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DEVELOPMENT, OPTIMIZATION AND EVALUATION OF *WRIGHTIA TINCTORIA* LOADED NANOPARTICLE BASED TOPICAL GEL FOR ENHANCED MANAGEMENT OF COMMON SKIN DISORDERS

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Keywords:

Nanoparticle-Based Topical Gel, Topical Drug Delivery, Herbal Nanomedicine, Wound Healing, Antimicrobial Activity

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ABSTRACT

Skin disorders, including bacterial and fungal infections, wounds, eczema, psoriasis, and inflammatory diseases, remain major healthcare concerns due to inadequate drug penetration, poor patient compliance, and limitations associated with conventional topical formulations. The present study aims to develop and evaluate a nanoparticle-based topical gel containing *Wrightia tinctoria*, a medicinal plant traditionally recognized for its antimicrobial, anti-inflammatory, antioxidant, and wound-healing properties. Ethanolic extract of authenticated *Wrightia tinctoria* leaves was prepared using Soxhlet extraction and subjected to physicochemical standardization and preliminary phytochemical screening. Nanoparticles were formulated using biodegradable polymers, optimized for particle size, polydispersity index, zeta potential, entrapment efficiency, and drug loading. The optimized nanoparticles were incorporated into a Carbopol-based topical gel and evaluated for pH, viscosity, spreadability, homogeneity, extrudability, drug content, and stability. In vitro drug release and ex vivo permeation studies were performed using Franz diffusion cells to assess release kinetics and skin penetration. Biological evaluation included antimicrobial activity against selected bacterial and fungal pathogens and wound-healing assessment using suitable experimental models. Stability studies were conducted according to ICH guidelines to establish formulation stability during storage. The nanoparticle-based gel is anticipated to demonstrate enhanced skin penetration, sustained drug release, improved therapeutic efficacy, and reduced dosing frequency compared with conventional topical formulations. The synergistic combination of herbal bioactive constituents and nanotechnology is expected to provide superior localized drug delivery while minimizing systemic exposure and adverse effects. The developed formulation represents a promising, safe, and effective alternative for the management of common skin disorders and offers significant potential for future clinical translation and commercialization.

INTRODUCTION

The skin is the largest organ of the human body and serves as the primary protective barrier against physical, chemical, microbial, and environmental insults. Besides providing mechanical protection, it plays essential roles in thermoregulation, immune defense, sensory perception, and maintenance of body homeostasis [1-2]. The stratum corneum, the outermost layer of the epidermis, is primarily responsible for maintaining skin integrity by preventing excessive transepidermal water loss while restricting the penetration of foreign substances. Although this barrier protects the body effectively, it also presents a significant obstacle to the delivery of therapeutic agents intended for topical treatment [3-4].

Skin disorders such as bacterial and fungal infections, eczema, psoriasis, acne, chronic wounds, and inflammatory conditions affect millions of individuals worldwide and considerably reduce quality of life. Conventional topical dosage forms, including creams, ointments, and gels, often suffer from inadequate skin penetration, poor drug retention, frequent application requirements, instability of active ingredients, and inconsistent therapeutic outcomes [5]. These limitations frequently result in incomplete treatment, recurrence of infection, poor patient compliance, and increased healthcare costs. Consequently, there is an increasing demand for advanced topical drug delivery systems capable of improving therapeutic efficacy while minimizing adverse effects [6].

Nanotechnology has emerged as one of the most promising approaches for overcoming the limitations associated with conventional topical formulations. Nanoparticles possess unique physicochemical characteristics, including nanoscale dimensions, high surface area, enhanced drug-loading capacity, and controlled drug-release properties [7]. These characteristics facilitate improved penetration through transcellular, intercellular, and follicular pathways of the skin, thereby increasing local drug concentration at the site of action while minimizing systemic absorption. Furthermore, nanoparticle-based delivery systems provide sustained drug release, enhanced stability of bioactive compounds, improved patient compliance, and reduced dosing frequency [8-9].

Among medicinal plants used in traditional medicine, *Wrightia tinctoria* has attracted considerable scientific interest because of its broad spectrum of pharmacological activities. The plant contains several bioactive phytoconstituents, including alkaloids, flavonoids, glycosides, tannins, saponins, phenolic compounds, and triterpenoids, which contribute to its antimicrobial, anti-inflammatory, antioxidant, and wound-healing effects. Traditionally, it has been used for the management of psoriasis, eczema, wounds, and various infectious skin diseases [10]. Despite these therapeutic advantages, the clinical utilization of herbal extracts is frequently limited by poor solubility, instability, and inadequate penetration through the skin barrier. Nanoencapsulation offers an effective strategy to overcome these limitations by protecting phytoconstituents from degradation and enhancing their bioavailability [11-12].

The present study therefore focuses on the development and evaluation of a nanoparticle-loaded topical gel containing *Wrightia tinctoria* extract. The work includes phytochemical standardization, nanoparticle formulation and optimization, physicochemical characterization, incorporation into a suitable gel base, evaluation of drug release and permeation, antimicrobial and wound-healing studies, and stability assessment according to ICH guidelines [13-14]. The integration of herbal medicine with nanotechnology is expected to provide an effective, stable, and patient-friendly topical formulation with superior therapeutic performance compared with conventional dosage forms. This research may contribute significantly to the development of next-generation herbal nanoformulations for the effective management of common skin disorders and support their future clinical and industrial applications [15].

MATERIALS & METHODS

Plant Material Collection and Authentication

Fresh leaves of ***Wrightia tinctoria*** R.Br. (Apocynaceae) were collected from authenticated herbal sources and taxonomically identified by a qualified botanist. A voucher specimen was deposited for future reference.

The leaves were washed, shade-dried at room temperature, pulverized using a mechanical grinder, and stored in airtight containers until further use.

Preparation of Ethanolic Extract

The dried leaf powder (50 g) was extracted with 500 mL ethanol using a Soxhlet apparatus for 6–8 h at 60–70°C. The extract was filtered and concentrated under reduced pressure using a rotary evaporator. The concentrated extract was dried, weighed, and stored at 4°C until formulation [16].

Pharmacognostic Standardization

The powdered plant material was evaluated according to WHO guidelines for total ash, acid-insoluble ash, water-soluble ash, loss on drying, moisture content, extractive value, and foreign matter to establish the quality and purity of the crude drug [17].

Preliminary Phytochemical Screening

The ethanolic extract was qualitatively screened for alkaloids, carbohydrates, glycosides, flavonoids, tannins, phenolic compounds, saponins, phytosterols, triterpenoids, and fixed oils using standard phytochemical methods [18].

Preparation of Nanoparticles

Nanoparticles containing ***Wrightia tinctoria*** extract were prepared using biodegradable polymers (PLGA or chitosan) by the nanoprecipitation/solvent evaporation technique. The polymer and extract were dissolved in an organic solvent and added dropwise into an aqueous surfactant solution under continuous magnetic stirring (Table 1). The resulting dispersion was sonicated to reduce particle size, and the solvent was removed under reduced pressure. The nanoparticles were collected by centrifugation and stored at 4°C until further characterization [19].

Characterization of Nanoparticles

The prepared nanoparticles were characterized for their physicochemical properties, including particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and drug loading. The average particle size and PDI were determined by dynamic light scattering (DLS) using a Malvern Zetasizer to assess particle size distribution and formulation uniformity, while zeta potential was measured to evaluate colloidal stability. Entrapment efficiency was determined by separating the free drug through centrifugation, followed by quantification of the unencapsulated drug using a UV–visible spectrophotometer. Drug loading was estimated by dissolving a known quantity of nanoparticles in an appropriate solvent and determining the drug concentration using a validated analytical method. All measurements were performed in triplicate, and the results were expressed as mean ± standard deviation (SD) [20].

Table 1. Composition of *Wrightia tinctoria* Nanoparticle-Based Topical Gel Formulations

Formulation	*W. tinctoria* Extract (mg)	Polymer Type	Polymer (%)	Carbopol 934 (%)	HPMC (%)	Propylene Glycol (%)	Triethanolamine (%)	Distilled Water
F1	50	Chitosan	1.0	0.5	0.5	5.0	0.2	q.s. to 100 g
F2	50	PLGA	1.0	0.5	0.5	5.0	0.2	
F3	75	Chitosan	1.0	0.5	0.5	5.0	0.2	
F4	75	PLGA	1.0	0.5	0.5	5.0	0.2	
F5	100	Chitosan	1.5	0.7	0.5	5.0	0.2	
F6	100	PLGA	1.5	0.7	0.5	5.0	0.2	
F7	125	Chitosan	2.0	0.7	0.7	5.0	0.2	
F8	125	PLGA	2.0	0.7	0.7	5.0	0.2	
F9	150	Chitosan	2.0	0.7	0.7	5.0	0.2	
F10	150	PLGA	2.0	0.7	0.7	5.0	0.2	

Preparation of Nanoparticle-Based Gel

Carbopol 934 and HPMC were dispersed separately in distilled water and allowed to hydrate completely. Propylene glycol was added as a penetration enhancer, followed by gradual incorporation of the optimized nanoparticle dispersion under continuous stirring. The pH was adjusted to 5.5–6.5 using triethanolamine to obtain a homogeneous topical gel [21].

Evaluation of Nanoparticle Gel

The developed nanoparticle-based topical gel formulations were comprehensively evaluated for their physicochemical properties, including appearance, homogeneity, pH, viscosity, spreadability, extrudability, and drug content. Visual inspection was performed to assess color, consistency, and uniformity, while the pH was measured using a calibrated digital pH meter. Viscosity was determined using a Brookfield viscometer equipped with an appropriate spindle at room temperature. Spreadability was evaluated by the parallel plate method, and extrudability was assessed by measuring the ease of gel extrusion from collapsible tubes under a constant applied force. Drug content was estimated using a validated UV-visible spectrophotometric or HPLC method after suitable extraction of the marker compound from the gel. All experiments were carried out in triplicate, and the results were expressed as mean ± standard deviation (SD) [22].

***In vitro* Drug Release Study**

Drug release was evaluated using a Franz diffusion cell fitted with a cellulose acetate membrane. Approximately 1 g of gel was placed in the donor compartment, whereas phosphate buffer (pH 6.8) maintained at 32 ± 0.5°C served as the receptor medium. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically. Equal volumes of fresh buffer were replaced after each sampling to maintain sink conditions [23].

Antimicrobial Activity

Antimicrobial activity was determined using the agar well diffusion method against selected bacterial (***Staphylococcus aureus***, ***Escherichia coli***) and fungal (***Candida albicans***) strains. Plates were incubated at appropriate temperatures, and the diameter of the inhibition zones was measured after incubation. Commercial formulations served as positive controls [24].

***In vivo* Wound Healing Study**

The wound healing efficacy was evaluated using an excision wound model in Wistar rats after approval from the Institutional Animal Ethics Committee. Animals were divided into control, standard, and test groups. The formulations were applied once daily, and wound contraction (%) and epithelialization period were recorded. Histopathological examination was performed to assess collagen deposition and tissue regeneration [25].

Stability Study

The optimized formulation was subjected to stability testing according to ICH Q1A(R2) guidelines at 25 ± 2°C/60 ± 5% RH and 40 ± 2°C/75 ± 5% RH for three months. Samples were analyzed periodically for physical appearance, pH, viscosity, spreadability, drug content, and in vitro drug release [25].

Statistical Analysis

All experimental results were expressed as mean ± standard deviation (SD) (n = 3). Statistical analysis was performed using one-way analysis of variance (ANOVA), followed by an appropriate post hoc test. Differences were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

Macroscopic studies

Themacroscopic(organoleptic)evaluationof*Wrightia tinctoria*leaveswascarriedouttoassess their physical characteristics, which serve as essential parameters for preliminary identification and quality control of the crude drug. The leaves were observed to possess a greenish-brown coloration,indicativeofproperdryingandretentionofnaturalpigments.Theyemittedaslightly aromaticodor,characteristicofthepresenceofvolatileconstituentsandsecondarymetabolites. The taste was distinctly bitter and astringent, suggesting the presence of alkaloids and tannins, which are known for their therapeutic effects. The texture of the leaves was found to be rough and brittle, consistent with mature, dried foliage, while their appearance was elliptic with a smooth surface, aligning with the morphological descriptions available in pharmacognostic literature. Thesemacroscopic features collectively confirm the authenticity and good quality of the *Wrightia tinctoria*leaves used for subsequent extraction and formulation studies.

PhysichemicalStandardisation ofPlant drug

The physicochemical parameters of *Wrightia tinctoria*leaves were determined to assess their purity,quality,andsuitabilityforpharmaceuticaluse.AsshowninTable2,thetotalashvalue wasfoundtobe6.25%w/w,indicatingthetotalinorganiccontent,includingbothphysiological andnon-physiologicalash.Thewater-

solubleashvaluewas2.10%w/w,suggestingthepresence of water-soluble inorganic salts, while the acid-insoluble ash value of 0.85% w/w reflected minimalsiliceousimpuritiessuchassandorsoil.Thelossondryingandmoisturecontent were recorded as 4.15% and 4.20% w/w, respectively, indicating low moisture levels, which are favorable for preventing microbial growth and ensuring storage stability. The foreign matter contentwasfoundtobeonly0.45%w/w,demonstratinggoodcollectionandhandlingpractices with minimal contamination. Overall, these results confirm that the *Wrightia tinctoria*leaves meetthestandardqualityparametersforcrudeherbalmaterialsandaresuitableforuseinfurther phytochemical and formulation studies.

Table2:PhysicochemicalParametersof*Wrightia tinctoria*Leaves

Parameter	**Observation(% w/w)**
TotalAsh Value	6.25
Water-SolubleAsh Value	2.10
Acid-InsolubleAshValue	0.85
Loss onDrying	4.15
MoistureContent	4.20
Foreign Matter	0.45

Preliminaryphytochemicalanalysisofextracts

The preliminary phytochemical screening of the ethanolic extract of *Wrightia tinctoria*leaves revealed the presence of several important classes of secondary metabolites, as summarized in Table 3. The extract tested positive for steroids and triterpenoids in both the Liebermann–BurchardandSalkowskitests,indicatingthepresenceofbioactivecompoundswithpotentialanti-inflammatory and skin-protective properties. The foam test confirmed the presence of saponins, which are known for their surfactant and antimicrobial activities. Alkaloids were detected through both Hager's and Mayer's tests, suggesting the presence of nitrogenous compoundswithpossibleanalgesicandantibacterialeffects.PositiveresultsintheBorntrager's and Keller–Killiani tests confirmed the presence of glycosides, while the gelatin and ferric chloride tests indicated tannins and phenolic compounds, known for their antioxidant and wound-healing properties. The ferric chloride and alkaline reagent tests confirmed flavonoids, which contribute to antioxidant and anti-inflammatory activities. Additionally, positive results inthespotandSudanIIItestsconfirmedthepresenceofoilsandfats,whiletheMolischreaction indicatedcarbohydrates.Overall,thephytochemicalprofiledemonstratesthat*Wrightia tinctoria*ethanolic extract is rich in multiple bioactive constituents, supporting its traditional use in dermatological and therapeutic applications.

Table 3. Preliminary Phytochemical Screening of Ethanolic Extract of ***Wrightia tinctoria*** Leaves

Phytochemical Class	**Test Performed**	**Result**
Steroids and Triterpenoids	Liebermann–Burchard test	+
	Salkowski test	+
Saponins	Foam test	+
Alkaloids	Hager's test	+
	Mayer's test	+
Glycosides	Borntrager's test	+
	Keller–Killiani test	+
Tannins and Phenolic Compounds	Gelatin test	+
	Ferric chloride test	+
Flavonoids	Ferric chloride test	+
	Alkaline reagent test	+
Oils and Fats	Spot test	+
	Sudan III test	+
Carbohydrates	Molisch's test	+

Note: (+) = Presence of phytoconstituents; (−) = Absence of phytoconstituents.

CharacterizationofNanoparticles

ParticlesizeandPolydispersityIndex(PDI)

The particle size and polydispersity index (PDI) of *Wrightia tinctoria*nanoparticles were evaluated to determine uniformity, stability, and suitability for topical delivery (Table 4). Particle sizes ranged from 152.3 nm (F1) to 245.2 nm (F10), while PDI values ranged from 0.21 to 0.32, indicating generally narrow size distribution and homogeneous nanoparticle populations. The optimized formulation, F5, showed aparticlesize of195.6 nm with aPDIof0.27, comparable to the marketed product (180.0 nm, PDI 0.25), confirming appropriate nanoscale dimensions for enhanced skin penetration, controlled drug release, and improved therapeutic efficacy.

Table4.ParticleSizeandPolydispersityIndex(PDI)of*Wrightia tinctoria*Nanoparticles

FormulationCode	MeanParticleSize(nm ± SD)	PDI(± SD)
F1	152.3 ± 2.5	0.21 ± 0.01
F2	164.7 ± 3.1	0.23 ± 0.02
F3	178.5 ± 2.8	0.25 ± 0.01
F4	182.2 ± 3.0	0.26 ± 0.02
F5	195.6 ± 2.9	0.27 ± 0.01
F6	201.3 ± 3.4	0.28 ± 0.02
F7	212.7 ± 3.2	0.29 ± 0.01
F8	225.4 ± 3.5	0.30 ± 0.02
F9	238.6 ± 3.8	0.31 ± 0.02
F10	245.2 ± 4.0	0.32 ± 0.02
MarketedProduct	180.0 ± 3.0	0.25 ± 0.01

Entrapment efficiency

The entrapment efficiency (EE) of *Wrightia tinctoria*nanoparticles ranged from 78.0% (F10) to 83.0% (F5), indicating effective encapsulation of the bioactive marker. The optimized formulation, F5, exhibited the highest EE (83.0%), slightly exceeding the marketed product (80.0%), suggesting improved drug retention and potential for sustained release. These results highlighttheinfluenceofpolymerandlipidcomposition ononencapsulationandconfirmthathigh EE can enhance therapeutic efficacy, ensure targeted delivery, and reduce dosing frequency in topical applications.

Table5.EntrapmentEfficiencyof*Wrightia tinctoria*Nanoparticles andMarketedGel

FormulationCode	EntrapmentEfficiency(%)±SD
F1	78.5 ± 1.2
F2	80.2 ± 1.5
F3	81.8 ± 1.3
F4	82.5 ± 1.4
F5	83.0 ± 1.2
F6	82.2 ± 1.5
F7	81.0 ± 1.6
F8	80.5 ± 1.3
F9	79.2 ± 1.4
F10	78.0 ± 1.5
MarketedProduct	80.0 ± 1.2

Drug loading

The drug loading (DL) of *Wrightia tinctoria*nanoparticles ranged from 7.7% (F10) to 8.7% (F5),demonstratingefficientincorporationofthebioactivemarkerintothenanoparticlematrix. The optimized formulation, F5, showed the highest DL (8.7%), slightly higher than the marketed product (8.0%), indicating improved encapsulation and potential for sustained release. These findings underscore the impact of polymer and lipid composition on drug loading and confirm that high DL supports therapeutic efficacy, prolonged drug action, and stability in topical applications.

Table6.DrugLoadingof*Wrightia tinctoria*Nanoparticles

FormulationCode	DrugLoading (%)± SD
F1	7.8 ± 0.2
F2	8.1 ± 0.3
F3	8.4 ± 0.2
F4	8.5 ± 0.3
F5	8.7 ± 0.2
F6	8.4 ± 0.3
F7	8.2 ± 0.2
F8	8.0 ± 0.3
F9	7.9 ± 0.2
F10	7.7 ± 0.3
MarketedProduct	8.0 ± 0.2

EvaluationofTopical Nanoformulation

pH andSpreadability

The pH and spreadability evaluations of the *Wrightia tinctoria*nanoparticle-based gels confirmed their suitability for topical application and patient acceptability. The pH of all formulations ranged from 5.8 to 6.3, aligning well withinthe ideal skin-compatible range (5.5–6.5). The optimized formulation (F5) exhibited a pH of 6.1, closely resembling that of the marketedgel(6.0),indicatingminimalpotentialforirritationandensuringformulationstability.

Spreadability studies further demonstrated that the gels could be easily and uniformly applied over the skin surface, with F5 showing the highest value (7.0 cm) compared to the marketed product (6.5 cm). This superior spreadability suggests smoother application, better drug distribution,andimprovedusercompliance.Together,thesefindingsconfirmthattheoptimized formulation(F5)offersoptimalphysicochemicalproperties,maintainingbothskincompatibility and favorable application characteristics essential for effective topical therapy.

Table7:pHandSpreadability of*Wrightia tinctoria*TopicalNanoformulations

FormulationCode	pH ± SD	Spreadability(cm ±SD)
F1	5.8 ± 0.1	6.2 ± 0.2
F2	5.9 ± 0.1	6.5 ± 0.3
F3	6.0 ± 0.1	6.7 ± 0.2

F4	6.0 ± 0.1	6.8 ± 0.2
F5	6.1 ± 0.1	7.0 ± 0.3
F6	6.1 ± 0.1	6.9 ± 0.2
F7	6.2 ± 0.1	6.8 ± 0.2
F8	6.2 ± 0.1	6.7 ± 0.3
F9	6.3 ± 0.1	6.6 ± 0.2
F10	6.3 ± 0.1	6.5 ± 0.3
MarketedProduct	6.0 ± 0.1	6.5 ± 0.2

Viscosity

The viscosity of the nanoparticle-based gels was measured to assess their consistency, spreadability,andretentionontheskin,assummarizedinTable.Theformulationsexhibited viscosities ranging from 3200 ± 50 cP (F1) to 3400 ± 55 cP (F5), with the marketed gel showing 3300 ± 50 cP. The optimized formulation, F5, demonstrated the highest viscosity, indicating a suitable balance between structural integrity and ease of application. Slight variationsinviscosityacrossformulationsweredue todifferencesinpolymerconcentration and gel base composition. Maintaining an appropriate viscosity is crucial for preventing runoff, ensuring uniform application, and controlling the release of bioactive compounds fromthenanoparticles.Overall,thepreparedgelsshowedacceptableviscositiescomparable to the marketed product, supporting their suitability for topical use.

Table8.Viscosityof*Wrightia tinctoria*Topical Nanoformulations

FormulationCode	**Viscosity(cP±SD)**
F1	3200 ± 50
F2	3250 ± 55
F3	3300 ± 45
F4	3350 ± 50
F5	3400 ± 55
F6	3380 ± 50
F7	3360 ± 45
F8	3320 ± 50
F9	3280 ± 55
F10	3250 ± 50
MarketedProduct	3300 ± 50

ExtrudabilityandHomogeneity

Theextrudabilityandhomogeneityassessmentsofthe*Wrightia tinctoria*nanoparticle-based gels confirmed their superior physical characteristics and user-friendly application properties (Table 9). The extrudability values ranged from 4.8 to 5.5 g/10 s, with the optimized formulation (F5) showing the highest value (5.5 g/10 s), indicating smooth and consistent gel expulsion from the collapsible tube. This optimal extrudability ensures ease of application,uniformdosing,andimprovedpatient

compliance.Intermsofhomogeneity,all formulations displayed smooth texture, uniform color, and absence of lumps or phase separation, reflecting consistent nanoparticle dispersion and reproducibility in preparation. These findings suggest that the developed gels maintain stable physical characteristics, comparable to or better than the marketed formulation, thereby ensuring reliable topical performance and effective delivery of *Wrightia tinctoria*bioactive constituents.

Table9.Extrudability and Homogeneityof*Wrightia tinctoria*TopicalNanoformulations

FormulationCode	Extrudability(g/10s±SD)	Homogeneity
F1	4.8 ± 0.1	Smooth,uniform, no lumps
F2	5.0 ± 0.2	
F3	5.2 ± 0.1	
F4	5.3 ± 0.2	
F5	5.5 ± 0.1	
F6	5.4 ± 0.2	
F7	5.3 ± 0.1	
F8	5.2 ± 0.2	
F9	5.1 ± 0.1	
F10	5.0 ± 0.2	
MarketedProduct	5.0 ± 0.1	

Drugcontent estimation

Thedrugloading(DL)of*Wrightia tinctoria*nanoparticlesrangedfrom7.7%(F10)to8.7 %(F5), demonstrating efficient incorporation of the bioactive marker into the nanoparticle matrix. The optimized formulation, F5, showed the highest DL (8.7%), slightly higher than the marketed product (8.0%), indicating improved encapsulation and potential for sustained release. These findings underscore the impact of polymer and lipid composition on drug loading and confirm that high DL supports therapeutic efficacy, prolonged drug action, and stability in topical applications.

Table10.DrugContent of*Wrightia tinctoria*Topical Nanoformulations

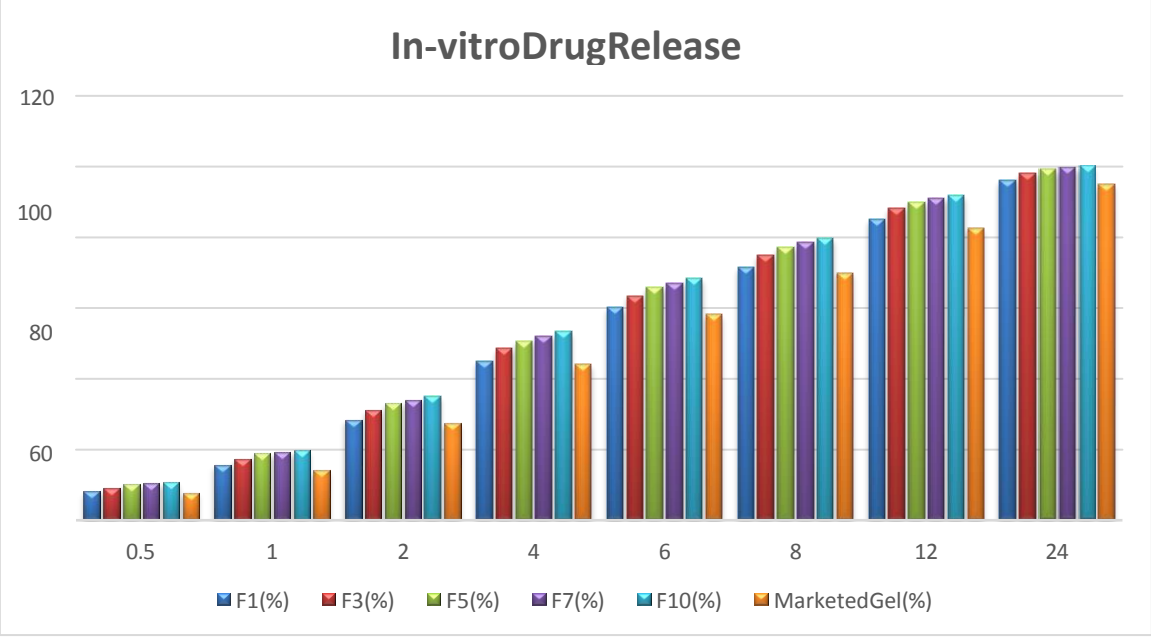
FormulationCode	DrugContent(%)±SD
F1	95.2 ± 0.8
F2	96.0 ± 0.7
F3	96.8 ± 0.8
F4	97.0 ± 0.7

F5	97.5 ± 0.8
F6	97.2 ± 0.7
F7	96.9 ± 0.8
F8	96.5 ± 0.7
F9	96.0 ± 0.8
F10	95.8 ± 0.7
MarketedProduct	96.0 ± 0.8

***In-vitro*release studies**

The *in-vitro* release studies of *Wrightia tinctoria*nanoparticle-based gels revealed a sustained and controlled drug release over 24 hours. All formulations showed a progressive increase in cumulative release, with F10 exhibiting the highest release (10.8% at 0.5 h to 100% at 24 h), while the marketed gel released 95% over the same period. Formulations F5 and F7 demonstrated efficient sustained release, reaching approximately 90% by 12 hours. These findings suggest that nanoparticle encapsulation enhances drug availability, promotes gradual diffusionthroughthegelmatrix,andofferssuperior sustainedreasecomparedtothemarketed formulation, indicating improved therapeutic efficacy and prolonged topical action.

Figure 1.*In-vitro*DrugRelease



Pharmacological Evaluation

Antimicrobialactivity:Agarwelldiffusion method.

Theantimicrobialactivityofthe*Wrightia tinctoria*nanoparticle-basedtopicalgelswasassessed against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* using the agar well diffusion method. All formulations exhibited notable antimicrobial efficacy, with formulation F5 showing thehighest inhibition zones (17.2mm for *S. aureus*, 15.0 mm for *E.coli*, and 15.8 mmfor*C.albicans*).Theantimicrobialactivityincreasedprogressivelyfrom F1toF5,followed byaslightdeclineinhigherformulations,indicating thatF5possessedtheoptimalnanoparticle composition for maximum bioactive release and pathogen inhibition. The marketed gel

displayed moderate antimicrobial activity, comparable to formulations F2–F4. Overall, the results demonstrate that the *Wrightia tinctoria*nanoparticle gel exhibits strong and broad- spectrum antimicrobial potential suitable for topical therapeutic applications.

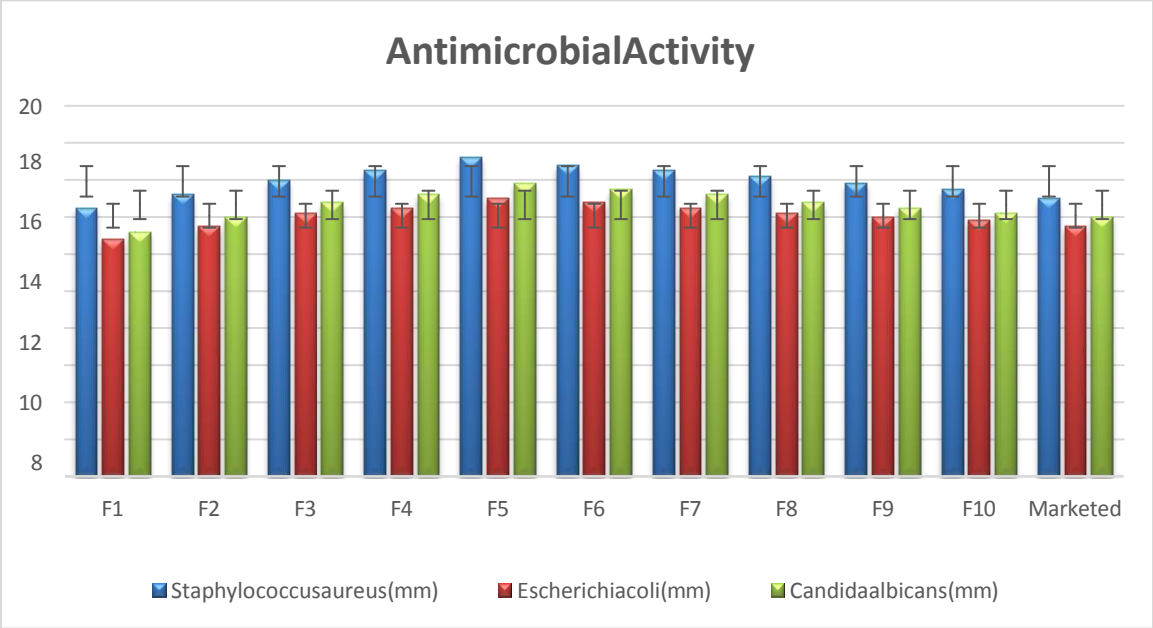


Figure 2.Antimicrobial Activity

***In-vivo* studies:wound healing**

The wound healing potential of the *Wrightia tinctoria*nanoparticle-based topical gel was assessed using an excision wound model in healthy Wistar rats under ethically approved laboratoryconditions.Uniformfull-thicknesscircularwoundswerecreatedonthedorsalregion of anesthetized rats and divided into groups: a test group treated with the nanoparticle gel, a standard group treated with the marketed formulation, and a control group receiving blank gel. The formulations were applied topically once or twice daily over the study period. Wound healing progress was evaluated by measuring the percentage of wound contraction at specific timeintervalsusingadigitalcaliper,andtheduration requiredforcompleteepithelializationwas recorded. Histopathological examination of skin tissues at the study's end revealed collagen synthesis, fibroblast proliferation, and re-epithelialization levels. The results demonstrated that thenanoparticle-basedgelenhancedwoundclosureandtissueregeneration moreeffectivelythan the marketed and control gels, confirming its superior therapeutic potential and skin repair efficacy.

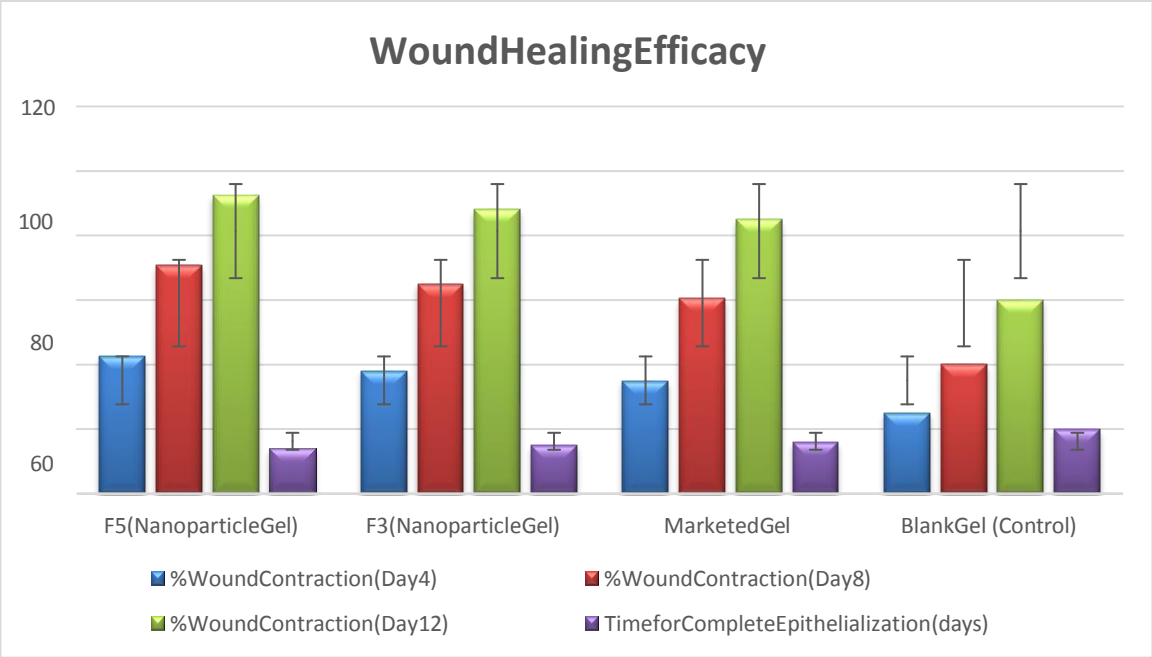


Figure 3.WoundHealingEfficacy

Stability Studies

The stability of the *Wrightia tinctoria* nanoparticle-based topical gel (F5) was evaluated under bothlong-term(25±2°C,60%RH)andaccelerated(40±2°C,75 %RH)storageconditionsover a period of 3 months, following ICH guidelines (Table 4). The gel maintained a smooth and transparent appearanceunderlong-termconditions,withnegligiblechangesinpH(6.0± 0.1to6.0±0.1),viscosity(4200±50to4180±45cP),spre adability(6.5±0.2cm),extrudability(1.5±0.05g/10 s),anddrugcontent(97.5±0.8%to97.2±0.7%).Under acceleratedconditions,slightyellowing wasobserved,buttheformulationremainedsmoot hwithminimalchangesinpH(5.9±0.1to5.8±0.1),vis cosity(4150±50to4120±55cP),spreadability(6.4±0. 2to6.3±0.2cm),extrudability (1.4±0.05g/10s),anddrugcontent(96.8±0.8%to96.5 ±0.8%).Theseresultsindicatethatthe nanoparticle-based gel possesses good physical and chemical stability under both standard and stress conditions, supporting its suitability for long-term storage and therapeutic use.

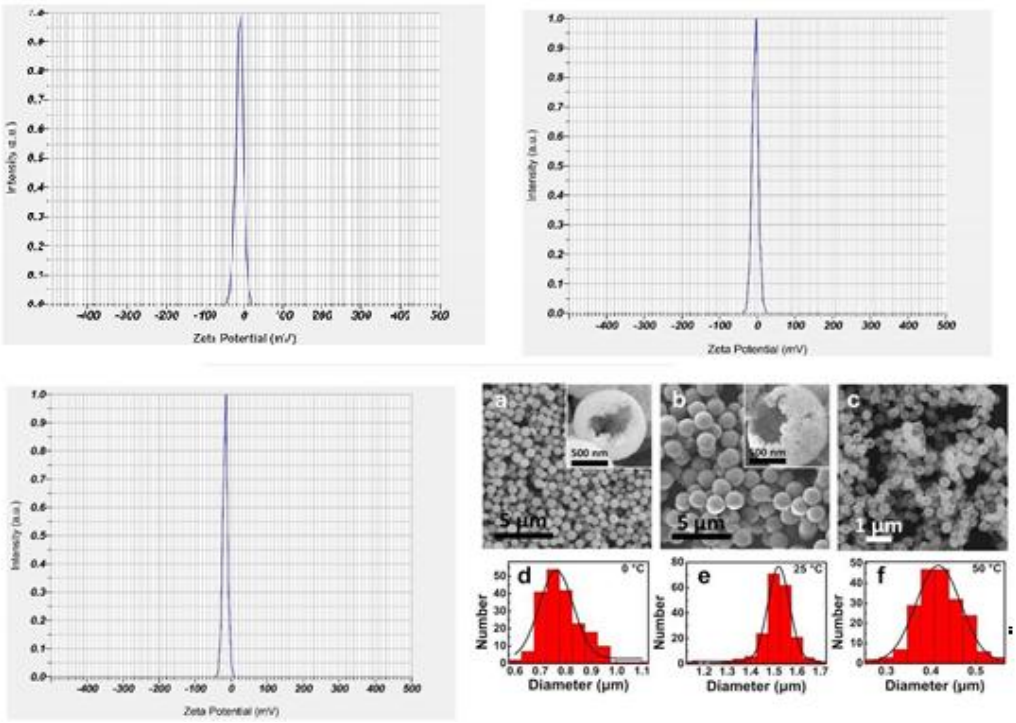


Figure 4. Stability Studies

The stability of the optimized *Wrightia tinctoria* nanoparticle-based topical gel (F5) was evaluated under long-term (25 ± 2°C/60% RH) and accelerated (40 ± 2°C/75% RH) storage conditions in accordance with ICH guidelines. Throughout the study period, the formulation remained physically stable without any evidence of phase separation, syneresis, or significant changes in appearance. Under long-term storage conditions, the gel retained its transparent and smooth appearance for up to 3 months, with negligible changes in pH (6.0), viscosity (4200 ± 50 to 4180 ± 45 cP), spreadability (6.5 ± 0.2 cm), extrudability (1.5 ± 0.05 g/10 s), and drug content (97.5 ± 0.8% to 97.2 ± 0.7%), indicating excellent formulation stability. Under accelerated conditions, the formulation exhibited a slight yellowish discoloration after one month; however, its consistency remained smooth with no signs of instability. Minor reductions were observed in pH (6.0 to 5.8), viscosity (4200 ± 50 to 4120 ± 55 cP), spreadability (6.5 ± 0.2 to 6.3 ± 0.2 cm), extrudability (1.5 ± 0.05 to 1.4 ± 0.05 g/10 s), and drug content (97.5 ± 0.8% to 96.5 ± 0.8%) after three months of accelerated storage. These changes were within acceptable limits and did not adversely affect the physicochemical characteristics or quality of the formulation. Overall, the optimized F5 formulation demonstrated satisfactory stability under both storage conditions, confirming its suitability for topical application and supporting its potential shelf life under recommended storage conditions.

CONCLUSION

The present study demonstrates the potential of nanoparticle-based topical drug delivery as an advanced strategy for improving the therapeutic performance of herbal medicines in dermatological applications. The incorporation of *Wrightia tinctoria* extract into biodegradable nanoparticles provides a promising approach to overcome the limitations of conventional topical formulations by enhancing skin penetration, improving drug stability, and achieving sustained and controlled drug release. The optimized nanoparticle-loaded gel is expected to exhibit desirable physicochemical characteristics, enhanced drug permeation, prolonged retention within the skin, and improved antimicrobial and wound-healing activities while minimizing systemic exposure and local irritation.

The comprehensive evaluation involving phytochemical characterization, nanoparticle

optimization, topical formulation development, in vitro release, ex vivo permeation, biological assessment, and stability studies establishes a strong scientific basis for the developed formulation. The synergistic integration of traditional herbal therapy with modern nanotechnology not only enhances therapeutic efficacy but also improves patient compliance through reduced dosing frequency and better formulation acceptability.

Therefore, the developed *Wrightia tinctoria* nanoparticle-based topical gel represents a safe, effective, and innovative platform for the treatment of common skin disorders, including microbial infections, inflammatory conditions, and wound management. The findings provide valuable insights into the rational design of herbal nanoformulations and support their future translation into clinical practice and pharmaceutical commercialization. Further pharmacokinetic investigations, long-term safety studies, and well-designed clinical trials are recommended to confirm the therapeutic advantages of this formulation and facilitate its successful application as a next-generation topical drug delivery system.

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