aerial extracts contain high levels of phenolics and flavonoids, compounds known to play key roles in antioxidant defense, tissue regeneration, and antimicrobial protection. These phytoconstituents act synergistically with silver nanoparticles, where flavonoids not only enhance antioxidant activity but also stabilize nanoparticles during green synthesis.[3]

Advancements in wound healing strategies are of great significance as they can significantly improve patient outcomes, enhance quality of life, and reduce healthcare costs. By incorporating natural compounds

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and nanoparticles, this research contributes to the development of novel therapeutic approaches for wound healing and anti-inflammatory therapy.[4]

Furthermore, recent reviews emphasize that eco-friendly AgNP systems, particularly when mediated by bioactive phytochemicals, can accelerate wound contraction, reduce oxidative stress, and improve collagen alignment in healing tissue This highlights the relevance of a *Lippia nodiflora*–based AgNP transdermal patch as an advanced and sustainable wound-healing system.

the combination of Lippia nodiflora and silver nanoparticles in a transdermal patch represents a promising avenue for localized wound healing and anti-inflammatory treatment. Further research and optimization of this approach can lead to the development of advanced transdermal patch formulations, offering improved therapeutic outcomes and better patient care.[5,6]

Materials and Methods

Plant Material Collection and Authentication

Fresh aerial parts of *Lippia nodiflora* were collected. The plant material was authenticated by a botanist. The collected material was washed thoroughly with distilled water, shade dried for 10–15 days at ambient temperature (25 ± 2 °C), and powdered using a mechanical grinder. The powder was stored in airtight containers at room temperature until extraction.

Preparation of Plant Extract

A total of 100 g of powdered *Lippia nodiflora* aerial parts was subjected to Soxhlet extraction using ethyl acetate (500 mL) as solvent for 6 h at 60 °C. The extract was concentrated under reduced pressure using a rotary evaporator and stored at 4 °C in amber glass bottles until further analysis.

Preliminary Phytochemical Screening

Qualitative phytochemical tests were carried out on the ethyl acetate extract using standard procedures to identify the presence of alkaloids, flavonoids, phenols, tannins, saponins, glycosides, and steroids[7]

Quantitative Estimation of Phytochemicals

Total Phenolic Content

The total phenolic content was determined using the Folin–Ciocalteu method. Extracts (1 mg/mL) were mixed with 0.5 mL of Folin–Ciocalteu reagent and 1.5 mL of sodium carbonate (7.5% w/v). The reaction mixture was incubated at room temperature for 30 min, and absorbance was measured at 765 nm using a UV–visible spectrophotometer (Shimadzu, Japan). Gallic acid was used as the standard, and results were expressed as mg gallic acid equivalent (GAE)/g extract.[8]

Total Tannin Content

Tannin content was estimated using the Folin–Ciocalteu method with gallic acid as standard. Extracts were mixed with Folin–Ciocalteu reagent and sodium carbonate, incubated, and absorbance was measured at 700 nm. Results were expressed as mg GAE/g extract.

Total Flavonoid Content

Flavonoid content was estimated using the aluminium chloride colorimetric method. Extracts were mixed with 5% aluminium chloride solution and incubated for 30 min at room temperature. Absorbance was read at 415 nm. Quercetin was used as the standard, and results were expressed as mg quercetin equivalent (QE)/g extract.[9]

Thin Layer Chromatography (TLC) Analysis[10]

TLC was performed on silica gel 60 F_{254} plates (20 × 20 cm). The mobile phase for flavonoid detection was ethyl acetate: formic acid: glacial acetic acid:water (10:1.1:1.1:2.6 v/v/v/v). For alkaloid detection, chloroform: methanol: ammonia (90:10:1 v/v/v) was used. Plates were pre-saturated in a chamber for 30 min before development. Spots were visualized under UV light (254 nm and 365 nm) after spraying with respective detecting reagents. Rf values were calculated using the formula:

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Rf value = Distance travelled by solute /Distance travelled by the solvent

Synthesis of Silver Nanoparticles (AgNPs)

A 1 mM aqueous silver nitrate ($AgNO_3$) solution was prepared. The *Lippia nodiflora* extract (10 mL, 1 mg/mL) was added dropwise to 90 mL of $AgNO_3$ solution under constant stirring at room temperature. The reaction was allowed to proceed for 24 h, during which a change in color from pale yellow to dark brown indicated nanoparticle formation. The synthesized AgNPs were collected by centrifugation at 12,000 rpm for 20 min, washed thrice with distilled water, and dried at 40 °C.

Characterization of Silver Nanoparticles

Particle size and distribution were determined by Dynamic Light Scattering (DLS) using a Malvern Zetasizer Nano ZS at 25 °C and 173° scattering angle. The nanoparticles were redispersed in deionized water, sonicated, and analyzed to obtain mean size (z-average) and polydispersity index (PDI), indicating size uniformity. Zeta potential was measured on the same instrument to assess surface charge and colloidal stability. Values greater than +30 mV or less than –30 mV suggest stable dispersions due to electrostatic repulsion. In this study, the negative zeta potential implied adsorption of anionic phytochemicals from *Lippia nodiflora*, providing stability and preventing aggregation. Such stability is essential for consistent performance in transdermal applications.

Antioxidant Activity

The antioxidant potential of biosynthesized silver nanoparticles (AgNPs) from *Lippia nodiflora* was assessed using two widely employed *in vitro* assays — DPPH radical scavenging and nitric oxide scavenging. Both assays were performed in triplicate, and results were expressed as percentage inhibition relative to a standard antioxidant (ascorbic acid). The inhibitory concentration values were calculated to compare the radical scavenging efficiency.

DPPH Radical Scavenging Assay

A 0.1 mM solution of 2,2-diphenyl-1-picrylhydrazyl (DPPH) was freshly prepared in methanol. Different concentrations of AgNPs (10, 20, 40, 60, 80, and 100 µg/mL) were prepared in methanol. To 1 mL of each sample, 1 mL of the DPPH solution was added and mixed thoroughly. The reaction mixtures were incubated in the dark at room temperature (25 ± 2 °C) for 30 min to allow complete interaction between the antioxidants and DPPH radicals. Absorbance was measured at 517 nm using a UV–visible spectrophotometer against methanol as the blank. Ascorbic acid was used as the positive control.[11] The percentage radical scavenging activity was calculated using the formula:

Percentage inhibition = (Abs control − Abs sample)/Abs control × 100

8.2 Nitric Oxide Scavenging Assay

Nitric oxide (NO) scavenging activity was determined using sodium nitroprusside (SNP) as a NO donor. A 10 mM SNP solution was prepared in phosphate-buffered saline (PBS, pH 7.4). Various concentrations of AgNPs (10–100 µg/mL) were added to 2 mL of SNP solution and incubated at 25 ± 2 °C for 2 h under light to induce NO production. After incubation, 0.5 mL of the reaction mixture was mixed with 0.5 mL of Griess reagent (1% sulfanilamide in 5% phosphoric acid and 0.1% naphthylethylenediamine dihydrochloride) and allowed to stand for 10 min at room temperature. The absorbance was measured at 546 nm using a UV–visible spectrophotometer. [12] Ascorbic acid served as the positive control. The percentage inhibition was calculated using the same formula as for the DPPH assay.

Percentage inhibition = (Abs control − Abs sample)/Abs control × 100

Formulation of Transdermal Patches.

Transdermal patches were prepared by the solvent casting method using hydroxypropyl methylcellulose (HPMC) as the film-forming polymer and glycerol as the

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plasticizer. HPMC was dissolved in distilled water under continuous stirring until a uniform viscous solution was obtained. The calculated amount of biosynthesized AgNPs, equivalent to the required therapeutic dose, was dispersed in the polymer solution using a magnetic stirrer to ensure homogeneous distribution. The final mixture was poured into a glass Petri dish (10 cm diameter) and spread evenly. The patches were dried at ambient temperature (25 ± 2 °C) for 48 h in a dust-free environment to allow solvent evaporation. Once dried, the patches were carefully peeled off, cut to the required dimensions, and stored in a desiccator containing silica gel until further evaluation.[12]

In Vitro Drug Release Study

The drug release profile of the prepared *Lippia nodiflora* silver nanoparticle transdermal patches was evaluated using a Franz diffusion cell. The receptor compartment was filled with 20 mL phosphate buffer solution (pH 7.4) maintained at 37 ± 0.5°C and stirred continuously at 600 rpm. A section of the patch (known surface area) was mounted on the donor compartment, with the release surface facing the receptor medium. At predetermined time intervals, 1 mL of sample was withdrawn from the receptor compartment and immediately replaced with fresh buffer of equal volume to maintain sink conditions. The withdrawn samples were filtered, and drug concentration was determined using a UV–visible spectrophotometer at λmax specific to the active compound.

Release Kinetics

The cumulative percentage drug release data were fitted into various mathematical models — zero-order, first-order, Higuchi, and Korsmeyer–Peppas — to elucidate the release mechanism. Zero-order and first-order models describe constant and concentration-dependent release, respectively, while the Higuchi model explains release governed by Fickian diffusion from a matrix. The Korsmeyer–Peppas model was applied to determine the diffusion exponent (n), which differentiates between Fickian diffusion (n ≤ 0.5), anomalous (non-Fickian) transport (0.5 < n < 1.0), and Case-II transport (n = 1). The best-fit model was determined based on the highest correlation coefficient (R^2) values.[13]

Results and Discussion

Percentage yield

The percentage yield was found to be 30.4 % w/w.

2. Phytochemical Screening

Qualitative analysis of the ethyl acetate extract of *Lippia nodiflora* revealed the presence of alkaloids, flavonoids, phenols, tannins, saponins, steroids, and glycosides (Table 1). These phytoconstituents have been widely reported for their antimicrobial (alkaloids, tannins), antioxidant (phenols, flavonoids), and wound healing (flavonoids, saponins) activities. The diversity of bioactive compounds in the extract supports its potential as a multifunctional wound healing agent.

1. Total Phenolic Content

The total phenolic content of the ethyl acetate extract of *Lippia nodiflora* was determined using the Folin–Ciocalteu method with gallic acid as the standard. At concentrations of 500 and 1000 µg/mL, absorbance values were recorded as 1.227 and 2.446, respectively, corresponding to a phenolic content of 7.5 mg GAE/g extract (Graph 1). This relatively high phenolic

Table 1: Preliminary phytochemical screening of *Lippia nodiflora* ethyl acetate extract

S.NO	CHEMICAL TESTS	OBSERVATION
1	Carbohydrates	+
2	Proteins	+
3	Amino acid	+
4	Alkaloids	+
5	Flavonoids	+
6	Steroids	+
7	Tannins	+
8	Saponin	+
9	Cardiac glycosides	+
10	Anthraquinones	-

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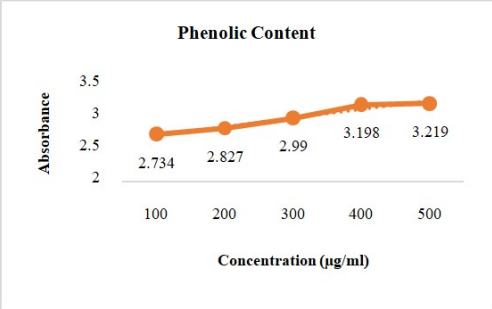
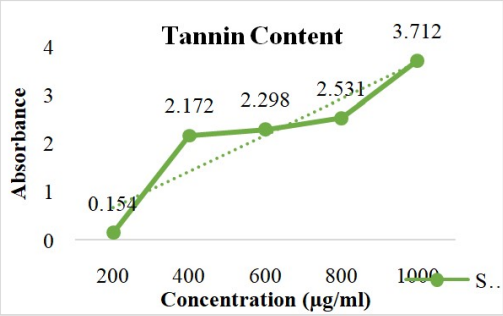


Graph 1: Phenolic content of gallic acid standard solution

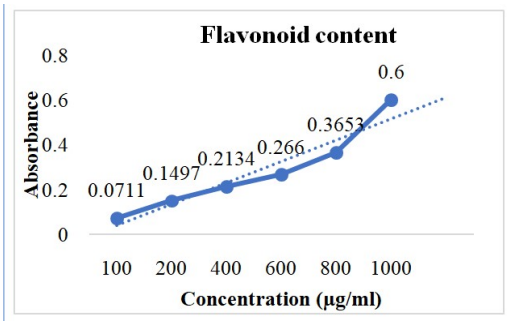


Graph 2: Phenolic content of *Lippia nodiflora* ethyl acetate extract

concentration reflects the abundance of bioactive antioxidant compounds in the extract. Phenolics are known for their capacity to neutralize reactive oxygen species (ROS) through hydrogen atom donation and metal ion chelation, preventing oxidative stress-induced damage to cellular components. Such protection is essential in wound healing, as oxidative stress can impair fibroblast proliferation, collagen deposition, and angiogenesis. The results obtained here are in agreement with previous reports where phenolic-rich extracts enhanced tissue regeneration and reduced healing time, thus supporting the potential application of *Lippia nodiflora* extract in antioxidant-based wound healing therapies.

2. Total Tannin Content

The total tannin content of the ethyl acetate extract of *Lippia nodiflora* was quantified using gallic acid as the standard, with absorbance values ranging from 0.154 at 200 µg/mL to 2.722 at 1000 µg/mL. The tannin content was found to be 50 mg GAE/g extract (Graph 2). Tannins exhibit strong astringent, antimicrobial, and antioxidant properties, enabling them to precipitate proteins and form a protective layer over wounds, thereby reducing microbial invasion and enhancing the healing process. Their antioxidant activity also helps in quenching free radicals and reducing inflammation, creating a favorable environment for tissue repair. The high tannin concentration observed here aligns with literature reports



Graph 3: Flavonoid content of tannic acid standard solution

where tannin-rich herbal extracts accelerated wound contraction and epithelialization by both antimicrobial and anti-inflammatory pathways. This suggests that the tannins in *Lippia nodiflora* may act synergistically with phenolics to promote effective wound healing.

Estimation of Flavonoid Content

The total flavonoid content of the ethyl acetate extract of *Lippia nodiflora* was determined using tannic acid as the standard (Graph 3). The flavonoid concentration was calculated from the calibration curve, and the extract was found to contain 60 mg QE/g. Flavonoids are known for their potent antioxidant, anti-inflammatory, and antimicrobial activities, all of which are beneficial in wound healing. Their antioxidant capacity arises from their ability to scavenge reactive oxygen species (ROS), thereby protecting cells from oxidative damage that

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can delay tissue repair. Additionally, flavonoids promote collagen synthesis, angiogenesis, and fibroblast proliferation, which accelerate the healing process. The high flavonoid content observed in the extract suggests its potential to enhance tissue regeneration and support faster wound closure, consistent with earlier studies on flavonoid-rich herbal formulations.

Thin Layer Chromatography (TLC)

Thin-layer chromatography (TLC) of the *Lippia nodiflora* ethyl acetate extract revealed distinct spots corresponding to flavonoids and alkaloids, with Rf values of 0.890 and 0.450, respectively (Figs. 1–2). These values, when compared with literature-reported standards, confirm the presence of these phytochemical classes in the extract. The higher Rf value of flavonoids suggests greater polarity compared to alkaloids under the selected solvent system. The detection of both classes is significant, as flavonoids are known to promote angiogenesis, collagen synthesis, and antioxidant defense, while alkaloids possess antimicrobial and anti-inflammatory properties. Together, these compounds contribute to a synergistic therapeutic effect in wound healing. Similar TLC profiles have been reported for medicinal plants with proven bioactivity, supporting the qualitative richness of *Lippia nodiflora* and its potential as a bioactive source for nanoparticle synthesis and transdermal delivery applications.

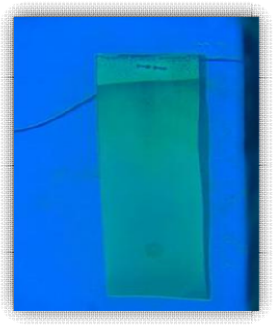

Fig. 1: Thin layer chromatography (TLC) plate showing flavonoid spots in *Lippia nodiflora* ethyl acetate extract

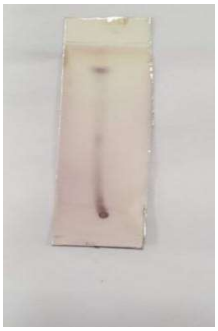

Fig. 2: Thin layer chromatography (TLC) plate showing alkaloid spots in *Lippia nodiflora* ethyl acetate extract

Particle Size and Zeta Potential

Dynamic Light Scattering (DLS) analysis of the synthesized silver nanoparticles (AgNPs) from *Lippia nodiflora* extract revealed a mean particle size of 355.3 nm with a narrow distribution. Zeta potential measurement showed a surface charge of –28.4 mV, indicating good colloidal stability due to electrostatic repulsion between particles. The particle size obtained is within the range suitable for topical delivery, ensuring effective skin penetration while maintaining stability in suspension. A negative zeta potential close to –30 mV suggests that the nanoparticles are unlikely to aggregate rapidly, which is advantageous for consistent drug release and bioactivity. The stability is likely enhanced by phytochemicals from *Lippia nodiflora* acting as natural capping agents, as reported in similar plant-mediated AgNP syntheses. This stability, combined with the bioactive surface chemistry, enhances the therapeutic potential of the nanoparticles for wound healing applications.

Antioxidant Activity

DPPH Radical Scavenging Activity

The DPPH assay demonstrated that silver nanoparticles synthesized from *Lippia nodiflora* exhibited strong, concentration-dependent free radical scavenging activity (Graph 4). The percentage inhibition increased

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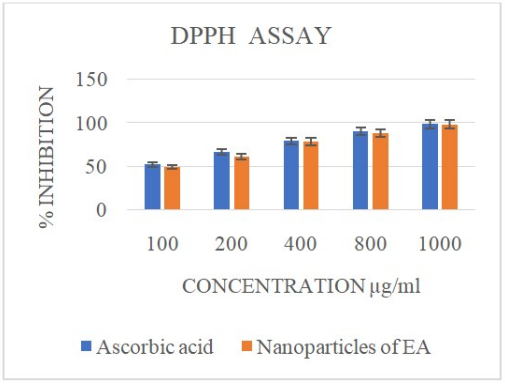
from 49.63% at 100 µg/mL to 98.38% at 1000 µg/mL, with an IC_{50} value of 95.69 µg/mL, which is comparable to the standard ascorbic acid. The high scavenging efficiency can be attributed to the synergistic interaction between silver nanoparticles and phenolic/flavonoid-rich phytochemicals capping their surface, which readily donate hydrogen atoms to neutralize DPPH radicals. This activity is crucial for wound healing, as neutralization of reactive oxygen species (ROS) minimizes oxidative stress, prevents damage to cellular macromolecules, and supports fibroblast proliferation and collagen synthesis. Comparable findings in previous studies have shown that plant-mediated AgNPs with high phenolic content accelerate wound closure through both antioxidant and anti-inflammatory pathways, supporting the therapeutic relevance of the present formulation.

5. Nitric Oxide Radical Scavenging Activity

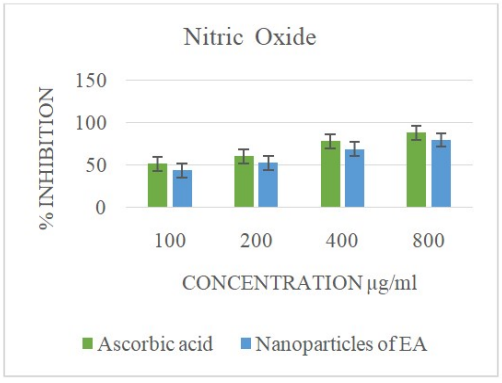
Nitric oxide scavenging activity results revealed that *Lippia nodiflora*-derived silver nanoparticles effectively inhibited nitric oxide radicals in a concentration-dependent manner (Graph 5). The percentage inhibition increased from 43.16% at 100 µg/mL to 96.07% at 1000 µg/mL, with an IC_{50} value of 97.88 µg/mL, which is also comparable to ascorbic acid. Excess nitric oxide in wounds can lead to peroxynitrite formation, causing oxidative tissue damage and prolonging inflammation. The observed scavenging effect suggests that the nanoparticles can regulate nitric oxide levels, thereby reducing oxidative damage and modulating the inflammatory phase of wound healing. The presence of phenolics and flavonoids on the nanoparticle surface likely enhances this bioactivity, working in synergy with silver's known antimicrobial and anti-inflammatory properties. Literature reports similarly confirm that nitric oxide scavenging contributes to improved wound contraction, reduced inflammation, and faster epithelialization, aligning with the current findings.

6. Evaluation of Transdermal Patches

The prepared transdermal patches (F1–F5) of *Lippia nodiflora* silver nanoparticles were evaluated for physicochemical parameters to ensure product uniformity and therapeutic reliability (Table 2). Patch weight ranged from 0.49 ± 0.2 mg (F2) to 0.54 ± 0.2 mg (F1), indicating minimal variation during casting. All formulations exhibited a yellowish-brown color, clear appearance, and flexible nature, suggesting good dispersion of nanoparticles and polymer homogeneity. Folding endurance values ranged from 100 ± 2 (F1) to 150 ± 2 (F5), demonstrating high mechanical strength for withstanding repeated bending without damage. The surface pH varied between 5.82 ± 0.1 (F5) and 8.15 ± 0.1(F3), with most



Graph 4: DPPH % inhibition of silver nanoparticles synthesized from *Lippia nodiflora*



Graph 5: Nitric oxide % inhibition of silver nanoparticles synthesized from *Lippia nodiflora*

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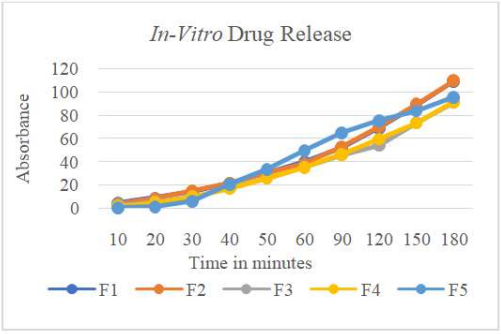
Table 2: Evaluation parameters of *Lippia nodiflora* transdermal patches

Evaluation Parameters / Formulation Code	Weight (mg)	Color	Clarity	Flexibility	Folding endurance	pH	Thickness (mm)	Drug content (%)
F1	0.50±0.2	Yellowish-brown	Clear	Flexible	100±2	7.9±0.1	55±4	85.12±0.1
F2	0.49±0.2	Yellowish-brown	Clear	Flexible	104±2	7.6±0.1	47±4	86.14±0.1
F3	0.52±0.2	Yellowish-brown	Clear	Flexible	120±25	8.15±0.1	51±4	80.94±0.1
F4	0.51±0.2	Yellowish-brown	Clear	Flexible	136±2	6.1±0.1	70±4	79.06±0.1
F5	0.53±0.2	Yellowish-brown	Clear	Flexible	150±2	5.28±0.1	42±4	90.04±0.1

values close to skin pH, reducing the risk of irritation. Thickness values were consistent, ranging from 42 ± 4 mm to 55 ± 4 mm, which is critical for maintaining drug release rates and mechanical performance. Drug content analysis revealed values between 79.06 ± 0.1**%** (F4) and 90.04 ± 0.1**%** (F5), meeting pharmacopeial limits for dosage uniformity. These results align with reported standards for transdermal patches, where optimal flexibility, pH compatibility, and high drug content contribute to effective drug permeation and patient comfort.

In Vitro Drug Release

The in vitro drug release study was performed for all prepared formulations (F1–F5) to evaluate the rate and extent of drug delivery from the transdermal patches (Table 3 & Graph 6). The cumulative percentage drug release after 24 hours was 88.36% for F1, 89.76% for F2, 91.28% for F3, 91.44% for F4, and 95.82% for F5. Among these, F5 exhibited the highest release, achieving maximum drug liberation within the initial 3 hours, which can be attributed to its optimal thickness (42 ± 4 mm), highest drug content (90.04 ± 0.1%), and favorable surface pH (5.82 ± 0.1), promoting enhanced diffusion. The uniform release



Graph 6: Cumulative % drug release profile for formulations F1–F5

Table 3: Release kinetics parameters for optimized formulation F5

Release kinetics model	Zero order	First order	Higuchi equation	Kosmeyer Peppas
R^2	0.9976	0.8405	0.9679	0.9951

pattern observed in all formulations indicates effective polymer–drug compatibility and sustained release potential. Based on these results, F5 was selected as the optimized formulation for further release kinetics studies.

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Drug Release Kinetics of Optimized Formulation (F5)

The release kinetics of F5 were analyzed using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models (Table 3). The correlation coefficients (R^2) were found to be 0.9976 for zero-order, 0.8405 for first-order, 0.9679 for Higuchi, and 0.9951 for Korsmeyer–Peppas, indicating that the drug release best fitted the zero-order model, signifying a constant release rate independent of drug concentration. The high R^2 value for the Higuchi model suggests that diffusion through the polymer matrix also contributes significantly to drug liberation. The Korsmeyer–Peppas analysis revealed an value indicating a non-Fickian (anomalous) diffusion mechanism, where both diffusion and polymer relaxation govern the release process. This kinetic profile confirms that the F5 patch is capable of providing controlled and sustained drug delivery, a desirable property for maintaining steady therapeutic levels.

Discussion

The phytochemical analysis of *Lippia nodiflora* confirmed the presence of alkaloids, flavonoids, phenols, tannins, saponins, steroids, and glycosides, all of which are well recognized for their antimicrobial, antioxidant, and wound-healing properties. The relatively high levels of flavonoids (60.0 mg QE/g) and phenolics (7.5 mg GAE/g) are likely responsible for enhancing both antioxidant activity and nanoparticle stabilization, in line with previous findings on plant-mediated AgNPs[15]. The biosynthesized AgNPs exhibited strong DPPH and nitric oxide scavenging activities, confirming their ability to modulate ROS, which is essential for reducing oxidative stress and supporting tissue repair.

These results are consistent with recent reports demonstrating that phytochemical-enriched AgNPs improve collagen deposition, regulate inflammation, and accelerate epithelialization[16,17]. The optimized formulation (F5) displayed sustained drug release with zero-order kinetics, a desirable characteristic for maintaining steady therapeutic levels at the wound site. Such controlled delivery minimizes infection risk while promoting faster tissue regeneration. Moreover, the high flavonoid content may confer additional protective effects against AgNP-induced oxidative stress, providing a synergistic balance between efficacy and safety[18,19]

Overall, these findings highlight the potential of *L. nodiflora*–mediated AgNP patches as multifunctional wound dressings with combined antimicrobial, antioxidant, and controlled-release properties. Future investigations should focus on *in vivo* wound-healing models, antimicrobial activity against multidrug-resistant pathogens, and comprehensive safety evaluations to establish clinical relevance and translational applicability.

Conclusion

This study successfully developed and evaluated a transdermal patch containing silver nanoparticles synthesized from the ethyl acetate extract of *Lippia nodiflora*. Phytochemical screening confirmed the presence of bioactive compounds such as flavonoids, phenols, and tannins, which are known for their antioxidant and wound healing properties. The biosynthesized silver nanoparticles exhibited strong free radical scavenging activity, while the optimized patch formulation (F5) demonstrated desirable physicochemical characteristics, high drug content, and a sustained *in vitro* drug release profile following non-Fickian diffusion kinetics. The combination of plant-derived phytoconstituents and silver nanoparticles presents a synergistic approach to wound management, offering antimicrobial, anti-inflammatory, and antioxidant benefits through a controlled transdermal delivery system. These findings highlight the therapeutic potential of *Lippia nodiflora*–based nanotechnology formulations for wound healing. Future work should focus on *in vivo* wound healing studies, detailed antimicrobial evaluations, and clinical investigations to validate efficacy, safety, and scalability for pharmaceutical applications.

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