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Original Article

# Formulation and Optimization of a Rifaximin Solid Dispersion-Based Hydrogel for Topical Delivery

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## ABSTRACT

**Background:** Rifaximin is a poorly water-soluble antibiotic that limits dissolution, formulation flexibility, and topical delivery. Enhancing its solubility is essential to improve therapeutic performance in localized applications. **Materials and Methods:** Solid Dispersions (SDs) were prepared using five hydrophilic polymers at drug-to-polymer ratios of 1:0.5-1:1.5 (w/w) by solvent evaporation. SDs were characterized by FTIR, XRD, and DSC. The optimized SD was incorporated into hydrogels and optimized using a $3^2$ factorial design with locust bean gum (2-4% w/v) and xanthan gum (0.2-0.4% w/v). Formulations were evaluated for drug content, pH, viscosity, *in vitro* release, and accelerated stability (40ºC/75% RH, 6 months). **Results:** The PVA-based SD (1:1.5) showed the highest solubility (>300 µg/mL; ~35-40-fold increase) due to amorphization and improved drug-polymer interactions. Hydrogels exhibited skin-compatible pH and pseudoplastic behavior. Drug release ranged from 23% to 47%, significantly higher than pure drug gel. Polymer concentration significantly affected viscosity and release. The optimized formulation (F3) showed balanced properties and stable performance. **Conclusion:** Solid dispersion-loaded hydrogels effectively enhance rifaximin solubility and support improved topical delivery, offering a promising strategy for poorly water-soluble drugs.

**Keywords:** Factorial design, Hydrogel, Rifaximin, Solid dispersion, Solubility enhancement.

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## INTRODUCTION

Rifaximin is a broad-spectrum, minimally absorbed antibiotic widely used for gastrointestinal infections due to its high local activity and negligible systemic absorption (Shayto *et al.*, 2016). However, it's low aqueous solubility limits dissolution, formulation versatility, and potential application in alternative delivery systems such as topical formulations (Tsakiridou *et al.*, 2025). Improving its solubility is therefore essential to expand its therapeutic utility. Solid dispersion is a well-established approach for solubility enhancement, primarily by converting crystalline drugs into amorphous forms and improving wettability using hydrophilic carriers. Hydrogels are promising topical delivery systems due to their biocompatibility, ease of application, and ability to provide controlled release and prolonged residence time. Natural polymers such as Locust Bean Gum (LBG) and Xanthan Gum (XG) are widely used due to their biocompatibility and gel-forming properties; however, their concentration significantly influences rheology and drug release.

Although solid dispersion has been extensively studied, limited research has explored its integration into hydrogel systems for the topical delivery of rifaximin, and optimization of polymer combinations remains underexplored.

Therefore, the present study aimed to develop and optimize a rifaximin solid dispersion-loaded hydrogel using a $3^2$ factorial design to evaluate the effects of LBG and XG on drug content, viscosity, and drug release.

## MATERIALS AND METHODS

Rifaximin was supplied by Alembic Pharmaceuticals Ltd., Mumbai, India. Polymers like Soluplus, HPMC E5, PEG 4000, HPC, and Polyvinyl Alcohol (PVA) were procured from Lob Chemie, Mumbai. Other chemicals were obtained from Merck Chemicals, Mumbai. Microsoft Excel® and Design-Expert® were used for statistical analysis.

### Preparation of Rifaximin Solid Dispersion by Solvent Evaporation Method

Solid dispersions of rifaximin were prepared using hydrophilic polymers (Soluplus, HPMC E5, PEG 4000, HPC, and PVA)

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at drug-to-polymer ratios of 1:0.5, 1:1, and 1:1.5 (w/w) by the solvent evaporation method.

Rifaximin (2 g) and the respective polymer were dissolved separately in ethanol (10 mL), mixed under continuous stirring, and the solvent was evaporated at 40°C to obtain solid dispersions. For PVA, distilled water was used as the solvent. The dried mass was pulverized, sieved (#80), and stored in airtight containers (Jadhav *et al.*, 2024). The composition of solid dispersions is presented in Table 1.

## Drug Content

Solid dispersion equivalent to 10 mg rifaximin was dissolved in ethanol, sonicated for 10 min, and suitably diluted. A standard rifaximin solution was prepared similarly. Aliquots were further diluted with ethanol, and absorbance was measured at 340 nm using a UV-visible spectrophotometer. Drug content (%) was calculated from the calibration curve. All measurements were performed in triplicate ($n$=3) (Sapkal *et al.*, 2020; Joshi *et al.*, 2023).

## Solubility Analysis

The solubility of pure rifaximin and solid dispersions was determined in acetate buffer (pH 5.0). An excess sample was added to 50 mL of buffer and shaken for 48 hr to achieve equilibrium. The solutions were filtered, and 1 mL was diluted to 10 mL with buffer. Absorbance was measured spectrophotometrically, and solubility was calculated. All experiments were conducted in triplicate (Mohana *et al.*, 2022; Kulawik *et al.*, 2025).

## FTIR Analysis

Fourier-Transform Infrared (FTIR) spectroscopy was performed to evaluate drug-polymer interactions. Samples were mixed with Potassium Bromide (KBr), compressed into pellets, and scanned over 4000-400 $cm^{-1}$ using a Jasco FT/IR-4600 spectrophotometer. Spectra were analysed for changes in characteristic peaks to assess possible interactions (Jadhav *et al.*, 2025).

## XRD Analysis

X-ray Diffraction (XRD) analysis was carried out to determine the crystalline or amorphous nature of rifaximin in the solid dispersions. Samples were analysed using a Bruker D8 Advance diffractometer with Cu Kα radiation (λ=1.5406 Å) at 40 kV and 30 mA. The scanning range was 2θ=5°-50° with a step size of 0.02° and a scanning speed of 2°/min (Jadhav *et al.*, 2025).

## DSC Analysis

Differential Scanning Calorimetry (DSC) was performed to evaluate thermal behaviour and confirm amorphization of the drug. Samples were sealed in aluminium pans and analysed using a TA Instruments Q2000 DSC. The samples were heated from 30°C to 300°C at a rate of 10°C /min under a nitrogen flow of 50 mL/min, using an empty pan as reference (Shah *et al.*, 2023).

## Formulation of Rifaximin Solid Dispersion Gel

Hydrogel formulations were prepared using a $3^2$ factorial design by varying locust bean gum (LBG: 2.0-4.0% w/v) and xanthan gum (XG: 0.2-0.4% w/v) to evaluate their combined effects on formulation properties. LBG was dispersed in propylene glycol, followed by gradual addition of cold distilled water and allowed to swell for 24 hr. XG was then added to form a uniform gel base. The optimized rifaximin solid dispersion (1% w/v), dissolved in propylene glycol, was incorporated under continuous stirring. The gels were deaerated, adjusted to final volume, and stored in airtight containers. The composition of formulations is presented in Table 2.

## Evaluation of gel

### *pH determination*

The pH of the gel was determined by dispersing 1 g of gel in 10 mL of ultrapure water under constant stirring. The pH was measured using a calibrated digital pH meter (Hanna Instruments, pH-21). All measurements were performed in triplicate ($n$=3) (Jadhav *et al.*, 2021).

## % drug content of Rifaximin solid dispersion gel

Gel equivalent to 1 g was dissolved in methanol and diluted to 100 mL to obtain a stock solution. The solution was filtered and further diluted appropriately. Absorbance was measured at the predetermined λmax, and drug content (%) was calculated using the calibration curve. All measurements were carried out in triplicate.

## Spreadability of Rifaximin solid dispersion gel

Spreadability was evaluated using the parallel-plate method under a 2 g load. Approximately 1 g of gel was placed between two glass plates (20 × 20 cm), and the load was applied for 1 minute at 25±1°C. The spread area (S, $cm^2$) was calculated using the equation:

$S=\pi d^2/4$,

Where d is the diameter of the spread circle (Borse *et al.*, 2020).

## Viscosity

Viscosity was measured using a Brookfield DV-I Prime rotational viscometer at 25±1°C. Approximately 60 g of gel was analysed using spindle RV06 at rotational speeds ranging from 5 to 100 rpm, maintaining torque within 10-90%. The rheological behaviour was assessed to determine flow characteristics (Jhawat *et al.*, 2016).

### *In vitro* Diffusion study

*In vitro* diffusion was performed using a Franz diffusion cell with pre-soaked excised goat skin as the membrane. Gel (0.5 g) was placed in the donor compartment, while the receptor contained phosphate buffer (pH 5.5) with 10% v/v methanol to maintain sink conditions. The system was maintained at 32±0.5°C with continuous stirring. Samples were withdrawn at predetermined intervals, replaced with fresh medium, and analysed spectrophotometrically. Cumulative drug release was calculated, and a pure drug gel was evaluated under identical conditions (Kumar *et al.*, 2020).

### Experimental design and statistical analysis

A $3^2$ full factorial design was employed to study the effects of LBG ($X_1$: 2-4% w/v) and XG ($X_2$: 0.2-0.4% w/v) on drug content ($Y_1$), viscosity at 20 rpm ($Y_2$), and cumulative drug release at 180 min ($Y_3$). Nine formulations (F1-F9) were prepared in triplicate. Data were analysed using Design-Expert® (Stat-Ease, USA). Analysis of Variance (ANOVA) was used to evaluate the significance of model terms, and numerical optimization based on a desirability function was applied to identify the optimal formulation.

### Antimicrobial Activity Study (Ring Diffusion Method)

Antimicrobial activity was evaluated using the ring diffusion method *against Staphylococcus aureus* and *Escherichia coli*. Sterile rings loaded with the formulation were placed on inoculated agar plates and incubated under suitable conditions. Zones of inhibition were measured to assess antimicrobial effectiveness.

### Accelerated Stability Study

The optimized gel was subjected to accelerated stability testing at 40±2°C/ 75±5% RH for 6 months as per ICH guidelines. Samples were collected at 0, 1, 3, and 6 months and evaluated for drug content, viscosity, and *in vitro* drug release, which were compared with initial values to assess stability (Zothanpuii *et al.*, 2020).

## RESULTS

### Drug Content

The drug content of rifaximin solid dispersions was influenced by polymer type and drug-to-polymer ratio. Soluplus-based formulations showed the highest drug content (61.00±1.12% to 87.00±1.46%), followed by PEG 4000 (61.00±0.92%-79.40±1.32%) ($n$=3). In contrast, HPMC E5 showed a marked reduction at a higher ratio (49.60±0.87% at 1:1.5), suggesting reduced drug-polymer affinity at elevated concentrations, while HPC and PVA showed moderate variation. These differences may be attributed to variations in polymer hydrophilicity and drug-polymer interactions, which influence drug entrapment. Overall, polymer type and concentration play a critical role in drug incorporation efficiency.

### Solubility study

Pure rifaximin exhibited very low solubility (8.6±0.42 µg/mL), confirming its poorly water-soluble nature. All solid dispersions showed a marked increase in solubility, depending on polymer type and ratio. Solubility increased to 93.12±3.25-107.45±4.10 µg/mL with Soluplus, 147.36±5.22-180.48±6.13 µg/mL with HPMC E5, and 144.28±4.95-164.32±5.84 µg/mL with PEG 4000, while HPC showed comparatively lower improvement (48.56±2.15-118.22±4.76 µg/mL). The highest enhancement was observed with PVA-based solid dispersion (187.03±6.34-302.67±8.92 µg/mL), with the maximum at 1:1.5 ratio (~35-40-fold increase). This improvement may be attributed to amorphization of rifaximin along with enhanced wettability and molecular dispersion in the hydrophilic polymer matrix. Additionally, possible hydrogen bonding between PVA and rifaximin may have contributed to stabilization of the amorphous form. These results highlight the critical role of polymer properties in solubility enhancement.

### FTIR analysis

The FTIR spectrum of pure rifaximin showed characteristic functional group peaks, which were retained in the optimized solid dispersion (Figure 1) without significant shifts or disappearance. This indicates the absence of chemical interaction or degradation, confirming compatibility between rifaximin and the polymer. The preservation of functional groups suggests that solubility enhancement is due to physical modifications rather than chemical changes.

### XRD

The XRD pattern of pure rifaximin showed sharp diffraction peaks, confirming its crystalline nature. In contrast, the optimized solid dispersion exhibited a diffuse halo pattern without characteristic peaks, indicating conversion to an amorphous form (Figure 2). The disappearance of crystalline peaks suggests successful molecular dispersion of the drug within the polymer matrix. This amorphization contributes to enhanced solubility due to higher free energy and improved dissolution compared to the crystalline form.

**Table 1: Composition of different solid dispersions.**

| Formulation Code | Polymer Used | Drug: Polymer Ratio (w/w) |
|---|---|---|
| SD1- SD3 | Soluplus | 1:0.5, 1:1, 1:1.5 |
| SD4- SD6 | HPMC E5 | 1:0.5, 1:1, 1:1.5 |
| SD7- SD9 | PEG 4000 | 1:0.5, 1:1, 1:1.5 |
| SD10- SD12 | HPC | 1:0.5, 1:1, 1:1.5 |
| SD13- SD15 | PVA | 1:0.5, 1:1, 1:1.5 |

SD: Solid Dispersion, HPMC: Hydroxy Propyl Methyl Cellulose, PEG: Polyethylene Glycol, HPC: Hydroxy Propyl Cellulose, PVA: PolyVinyl Alcohol.

## DSC

The DSC thermogram of pure rifaximin showed a sharp endothermic peak at 245-246°C, confirming its crystalline nature. In contrast, the optimized rifaximin-PVA solid dispersion showed no distinct melting peak, indicating loss of crystallinity and formation of an amorphous system (Figure 3). The absence of the melting endotherm, along with a broad transition, suggests drug-polymer interaction and uniform dispersion within the polymer matrix. These findings are consistent with XRD results and support the role of amorphization in solubility enhancement.

## Evaluation of gel

### *pH determination*

The pH of all gel formulations ranged from 6.89±0.04 to 7.15±0.06, indicating near-neutral conditions with minimal variation. This pH range is suitable for topical application and is unlikely to cause skin irritation, confirming the compatibility of the formulation with physiological skin conditions.

## % drug content of Rifaximin solid dispersion gel

Drug content of hydrogel formulations ranged from 76.57±1.28% to 91.21±1.61% and was significantly influenced by polymer concentration. Formulations containing moderate levels of LBG

**Table 2: Composition of Rifaximin Solid Dispersion-Loaded Gel Formulations Using LBG and XG.**

| Formulation Code | LBG (% w/v) | XG (% w/v) | Rifaximin SD (% w/v) | PG (base) (mL) | PG (for SD) (mL) | Water (mL) |
|---|---|---|---|---|---|---|
| F1 | 2.0 | 0.2 | 1.0 | 6 | 1 | 52 |
| F2 | 2.0 | 0.3 | 1.0 | 6 | 1 | 52 |
| F3 | 2.0 | 0.4 | 1.0 | 6 | 1 | 52 |
| F4 | 3.0 | 0.2 | 1.0 | 6 | 1 | 52 |
| F5 | 3.0 | 0.3 | 1.0 | 6 | 1 | 52 |
| F6 | 3.0 | 0.4 | 1.0 | 6 | 1 | 52 |
| F7 | 4.0 | 0.2 | 1.0 | 6 | 1 | 52 |
| F8 | 4.0 | 0.3 | 1.0 | 6 | 1 | 52 |
| F9 | 4.0 | 0.4 | 1.0 | 6 | 1 | 52 |

LBG: Locust Bean Gum, XG: Xanthan Gum, PG: Propylene Glycol.

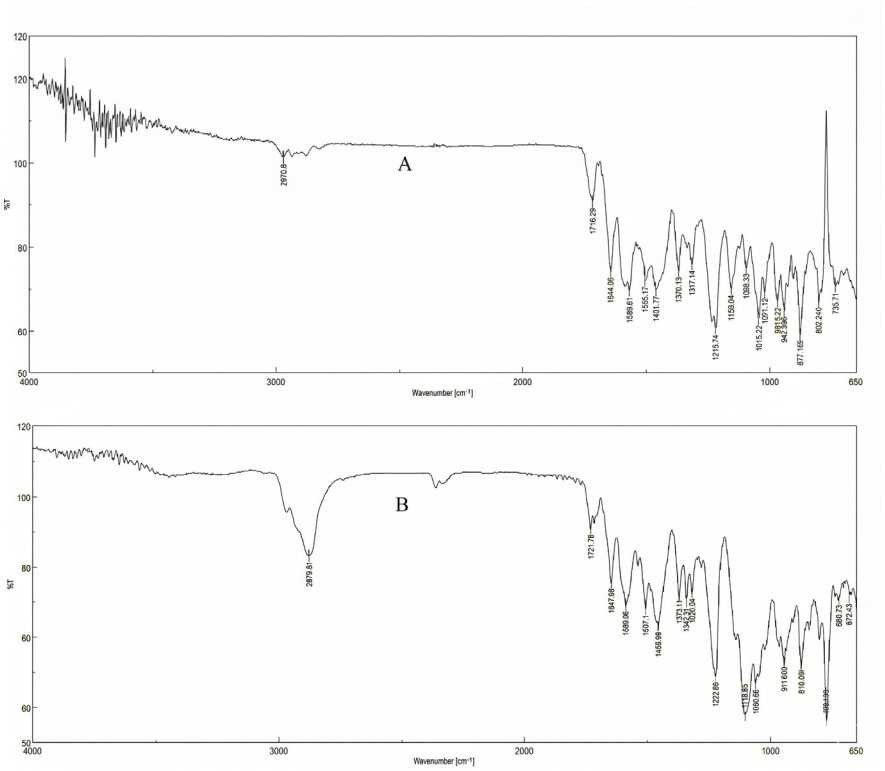


**Figure 1:** FTIR of pure rifaximin (A) and Solid dispersion with PVA (B).

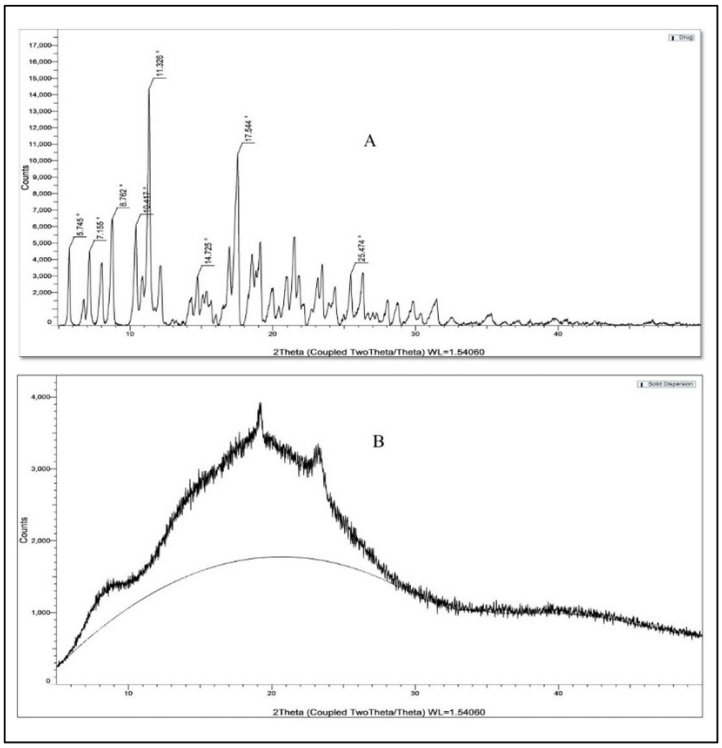


**Figure 2:** XRD spectra of pure rifaximin (A) and Solid dispersion with PVA (B).

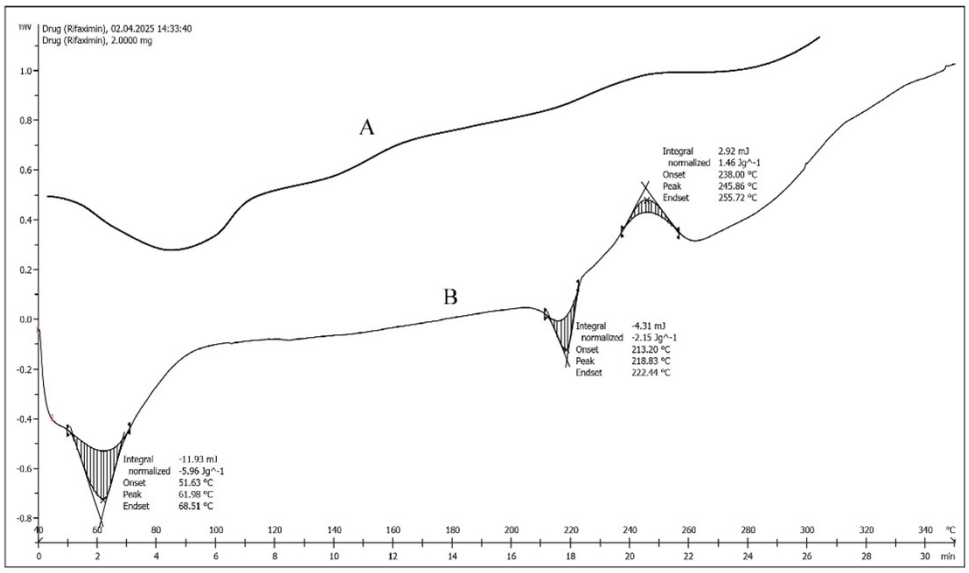


**Figure 3:** DSC graphs of pure rifaximin (B) and solid dispersion with PVA (A).

and XG (F3 and F5) exhibited the highest drug content, indicating optimal entrapment and uniform distribution. At higher polymer concentrations (e.g., F9), drug content decreased, which may be attributed to increased viscosity hindering uniform mixing and drug distribution. Excessive polymer entanglement can also limit proper incorporation of the drug into the gel matrix. These results suggest that an optimal polymer concentration is essential to achieve efficient drug loading and homogeneity.

## Spreadability of Rifaximin solid dispersion gel

Spreadability ranged from 1.24±0.05 to 2.40±0.08 cm² and decreased with increasing polymer concentration. Formulations with lower polymer content (F1) showed higher spreadability, while higher polymer concentrations resulted in stiffer gels. This inverse relationship can be attributed to increased viscosity and structural rigidity of the gel matrix at higher polymer levels, which reduces its ability to spread. These findings highlight the

importance of optimizing polymer concentration to achieve a balance between mechanical strength and ease of application.

## Viscosity

Viscosity increased with increasing polymer concentration, ranging from 1400±243 cP (F1) to 46500±875 cP (F6 at 5 rpm). This increase is attributed to enhanced polymer chain entanglement and formation of a dense three-dimensional network structure, which restricts flow. All formulations exhibited a decrease in viscosity with increasing shear rate (5-100 rpm), confirming pseudoplastic (shear-thinning) behavior. This rheological property is desirable for topical formulations, as it allows ease of application under shear while maintaining structural integrity at rest. Overall, viscosity was directly proportional to polymer concentration.

## *In vitro* diffusion study

Cumulative drug release increased over 180 min, ranging from 23.50±1.84% (F9) to 46.50±2.12% (F1). Faster release was observed at lower polymer concentrations, while higher polymer content slowed diffusion. This may be attributed to the formation of a dense polymeric network, increasing diffusional resistance and reducing drug mobility within the matrix. Kinetic modelling showed first-order release ($R^2$=0.9957), indicating concentration-dependent behavior. The Korsmeyer-Peppas model (n ≈ 1) suggested a combined mechanism of diffusion and polymer relaxation. Minimal release from the pure drug gel further confirms the enhancement achieved by solid dispersion (Figure 4).

## Experimental design, model fitting and optimisation

The $3^2$ factorial design effectively modelled the responses, including drug content ($Y_1$), viscosity ($Y_2$), and cumulative drug release ($Y_3$), with all models showing good statistical significance and adequacy. The polynomial equations generated for the responses were as follows:

$$Y_1 = 89.29 + 0.86A + 2.06B - 4.97AB - 4.315A^2 - 0.865B^2$$

$$Y_2 = 16319.78 + 5263A + 11529.67B$$

$$Y_3 = 34.8333 - 9.3667A - 2.4B$$

where A represents Locust Bean Gum (LBG), and B represents Xanthan Gum (XG) concentration. The polynomial coefficients indicate the magnitude and direction of variable effects. Positive coefficients in $Y_1$ suggest that both polymers increase drug content up to an optimal level, while negative quadratic and interaction terms indicate a decline at higher concentrations due to polymer overcrowding. For viscosity ($Y_2$), both variables showed positive effects, with XG having a greater impact, reflecting its stronger thickening ability due to higher water-binding capacity. In contrast, negative coefficients in $Y_3$ indicate that increasing polymer concentration reduces drug release, likely due to the formation of a dense matrix that limits diffusion. Desirability optimization identified formulation F3 as optimal, showing a balanced response profile. Experimental values closely matched predicted values ($Y_1$: 0.78%, $Y_2$: 4.48%, $Y_3$: 0.48% deviation), confirming model reliability. ANOVA indicated statistical significance ($p < 0.05$), and response surface plots (Figure 5) further illustrated variable interactions.

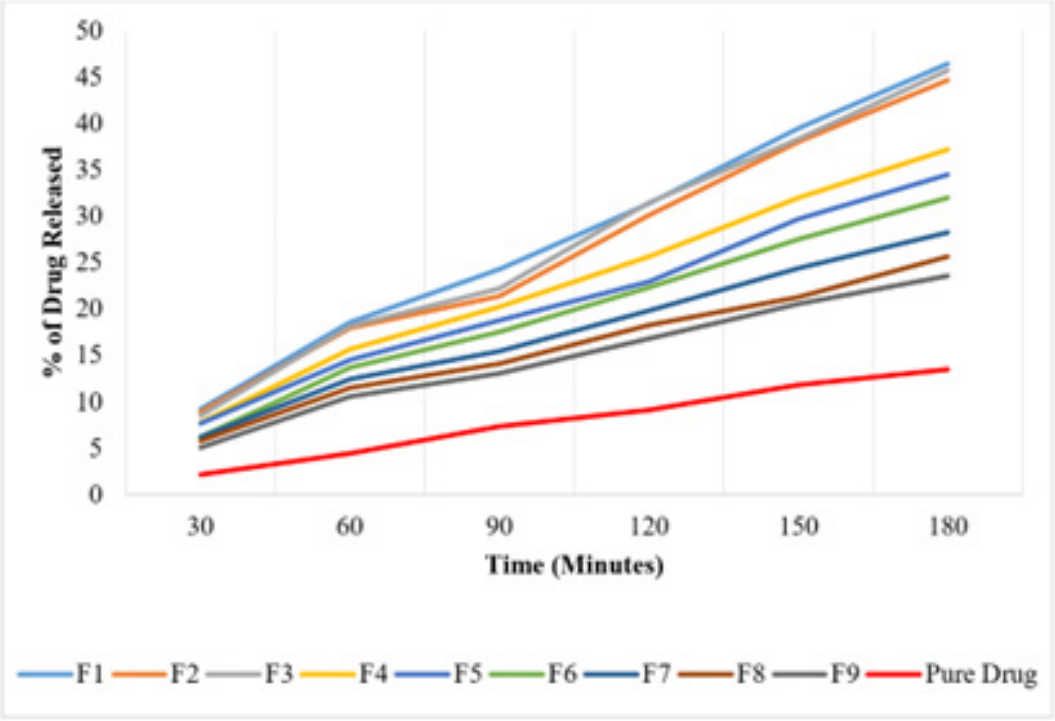


**Figure 4:** *In vitro* drug release profile of rifaximin formulations.

## Antimicrobial Activity Study (Ring Diffusion Method)

The optimized formulation (F3) exhibited significantly higher antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli*, with zones of inhibition of 20.2±0.4 mm and 18.5±0.3 mm, respectively, compared to the pure drug gel (8.2±0.3 mm and 7.1±0.3 mm). The enhanced antimicrobial activity can be attributed to improved solubility and release of rifaximin from the solid dispersion-loaded hydrogel, leading to increased drug diffusion and availability at the site of action.

## Accelerated Stability Testing

The optimized formulation showed a gradual decrease in drug content and *in vitro* release over time, accompanied by an increase in viscosity. These changes may be attributed to minor solvent loss and progressive densification of the polymer matrix under accelerated conditions. However, the observed variations remained within acceptable limits, indicating good physical and chemical stability of the formulation over the study period (Table 3).

# DISCUSSION

The present study demonstrates a systematic approach to overcoming the solubility limitations of rifaximin through the development of a solid dispersion-loaded hydrogel system. The significant enhancement in solubility observed in the PVA-based solid dispersion can be primarily attributed to the transformation of rifaximin from a crystalline to an amorphous state, as confirmed by XRD and DSC analyses. Amorphous systems possess higher free energy and greater molecular mobility, which contribute to improved wettability and dissolution behavior. Rusdin *et al.* (2024) reported that hydrophilic polymers facilitated solubility enhancement by stabilizing the amorphous form and preventing recrystallization. The role of polymer type was found to be critical in determining solubility enhancement. Among the polymers evaluated, PVA demonstrated superior performance, which may be attributed to its strong hydrophilic nature and potential to form intermolecular hydrogen bonding with the drug. This interaction likely promotes uniform molecular dispersion and inhibits drug aggregation. Comparable observations have been reported for other poorly soluble drugs, where polymer-drug interactions significantly influenced solubility and dissolution profiles. Incorporation of the optimized solid dispersion into a

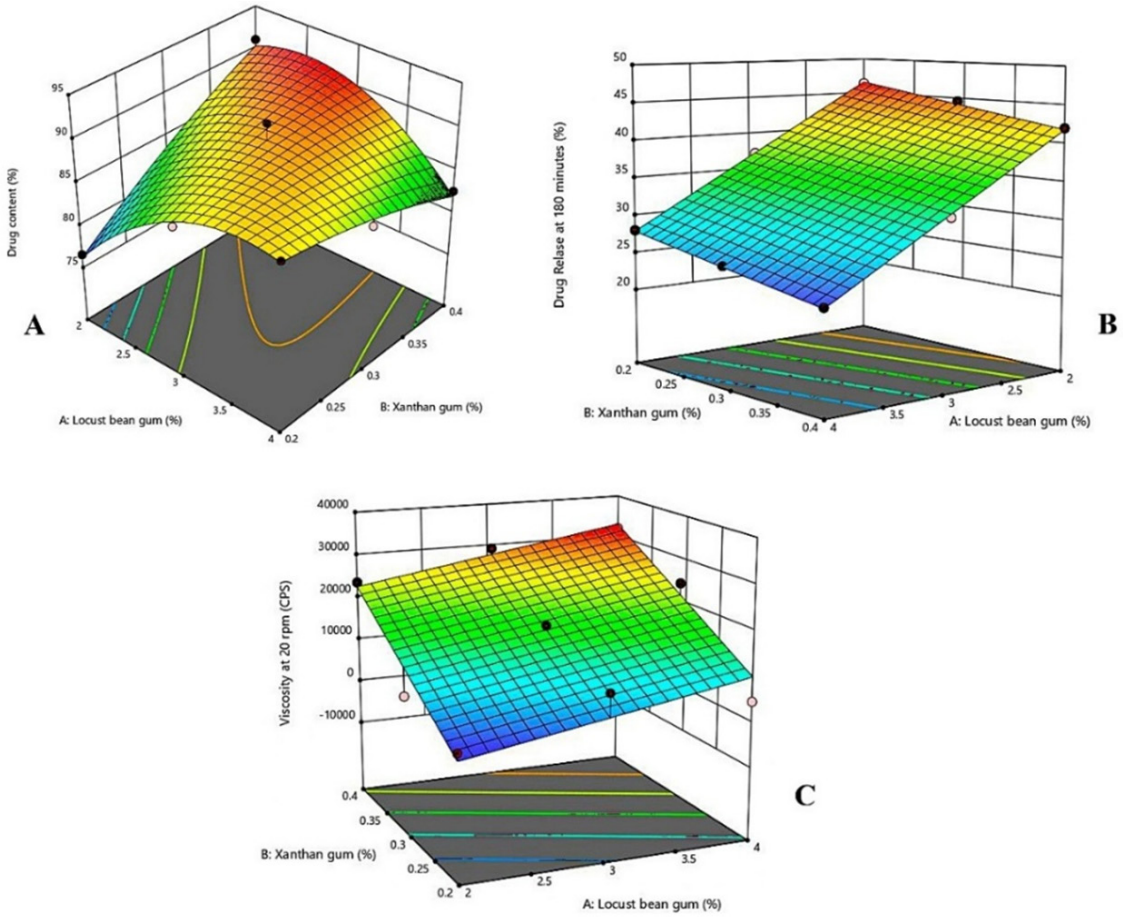


**Figure 5:** Response surface plots showing the effect of LBG and XG on (A) Drug content, (B) Drug release, and (C) Viscosity.

**Table 3: Results of the stability study.**

| Time Point | Drug Content (%) | Viscosity (cP) at 20 rpm | *In vitro* Drug Release at 180 min (%) |
|---|---|---|---|
| 0 Months | 91.07±1.37 | 23600±325 | 45.66±2.36 |
| 1 Month | 90.45±2.43 | 24200±231 | 42.32±3.24 |
| 3 Months | 88.12±3.23 | 26120±327 | 39.23±2.88 |
| 6 Months | 86.45±2.34 | 28532±235 | 36.34±3.23 |

All values are expressed in Mean±SD, $n$=3. Viscosity measured at 20 rpm using Brookfield viscometer. Drug release determined using Franz diffusion cell. Statistical analysis performed using one-way ANOVA ($p < 0.05$). cP: CentiPoise.

hydrogel matrix further enhanced drug release and functional performance. Hydrogels are known to provide a hydrated environment that facilitates drug diffusion while maintaining prolonged contact with the application site. The near-neutral pH of all formulations indicates their compatibility with skin physiology, reducing the risk of irritation and supporting their suitability for topical application. The rheological evaluation revealed that viscosity increased with polymer concentration due to enhanced polymer chain entanglement and formation of a three-dimensional network structure. All formulations exhibited pseudoplastic behavior, which is advantageous for topical delivery as it allows easy spreading under shear stress while maintaining structural integrity at rest. Similar rheological characteristics have been reported by Calienni *et al.* (2023) in polysaccharide-based hydrogels used for topical drug delivery. The *in vitro* diffusion study demonstrated that drug release decreased with increasing polymer concentration, which can be explained by the formation of a denser gel matrix that increases diffusional resistance. This behavior is consistent with previously reported hydrogel systems, where higher polymer content reduces drug mobility and slows release. The kinetic analysis indicated that drug release followed first-order kinetics with a combined diffusion and polymer relaxation mechanism, suggesting that both matrix structure and swelling behavior contribute to drug release. The factorial design provided valuable insights into the influence of formulation variables on key responses. Both locust bean gum and xanthan gum significantly affected viscosity and drug release, with xanthan gum showing a stronger impact on gel viscosity. The optimized formulation (F3) achieved a desirable balance between drug content, viscosity, and release, demonstrating the effectiveness of statistical optimization in formulation development. The close agreement between predicted and experimental values further confirms the robustness and reliability of the model. The enhanced antimicrobial activity observed in the optimized formulation compared to the pure drug gel can be attributed to improved solubility and drug release, resulting in higher drug availability at the site of action. This indicates that the developed system not only improves physicochemical properties but also enhances functional therapeutic performance. Stability studies indicated that the formulation remained stable under accelerated conditions, with only minor changes in drug content, viscosity, and drug release. These changes may be attributed to slight moisture loss and polymer matrix densification over time; however, the overall performance remained within acceptable limits, confirming the robustness of the formulation. This study provides a novel and systematic approach by integrating solid dispersion and hydrogel systems for the topical delivery of rifaximin. While solid dispersion has been widely used for solubility enhancement, its incorporation into a hydrogel matrix for the topical application of rifaximin has not been extensively explored. The use of factorial design further strengthens the study by enabling optimization of formulation variables and establishing their quantitative influence on product performance.

## CONCLUSION

The present study successfully developed and optimized a rifaximin solid dispersion-loaded hydrogel system to overcome solubility limitations and enhance topical drug delivery. The PVA-based solid dispersion (1:1.5) achieved significant solubility enhancement through amorphous transformation, while the optimized hydrogel formulation (F3) demonstrated an optimal balance of drug content, viscosity, and controlled drug release. Factorial design effectively established the influence of polymer concentrations on formulation performance, and stability studies confirmed the robustness of the system. Overall, the developed formulation represents a promising and scalable strategy for improving the topical delivery of poorly water-soluble drugs. Further *in vivo* and clinical studies are warranted to establish its therapeutic potential.

## ABBREVIATIONS

**SD:** Solid Dispersion; **LBG:** Locust Bean Gum; **XG:** Xanthan Gum; **PVA:** Polyvinyl Alcohol; **FTIR:** Fourier-Transform Infrared Spectroscopy; **XRD:** X-ray Diffraction; **DSC:** Differential Scanning Calorimetry; **HPMC:** Hydroxypropyl Methylcellulose; **HPC:** Hydroxypropyl Cellulose; **PEG:** Polyethylene Glycol; **PG:** Propylene Glycol; **ANOVA:** Analysis of Variance.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## REFERENCES

Borse VA, Gangude AB, Deore AB. (2020). Formulation and evaluation of antibacterial topical gel of doxycycline hyclate, neem oil and tea tree oil. Indian Journal of Pharmaceutical Education and Research, 54(1), 206-212. https://doi.org/10.5530/ijper.54.1.24

Calienni MN, Martínez LM, Izquierdo MC, Alonso SDV, Montanari J. (2023). Rheological and viscoelastic analysis of hybrid formulations for topical application. Pharmaceutics, 15(10), 2392. https://doi.org/10.3390/pharmaceutics15102392

Jadhav K, Jadhav S, Sonawane D, Somvanshi D, Shah H, Patil P. (2021). Formulation and evaluation of miconazole nitrate-loaded novel nanoparticle gel for topical delivery. Journal of Pharmaceutical Research International, 33(44A), 292-307. https://doi.org/10.9734/JPRI/2021/v33i44A32616

Jadhav SP, Dhakad PK, Gupta T, Gilhotra R. (2025). Formulation development and evaluation of iloperidone-loaded nanosuspension for solubility enhancement. Indian Journal of Pharmaceutical Education and Research, 59(4), 1323-1333. https://doi.org/10.5530/ijper.20250282

Jadhav V, Kashid P, Otari K, Yadav M. (2024). Solubility enhancement by solid dispersion method: An overview. Asian Journal of Pharmaceutical Research and Development, 12(4), 113-118. https://doi.org/10.22270/ajprd.v12i4.1450

Jhawat V, Gupta S, Saini V. (2016). Formulation and evaluation of novel controlled-release topical pluronic lecithin organogel of mefenamic acid. Drug Delivery, 23(9), 3573-3581. https://doi.org/10.1080/10717544.2016.1212439

Joshi S, Dhingra AK, Chopra B, Dass R, Guarve K, Sapra S. (2023). Formulation and evaluation of solid dispersions of poorly water-soluble drug hesperidin. Letters in Interdisciplinary and National Science, 12(2), Article 50. https://doi.org/10.33263/LIANBS122.050

Khodaverdi E, Khalili N, Zangiabadi F, Homayouni A. (2012). Preparation, characterization and stability studies of glassy solid dispersions of indomethacin using PVP and isomalt as carriers. Iranian Journal of Basic Medical Sciences, 15(3), 820-832.

Kulawik A, Kulawik M, Rosiak N, Lu W, Cielecka-Piontek J, Zalewski P. (2025). Amorphous lycopene-PVP K30 dispersions prepared by ball milling: Improved solubility and antioxidant activity. Polymers, 17(21), 2916. https://doi.org/10.3390/polym17212916

Kumar SR, Mohan V, Srilekha K, Ryaz S, Koteshwara KB, Tippavajhala VK, *et al.* (2020). Diffusion studies of diclofenac sodium topical gel using different synthetic membranes. Research Journal of Pharmacy and Technology, 13(7), 3098-3102. https://doi.org/10.5958/0974-360X.2020.00549.1

Mohana M, Vijayalakshmi S. (2022). Development and characterization of solid dispersion-based orodispersible tablets of cilnidipine. Beni-Suef University Journal of Basic and Applied Sciences, 11, Article 83. https://doi.org/10.1186/s43088-022-00259-3

Raina N, Rani R, Thakur VK, Gupta M. (2023). New insights in topical drug delivery for skin disorders: From a nanotechnological perspective. ACS Omega, 8(22), 19145-19167. https://doi.org/10.1021/acsomega.2c08016

Rusdin A, Mohd Gazzali A, Ain Thomas N, *et al.* (2024). Advancing drug delivery paradigms: Polyvinyl pyrrolidone (PVP)-based amorphous solid dispersion for enhanced physicochemical properties and therapeutic efficacy. Polymers, 16(2), 286. https://doi.org/10.3390/polym16020286

Sapkal SB, Adhao VS, Thenge RR, Darakhe RA, Shinde SA, Shrikhande VN. (2020). Formulation and characterization of solid dispersions of etoricoxib using natural polymers. Turkish Journal of Pharmaceutical Sciences, 17(1), 7-19. https://doi.org/10.4274/tjps.galenos.2018.04880

Shah N, Patel K. (2023). Formulation, development and characterization of liposome-based gel of eberconazole nitrate for topical delivery. International Journal of Pharmaceutical Investigation, 13(3), 485-495. https://doi.org/10.5530/ijpi.13.3.060

Shayto RH, Abou Mrad R, Sharara AI. (2016). Use of rifaximin in gastrointestinal and liver diseases. World Journal of Gastroenterology, 22(29), 6638-6651. https://doi.org/10.3748/wjg.v22.i29.6638

Tsakiridou G, Papanastasiou AM, Efentakis P, Angelerou MFG, Kalantzi L. (2025). Challenges in the investigation of therapeutic equivalence of locally applied/locally acting drugs in the gastrointestinal tract: The rifaximin case. Pharmaceutics, 17(7), 839. https://doi.org/10.3390/pharmaceutics17070839

Zothanpuii F, Rajesh R, Selvakumar K. (2020). A review on stability testing guidelines of pharmaceutical products. Asian Journal of Pharmaceutical and Clinical Research, 13(10), 3-9. https://doi.org/10.22159/ajpcr.2020.v13i10.38848

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