RESEARCH PAPER

Formulation and Evaluation of a Plant Polysaccharide-Based Hydrogel for Topical Delivery of an Antibiotic for Chronic Wound Management

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ABSTRACT

The present study aimed to formulate and evaluate a plant polysaccharide-based hydrogel containing gentamicin for chronic wound management. Polysaccharide was isolated from Eulophia herbacea tubers and characterized for its physicochemical properties. Compatibility studies using FTIR and DSC confirmed the absence of significant drug–polymer interactions. Gentamicin-loaded hydrogels were prepared and optimized using a Box–Behnken Design by evaluating the effects of polysaccharide, calcium chloride, and glycerol concentrations on viscosity, swelling index, spreadability, drug content, and drug release. Among fifteen formulations, Run 7 containing 1.0% polysaccharide, 1.0% calcium chloride, and 15% glycerol was identified as the optimized batch. The optimized hydrogel exhibited skin-compatible pH (6.45), high swelling capacity (95.37%), satisfactory spreadability, and uniform drug content (95.90%). Sustained in-vitro release of gentamicin (91.6%) over 12 h demonstrated its potential as an effective topical delivery system for chronic wound treatment.

Keywords: Eulophia herbacea, Plant polysaccharide, Hydrogel, Gentamicin, Chronic wound management, Topical drug delivery, Box–Behnken Design, Sustained drug release

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INTRODUCTION

Wound healing is a highly coordinated and essential physiological process that restores the structural and functional integrity of damaged tissue following injury. A wound is defined as a disruption in the continuity of skin and underlying tissues caused by physical, chemical, thermal, or microbial insults.1 The healing process involves a complex cascade of overlapping cellular and molecular events traditionally divided into four phases: hemostasis, inflammation, proliferation, and remodeling.2 These phases are tightly regulated in acute wounds, enabling timely repair and restoration of tissue integrity with minimal complications 3.

However, when this finely tuned process is disrupted due to local or systemic factors, wounds may fail to progress through the normal stages of healing and instead enter a chronic state.[4] Chronic wounds, including diabetic foot ulcers, venous leg ulcers, and pressure ulcers, represent a major global healthcare burden due to their prolonged healing time, high recurrence rate, susceptibility to infection, and significant socioeconomic impact.5 These wounds are typically defined by their failure to achieve anatomical and functional restoration within an expected time frame and are often associated with underlying comorbidities such as diabetes mellitus, vascular insufficiency, and immunosuppression 6.

The pathophysiology of chronic wounds is complex and multifactorial. A key feature is the persistent inflammatory phase characterized by continuous infiltration of neutrophils and macrophages, resulting in sustained release of pro-inflammatory cytokines, proteases, and reactive oxygen species.7 This prolonged inflammatory environment leads to degradation of extracellular matrix components and growth factors, thereby impairing progression into the proliferative phase of healing. Additionally, chronic wounds exhibit reduced angiogenesis,

impaired fibroblast proliferation, and defective re-epithelialization, all of which contribute to delayed tissue regeneration .8,9

Microbial colonization and biofilm formation further complicate chronic wound healing. Biofilms provide a protective matrix for microorganisms, significantly reducing their susceptibility to host immune responses and antimicrobial therapy.[10] This contributes to persistent infection, increased inflammation, and antibiotic resistance, making effective treatment more challenging. Furthermore, systemic conditions such as diabetes mellitus, peripheral vascular disease, malnutrition, and advanced age exacerbate wound chronicity by impairing immune function, reducing tissue perfusion, and limiting cellular repair mechanisms .11,12

Conventional topical therapies, including creams, ointments, and liquid formulations, often fail to provide sustained therapeutic concentrations at the wound site due to rapid removal by wound exudate and limited retention on the tissue surface.13 Additionally, these formulations are generally unable to maintain an optimal moist environment, manage exudate effectively, or provide controlled and localized drug delivery, all of which are critical for efficient wound healing .14,15

In this context, hydrogel-based drug delivery systems have emerged as promising biomaterials for advanced wound management. Hydrogels are three-dimensional hydrophilic polymer networks capable of retaining large amounts of water while maintaining structural integrity.[16] Their high water content mimics natural extracellular tissue, thereby promoting cell migration, angiogenesis, and epithelialization. Moreover, hydrogels provide a moist wound environment, facilitate autolytic debridement, reduce pain during dressing changes, and enhance overall patient comfort .17,18

Among various hydrogel-forming materials, plant-derived polysaccharides have gained considerable attention due to their excellent biocompatibility, biodegradability, non-toxicity, and structural versatility.[19] Natural polymers such as chitosan, alginate, pectin, cellulose derivatives, and guar gum possess favorable physicochemical properties for hydrogel formation and can be easily modified to achieve desired mechanical strength, swelling behavior, and drug release profiles.20 In addition, several polysaccharides exhibit inherent antimicrobial and wound-healing properties, further enhancing their suitability for biomedical applications .21,22

The incorporation of antibiotics into hydrogel matrices provides a targeted and sustained drug delivery approach for infected chronic wounds. Localized delivery ensures high drug concentration at the wound site while minimizing systemic exposure and adverse effects.[23] Sustained release systems also reduce dosing frequency and improve patient compliance, which is particularly important in long-term chronic wound management. Furthermore, such systems help in reducing microbial burden and controlling biofilm-associated infections, thereby supporting the natural healing cascade .24

Despite significant advances in wound care technologies, there remains a need for an ideal multifunctional dressing that can simultaneously provide antimicrobial activity, maintain moisture balance, absorb wound exudate, and support tissue regeneration.25 Plant polysaccharide-based hydrogels offer a promising platform to address these challenges by integrating biocompatibility, controlled drug delivery, and wound-friendly physicochemical properties into a single system .26

Therefore, the present study focuses on the formulation and evaluation of a plant polysaccharide-based hydrogel loaded with an antibiotic for the effective management of chronic wounds. The objective is to develop a stable, biocompatible hydrogel system with suitable physicochemical characteristics, controlled swelling behavior, sustained drug release, and enhanced antimicrobial efficacy to promote optimal wound healing.

In conclusion, chronic wounds represent a significant clinical challenge due to their complex pathophysiology and impaired healing mechanisms. Conventional therapies are often insufficient to address the multifactorial nature of these wounds. Plant polysaccharide-based hydrogel systems provide an advanced and promising strategy for wound management by combining natural polymer advantages with controlled drug delivery systems. Such formulations have the potential to significantly improve therapeutic outcomes and advance the field of topical drug delivery in chronic wound care .

MATERIAL AND METHOD

MATERIAL

Gentamicin was obtained in pure form from Taj Pharma India Ltd., Vapi, Gujarat, India. The plant material used for polysaccharide extraction was procured from a reliable local supplier in Nandurbar district and authenticated prior to use. All chemicals and reagents employed in the study were of analytical reagent (AR) grade and were purchased from Merck Pvt. Ltd. and Qualigens Fine Chemicals, India.

EXTRACTION AND ISOLATION OF PLANT POLYSACCHARIDE

The tubers of Eulophia herbacea were thoroughly washed, shade dried at room temperature, and pulverized using a mechanical grinder. The dried powder was passed through sieve no. 60 and stored in airtight containers. For extraction, 500 g of powdered material was extracted with 5.0 L of distilled water at 80 ± 2 °C for 3 h under continuous stirring. The extraction was repeated three times, and the combined extracts were filtered through muslin cloth followed by Whatman No. 1 filter paper and concentrated under reduced pressure.

The concentrated extract was precipitated by adding three volumes of 95% ethanol with continuous stirring and kept at 4 °C for 24 h. The precipitate was collected by centrifugation at 5000 rpm for 15 min, washed with ethanol, redissolved in distilled water, and dialyzed using a 3500 Da molecular weight cut-off membrane for 48 h. The purified polysaccharide was reprecipitated with ethanol, centrifuged, and dried at 45 ± 2 °C to obtain a constant weight. The dried polysaccharide was finally powdered and stored in airtight containers protected from moisture and light.

CHARACTERIZATION OF ISOLATED PLANT POLYSACCHARIDE (BRIEF METHODOLOGY)

The isolated polysaccharide was characterized by standard physicochemical and instrumental methods. Organoleptic properties including color, odor, appearance, and texture were evaluated visually. Solubility was determined in water and organic solvents by stirring a fixed amount of sample and observing its dissolution behavior.

Swelling index was measured by hydrating a known weight of polysaccharide in distilled water for 24 h and recording volume change. pH of a 1% w/v aqueous solution was measured using a digital pH meter, while viscosity was determined using a Brookfield viscometer at controlled temperature.FTIR spectroscopy was used to identify functional groups and confirm polysaccharide structure. Thermal behavior was analyzed by DSC to assess stability. Total carbohydrate content was estimated by the phenol–sulfuric acid method using glucose as standard and measuring absorbance at 490 nm.27

PREFORMULATION STUDIES

Preformulation studies were performed to evaluate the physicochemical properties of gentamicin and its compatibility with the extracted plant polysaccharide. Drug identification was confirmed by visual inspection and FTIR spectroscopy. The λmax was determined using UV–Visible spectrophotometry after derivatization with ninhydrin, and a calibration curve was constructed over 10–60 µg/mL at 400 nm. Drug–polymer compatibility was assessed using FTIR and DSC analysis of the pure drug, polymer, and physical mixture to detect possible interactions affecting formulation stability and performance

PREPARATION OF FORMULATION

OPTIMIZATION OF FORMULATION

The present study aimed to develop and optimize a gentamicin-loaded plant polysaccharide hydrogel for topical drug delivery using a Box–Behnken Design (BBD). Three critical formulation variables—plant polysaccharide concentration (X_1), crosslinker concentration (X_2), and plasticizer concentration (X_3)—were evaluated for their influence on viscosity, swelling index, spreadability, drug content, and in-vitro drug release. The statistical design enabled efficient optimization with reduced experimental runs and facilitated identification of an optimized

hydrogel formulation with desirable physicochemical and drug release characteristics suitable for chronic wound management.

EXPERIMENTAL DESIGN

Gentamicin-loaded hydrogels were developed using a 3-factor, 3-level Box–Behnken Design (BBD) to optimize formulation characteristics. A total of 15 experimental runs were generated. Three independent variables were selected and studied at low (−1), medium (0), and high (+1) levels as follows:

Table 1. Independent variable Design

Factor	Level used, actual (coded)		
Independent Variables	Low (-1)	Medium (0)	High (+1)
X1 = Plant polysaccharide concentration (% w/w)	1.0	1.5	2.0
X2 = Crosslinker concentration (% w/w)	0.5	1.0	1.5
X3 =Plasticizer concentration (% w/w)	5	10	15

PROCEDURE

Fifteen hydrogel formulations were prepared according to the Box–Behnken experimental design using a standardized method. The plant polysaccharide was dispersed in distilled water under continuous stirring and allowed to hydrate completely. Gentamicin solution was then incorporated into the polymer dispersion with uniform mixing. Subsequently, plasticizer and crosslinking agent were added sequentially to form a stable hydrogel network. The prepared formulations were evaluated for viscosity, swelling index, spreadability, drug content, and in-vitro drug release. The experimental data were analyzed using Design-Expert® software, and the optimized formulation was selected based on desirability criteria.28

Table 02. Box–Behnken design matrix for experimental batches

Run	Factor 1	Factor 2	Factor 3
	A:Plant polysaccharide	B:Crosslinker	C:Plasticizer
	%	%	%
1	1	0.5	10
2	2	0.5	10
3	1	1.5	10
4	2	1.5	10
5	1	1	5
6	2	1	5
7	1	1	15
8	2	1	15
9	1.5	0.5	5
10	1.5	1.5	5
11	1.5	0.5	15
12	1.5	1.5	15
13	1.5	1	10
14	1.5	1	10
15	1.5	1	10

EVALUATION OF HYDROGEL FORMULATIONS

PHYSICAL APPEARANCE AND HOMOGENEITY

The hydrogel formulations were visually examined for color, transparency, consistency, and homogeneity. Each formulation was checked against black and white backgrounds to detect phase separation, aggregation, or presence of particulate matter. Uniformity was further confirmed by pressing a small quantity of gel between glass slides to ensure smooth texture and absence of lumps.

PH DETERMINATION

The pH of each formulation was measured to ensure compatibility with skin physiology. One gram of hydrogel was dispersed in 10 mL of distilled water and stirred to obtain a uniform dispersion. The pH was measured using a calibrated digital pH meter at room temperature (25 ± 2 °C), and readings were taken in triplicate.

VISCOSITY MEASUREMENT

The viscosity of hydrogel formulations was determined using a Brookfield viscometer at 25 ± 2 °C. Approximately 20 g of sample was placed in the sample holder, and viscosity readings were recorded using suitable spindle numbers at varying rotational speeds (10, 20, and 50 rpm) depending on gel consistency.

DRUG CONTENT DETERMINATION

Drug content was evaluated by dissolving 1 g of hydrogel in distilled water, followed by sonication for complete drug extraction. The solution was filtered and analyzed using UV–Visible spectrophotometry at 400 nm after appropriate derivatization. Drug concentration was calculated using a previously prepared calibration curve. Content uniformity was assessed by analyzing samples from different regions of each batch.

SWELLING INDEX AND SPREADABILITY

Swelling behavior was determined by measuring weight gain of hydrogel after immersion in distilled water. The swelling index was calculated using the ratio of swollen weight to dry weight.

Spreadability was evaluated by placing 0.5 g of hydrogel between two glass slides under a 500 g weight for 5 min. The time required for the upper slide to travel a fixed distance was recorded, and spreadability was expressed based on the applied load and time taken for movement.

MOISTURE CONTENT

Moisture content was determined by drying 1 g of hydrogel in a hot air oven at 105 °C until constant weight was achieved. The percentage moisture content was calculated from the difference between initial and final weights, indicating water retention capacity and formulation stability.

IN-VITRO DRUG RELEASE STUDY (BRIEF METHODOLOGY)

The in-vitro release of gentamicin from the developed hydrogel formulations was evaluated using a dialysis membrane diffusion technique. The membrane was pre-soaked in distilled water for 12 h and mounted between donor and receptor compartments. Hydrogel equivalent to 10 mg of gentamicin was placed in the donor compartment, while phosphate buffer (pH 7.4) was used as the receptor medium and maintained at 37 ± 0.5 °C under continuous stirring at 50 rpm.At predetermined time intervals, samples were withdrawn and replaced with fresh buffer to maintain sink conditions. The collected samples were analyzed spectrophotometrically at 400 nm after suitable derivatization. The cumulative percentage drug release was calculated using the standard calibration curve.29

RESULT

Table 1. Preformulation Studies

Parameters	Observation
Gentamycin	
Organoleptic propertiesColour	white
Appearance	fine
odour	odourless
Solubility	Hydrophilic,insoluble in organic solvents
λmax	400
Isolated Polysaccride	
Colour	Creamish
Appearance	Fine
odour	odourless
Swelling index	7.84 ± 0.13
pH (1% w/v)	6.32 ± 0.04
Viscosity	684.00 ± 11.54 cP
Suitability	Suitable for hydrogel formulation

Table 3. Composition and Response Profile of Optimized Formulation

Parameter	Optimized Formulation Result
Optimized batch	Run 7
Plant polysaccharide concentration	1.0%
Calcium chloride concentration	1.0%
Glycerol concentration	15%
Viscosity	8600 cP
Swelling index	95.4%
Spreadability	24.3 g·cm/sec
Drug content	95.9%
Cumulative drug release	91.6%
Prediction error	< 3%

Table 4. Evaluation Results of Optimized Hydrogel

Parameter	Result (Mean ± SD)
Appearance	Pale cream to off-white, smooth and homogeneous
pH	6.45 ± 0.04
Viscosity (cP)	8601.67 ± 92.52
Swelling Index (%)	95.37 ± 0.55
Moisture Content (%)	73.47 ± 0.65
Spreadability (g·cm/sec)	24.33 ± 0.35
Drug Content (%)	95.90 ± 0.30

Table 5. In-vitro gentamicin release profile of optimized hydrogel

Time (h)	Trial 1 (%)	Trial 2 (%)	Trial 3 (%)	Mean ± SD (%)
0.5	18.4	19.1	19.5	19.0 ± 0.6
1	29.6	30.4	31.1	30.4 ± 0.8
2	41.8	42.6	43.2	42.5 ± 0.6
4	57.9	58.6	59.4	58.6 ± 0.8
6	69.8	70.6	71.3	70.6 ± 0.7
8	78.2	79.0	79.8	79.0 ± 0.8
10	85.7	86.4	87.1	86.4 ± 0.7
12	91.1	91.6	92.1	91.6 ± 0.5

PREFORMULATION STUDIES

Preformulation studies confirmed the suitability of gentamicin and isolated plant polysaccharide for hydrogel formulation.

DRUG POLYMER COMPATIBILITY

FTIR and DSC compatibility studies demonstrated retention of characteristic peaks and thermal transitions, indicating no significant drug–Physical mixture(Drug-Polysaccride) interaction and confirming compatibility of gentamicin with the isolated plant polysaccharide for hydrogel formulation

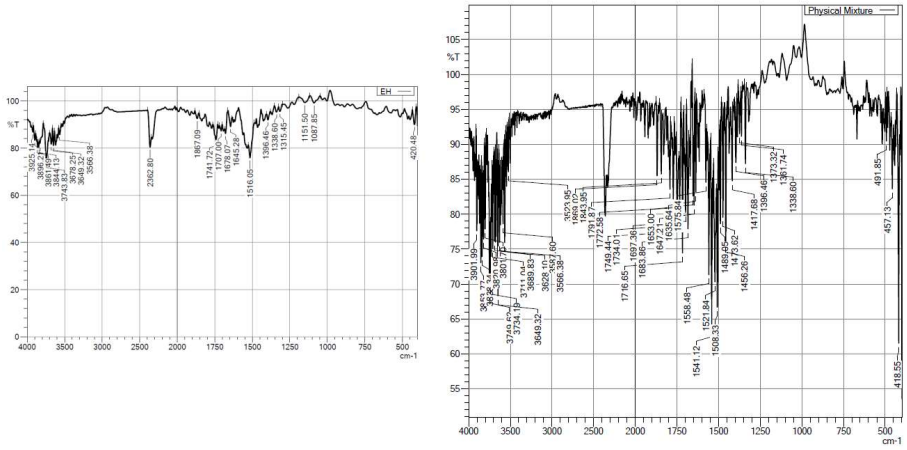

Figure FTIR spectrum of gentamicin (A) and physical mixture

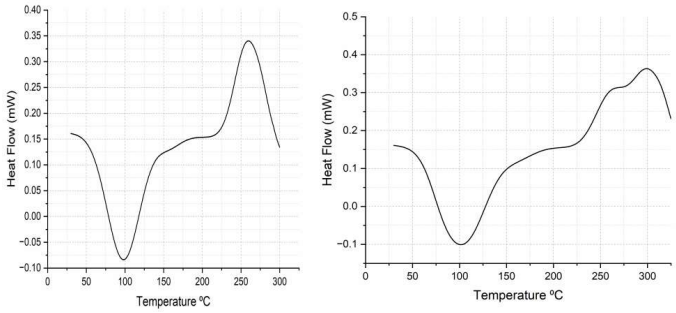

Figure DSC Theogram of gentamicin (A) and physical mixture(B)

PREPARATION OF FORMULATION

The prepared gentamicin-loaded Eulophia herbacea polysaccharide hydrogel formulations were evaluated for five dependent responses, namely viscosity, swelling index, spreadability, drug content, and cumulative drug release. The experimental response values obtained for all 15 Box–Behnken design runs are presented in Table 18. The viscosity of the formulations ranged from 8200 to 14860 cP, indicating a significant influence of plant polysaccharide and calcium chloride concentrations on the rheological behavior of the hydrogel system. The swelling index varied between 65.9% and 95.4%, demonstrating the effect of polymer network density and plasticizer concentration on water uptake. Drug content ranged from 95.7% to 98.5%, confirming efficient incorporation and uniform distribution of gentamicin within the hydrogel matrix. Spreadability values ranged from 16.8 to 32.4 g·cm/sec, showing an inverse relationship with viscosity and crosslinking density. The cumulative drug release varied from 69.8% to 91.6%, with higher release observed in formulations containing lower polymer and crosslinker concentrations and higher glycerol levels. These findings confirmed that the selected formulation variables significantly influenced the physicochemical characteristics and release performance of the gentamicin-loaded hydrogel system.

OPTIMIZED FORMULATION SELECTION

Statistical analysis indicated that the quadratic model was suitable for optimization of the gentamicin-loaded hydrogel formulation. Among all experimental batches, Run 7 was selected as the optimized formulation based on its desirable balance of viscosity, swelling behavior, spreadability, drug content, and maximum cumulative drug release. The optimized formulation contained 1.0% plant polysaccharide, 1.0% calcium chloride, and 15% glycerol, and exhibited a viscosity of 8600 cP, swelling index of 95.4%, spreadability of 24.3 g·cm/sec, drug content of 95.9%, and cumulative drug release of 91.6%. The low

prediction error (<3%) between predicted and observed responses confirmed the reliability of the Box–Behnken design model. Therefore, Run 7 was considered the most suitable formulation for further characterization and wound-healing applications.

Evaluation of Optimized Gentamicin-Loaded Eulophia herbacea Polysaccharide Hydrogel The optimized hydrogel exhibited suitable physicochemical properties, skin-compatible pH, high swelling capacity, uniform drug content, acceptable spreadability, and good mechanical strength.

IN-VITRO DRUG RELEASE STUDY OF OPTIMIZED GENTAMICIN-LOADED HYDROGEL

The optimized gentamicin-loaded Eulophia herbacea polysaccharide hydrogel exhibited a controlled and sustained drug release pattern over 12 h in phosphate buffer (pH 7.4). The formulation released 91.6 ± 0.5% of gentamicin at the end of 12 h, indicating efficient drug diffusion through the hydrated hydrogel network. The initial release was attributed to surface-associated drug, followed by sustained release governed by matrix swelling and diffusion. This prolonged release profile supports its potential application in chronic wound management by maintaining therapeutic drug levels for an extended period.

CONCLUSION

The present study successfully developed and optimized a gentamicin-loaded hydrogel based on the isolated polysaccharide obtained from Eulophia herbacea tubers for potential application in chronic wound management. Preformulation studies confirmed the suitability of gentamicin and the extracted plant polysaccharide for hydrogel development. FTIR and DSC compatibility studies demonstrated the absence of significant drug–polymer interactions, indicating good compatibility and stability of the formulation components.

Optimization using the Box–Behnken Design revealed that plant polysaccharide concentration, calcium chloride concentration, and glycerol concentration significantly influenced the physicochemical properties and drug release behavior of the hydrogel. Among the fifteen experimental formulations, Run 7 containing 1.0% plant polysaccharide, 1.0% calcium chloride, and 15% glycerol was identified as the optimized formulation. The optimized hydrogel exhibited desirable characteristics including suitable viscosity (8601.67 ± 92.52 cP), high swelling index (95.37 ± 0.55%), acceptable spreadability (24.33 ± 0.35 g·cm/sec), uniform drug content (95.90 ± 0.30%), and skin-compatible pH (6.45 ± 0.04).

The optimized formulation demonstrated a sustained in-vitro drug release profile, releasing 91.6 ± 0.5% gentamicin over 12 h, which is advantageous for maintaining prolonged antimicrobial activity at the wound site. The high moisture retention and swelling capacity further support its suitability for creating a moist wound environment conducive to healing. Overall, the developed Eulophia herbacea polysaccharide-based hydrogel represents a promising natural polymer-based topical drug delivery system for chronic wound management. Further in-vivo wound healing and stability studies are recommended to establish its clinical applicability and therapeutic effectiveness.

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