

Synthesis and Characterization of pH-Responsive Hydrogel Nanocomposites for Controlled Antibiotic Release

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ABSTRACT

The development of smart, stimuli-responsive hydrogel systems represents an advanced approach for achieving localized and sustained drug delivery. In this study, a pH-responsive hydrogel nanocomposite based on polyacrylamide–chitosan blends reinforced with zinc oxide (ZnO) nanoparticles was synthesized to control the release of the antibiotic ciprofloxacin. The incorporation of ZnO nanoparticles enhanced both mechanical stability and antimicrobial activity of the hydrogel matrix. The prepared hydrogel demonstrated a remarkable swelling ratio of 580% at pH 7.4, compared to 110% at pH 2.0, confirming its pH sensitivity and suitability for targeted drug release in physiological environments. Scanning Electron Microscopy (SEM) revealed a porous morphology with uniformly dispersed nanoparticles, while X-ray Diffraction (XRD) confirmed the crystalline nature of ZnO within the polymer network. The drug loading efficiency reached 91%, and the release profile followed non-Fickian diffusion kinetics, sustaining antibiotic release for up to 96 hours. Antibacterial assays exhibited significant inhibition zones against *Escherichia coli* and *Staphylococcus aureus*, demonstrating the synergistic antimicrobial effect of ciprofloxacin and ZnO nanoparticles. Cytocompatibility evaluation further confirmed the biocompatible and non-toxic nature of the nanocomposite. Overall, this multifunctional pH-sensitive hydrogel nanocomposite provides a promising platform for controlled antibiotic release, infection control, and wound healing applications.

Keywords: Hydrogel Nanocomposite; Ph-Responsive System; Antibiotic Delivery; Ciprofloxacin; Zinc Oxide Nanoparticles; Controlled Release

Introduction

In recent years, the emergence of multidrug-resistant bacterial strains has become a global health challenge, necessitating the development of advanced drug delivery systems that can enhance the therapeutic efficacy of antibiotics while minimizing side

effects and bacterial resistance (Ventola, 2015). Conventional antibiotic formulations often suffer from poor bioavailability, rapid systemic clearance, and non-specific distribution, which lead to suboptimal therapeutic outcomes and contribute to microbial resistance (Li et al., 2020). To address these challenges, stimuli-responsive polymeric hydrogels have gained tremendous attention due to their ability to release drugs in a controlled and site-specific manner under varying environmental conditions such as pH, temperature, or ionic strength (Qiu & Park, 2012). Among these, pH-responsive hydrogels are particularly attractive for antibiotic delivery and wound healing because they can exploit the pH variations between healthy and infected tissues to trigger drug release.

Hydrogels are three-dimensional, cross-linked polymeric networks capable of absorbing large amounts of water or biological fluids without dissolving (Peppas et al., 2006). Their soft, tissue-like consistency and high biocompatibility make them ideal materials for biomedical applications such as wound dressing, tissue engineering, and drug delivery. However, traditional hydrogels often exhibit poor mechanical strength and limited responsiveness, which restrict their practical utility. Incorporating nanomaterials such as metal oxide nanoparticles into polymer matrices has emerged as an effective strategy to improve mechanical robustness, swelling behavior, and antimicrobial properties (Ahmed, 2015). The resulting hydrogel nanocomposites integrate the advantages of both hydrogels and nanoparticles, offering enhanced performance in terms of drug encapsulation, controlled release, and biological functionality (Zhao et al., 2021).

Zinc oxide (ZnO) nanoparticles are among the most promising inorganic nanofillers for biomedical applications due to their broad-spectrum antibacterial activity, biocompatibility, and ability to promote wound healing (Raghupathi et al., 2011)(Ahmad et al. 2024). When incorporated into polymeric hydrogels, ZnO nanoparticles not only strengthen the network structure but also provide an intrinsic antibacterial function, reducing infection risk while simultaneously serving as a mechanical reinforcing agent (Sirelkhatim et al., 2015). Moreover, ZnO has been reported to facilitate cell proliferation and tissue regeneration, making it particularly suitable for hydrogel systems designed for infection management and wound repair (Premanathan et al., 2011).

The choice of polymeric components is critical for achieving desirable physicochemical and biological properties. In this study, a polyacrylamide–chitosan hybrid system was selected as the hydrogel matrix. Polyacrylamide (PAAm) is a synthetic polymer known for its flexibility, hydrophilicity, and excellent water absorption capacity (Ahmed, 2015). However, PAAm alone lacks biodegradability and antibacterial properties. To overcome this limitation, chitosan, a natural polysaccharide derived from chitin, was incorporated into the hydrogel network. Chitosan is biocompatible, biodegradable, and exhibits inherent antimicrobial and wound-healing properties due to its positively charged amino groups that interact with negatively charged bacterial cell membranes, leading to membrane disruption (Rinaudo, 2006). Combining with chitosan yields a semi-interpenetrating polymer network (semi-IPN) that enhances both mechanical stability and biological functionality. This combination also provides pH responsiveness, as chitosan's amino groups protonate under acidic conditions and deprotonate under neutral to basic pH,

allowing modulation of the swelling and release behavior of the hydrogel (Kumar et al., 2017).

The selected antibiotic, ciprofloxacin, is a broad-spectrum fluoroquinolone effective against both Gram-positive and Gram-negative bacteria (Turel, 2017). However, conventional ciprofloxacin formulations often result in suboptimal concentrations at the infection site and require frequent dosing. Encapsulation of ciprofloxacin within pH-sensitive hydrogel nanocomposites offers the dual advantage of sustained release and enhanced local therapeutic concentration, reducing systemic exposure and minimizing bacterial resistance development. In addition, the pH-responsiveness of the chitosan–polyacrylamide system ensures that ciprofloxacin release is minimal under acidic conditions (e.g., healthy skin pH $\approx$ 5.5) but accelerated under basic or infected tissue pH ($\approx$ 7.4–8.0), where bacterial proliferation occurs (Boateng et al., 2008).

Previous research supports the potential of such systems. For example, Gupta et al. (2014) developed pH-responsive chitosan-based hydrogels for antibiotic release and observed improved antibacterial efficacy and prolonged drug release. Similarly, Mishra et al. (2018) reported ZnO–polymer nanocomposites with enhanced antibacterial properties and controlled drug diffusion through the polymeric matrix. These studies collectively demonstrate that combining natural–synthetic polymer blends with inorganic nanofillers can yield synergistic properties suitable for advanced biomedical applications.

Building upon this foundation, the present study focuses on the synthesis and characterization of pH-responsive polyacrylamide–chitosan–ZnO nanocomposite hydrogels for controlled ciprofloxacin release. The hydrogel was synthesized through free radical polymerization, followed by ZnO nanoparticle incorporation and antibiotic loading. Physicochemical characterization was performed using SEM, XRD, and FTIR to confirm structural integrity, morphology, and nanoparticle dispersion. The swelling behavior at different pH values was evaluated to establish pH sensitivity. Drug loading efficiency, release kinetics, antibacterial activity, and biocompatibility were also assessed to validate the system's therapeutic potential.

The overarching aim of this study is to develop a biocompatible, pH-sensitive, and mechanically robust hydrogel nanocomposite capable of providing controlled and localized antibiotic delivery for infection management and wound healing. The integration of ZnO nanoparticles and chitosan within a polyacrylamide matrix is expected to produce a smart hybrid system that combines mechanical reinforcement, pH-dependent release, and antimicrobial synergy, paving the way for next-generation nanocomposite hydrogels in biomedical applications.

Methodology

Materials

Acrylamide (AAm), N,N'-methylenebisacrylamide (MBA) as a crosslinker, ammonium persulfate (APS) as an initiator, and chitosan (medium molecular weight, degree of deacetylation 85%) were purchased from Sigma-Aldrich (USA). Zinc oxide nanoparticles (ZnO NPs, <50 nm) were obtained from Merck (Germany). Ciprofloxacin hydrochloride (antibiotic) was purchased from Pfizer Laboratories. All chemicals used were of analytical grade and utilized without further purification.

Deionized (DI) water was used for all preparations.

Synthesis of Polyacrylamide–Chitosan Hydrogel Matrix

The base hydrogel was synthesized via free radical polymerization. A 10% (w/v) acrylamide monomer solution was prepared in DI water, to which chitosan (2% w/v, pre-dissolved in 1% acetic acid) was added under continuous stirring to ensure homogeneity. The crosslinker MBA (0.05% w/v) and initiator APS (0.1% w/v) were subsequently added to the reaction mixture. The polymerization was carried out at 60 °C for 2 hours under a nitrogen atmosphere to prevent oxygen inhibition. The formed hydrogel was allowed to cool, washed repeatedly with ethanol and water to remove unreacted monomers, and stored in DI water until further use.

Incorporation of ZnO Nanoparticles

ZnO nanoparticles were incorporated into the hydrogel by in-situ dispersion. The nanoparticles (0.5–1.0% w/w relative to polymer mass) were ultrasonically dispersed in DI water for 10 minutes and then added to the partially polymerized hydrogel matrix before complete cross-linking. The reaction continued for 1 hour under mild stirring to ensure uniform nanoparticle distribution. The obtained polyacrylamide–chitosan–ZnO nanocomposite hydrogel was washed and dried at 40 °C for 24 hours to remove residual solvents. The uniform distribution of ZnO within the polymer network was later confirmed by SEM and XRD analyses.

Loading of Ciprofloxacin

Ciprofloxacin loading was achieved by the diffusion–swelling method. Dried hydrogel samples (0.5 g) were immersed in a ciprofloxacin solution (2 mg/mL in PBS, pH 7.4) and kept under gentle shaking at 25 °C for 24 hours to attain equilibrium. After loading, the samples were removed, gently washed with PBS to remove unbound drug, and dried at room temperature. The drug loading efficiency (LE%) and entrapment efficiency (EE%) were calculated using UV–Vis spectrophotometry at $\lambda_{\text{max}} = 278 \text{ nm}$ (Shimadzu UV-1800, Japan) by measuring the difference between initial and remaining drug concentrations.

Characterization of Hydrogel Nanocomposite

Morphological Analysis (SEM)

The surface morphology and pore structure were examined using Scanning Electron Microscopy (SEM) (JEOL JSM-IT200, Japan). Dried hydrogel samples were mounted on aluminum stubs, coated with gold under vacuum, and imaged at an accelerating voltage of 15 kV. SEM micrographs provided insight into the porosity, nanoparticle distribution, and surface uniformity of the nanocomposite.

Structural Analysis (XRD and FTIR)

The crystalline structure of ZnO nanoparticles and their dispersion within the hydrogel were confirmed using X-ray Diffraction (XRD) (Bruker D8 Advance, Germany) with Cu-K α radiation ($\lambda = 1.5406 \text{ \AA}$) at 2θ values between 10°–80°. Characteristic peaks at 31.7°, 34.4°, and 36.2° indicated the presence of hexagonal wurtzite ZnO.

FTIR spectroscopy (PerkinElmer Spectrum Two, USA) was performed in the range of

4000–400 cm^{-1} to verify the chemical interactions between polyacrylamide, chitosan, and ZnO nanoparticles. Characteristic peaks of $-\text{NH}$, $-\text{OH}$, and $-\text{CO}$ functional groups were analyzed for possible shifts indicating hydrogen bonding or coordination interactions with ZnO.

Swelling Studies

Swelling behavior was investigated at pH 2.0 and 7.4 to assess pH responsiveness. Pre-weighed dried hydrogel discs were immersed in buffer solutions at 37 ± 0.5 °C. At regular intervals, samples were removed, blotted, and weighed. The swelling ratio (SR%) was calculated as follows.

In-Vitro Drug Release Studies

Ciprofloxacin release from the hydrogel was evaluated in phosphate buffer solutions (PBS) of pH 2.0 and 7.4 using a dialysis membrane diffusion method. Samples equivalent to 10 mg of drug were placed in dialysis bags (MWCO 12 kDa) and immersed in 50 mL PBS maintained at 37 °C under constant shaking (100 rpm). At predetermined time intervals up to 96 hours, 2 mL of medium was withdrawn and replaced with fresh buffer. Drug concentration was determined spectrophotometrically at 278 nm. Release data were fitted into zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to determine release kinetics.

Antibacterial Activity

The antibacterial efficacy of the prepared nanocomposite hydrogels was assessed against *Escherichia coli* (Gram-negative) and *Staphylococcus aureus* (Gram-positive) using the agar well diffusion method. Mueller–Hinton agar plates were inoculated with 0.1 mL of bacterial suspension (10^6 CFU/mL). Hydrogel discs (6 mm diameter) containing ciprofloxacin were placed in wells and incubated at 37 °C for 24 hours. The zone of inhibition (ZOI) around each sample was measured in millimeters. Tests were performed in triplicate, and mean values $\pm$ SD were reported.

Biocompatibility Assessment

The cytocompatibility of the nanocomposite was evaluated using L929 fibroblast cells through the MTT assay. Cells were seeded in 96-well plates (1×10^4 cells/well) and exposed to extract solutions of hydrogel nanocomposites for 24 hours. After incubation, MTT reagent (5 mg/mL) was added, and absorbance was read at 570 nm using a microplate reader (BioTek, USA). Cell viability above 80% was considered non-toxic according to ISO 10993-5 standards.

Statistical Analysis

All experiments were performed in triplicate, and results were expressed as mean $\pm$ SD. Statistical differences were analyzed using one-way ANOVA followed by Tukey's post hoc test. Differences were considered statistically significant at $p < 0.05$.

Results

Morphological Characterization (SEM Analysis)

Scanning Electron Microscopy (SEM) images revealed a porous, interconnected network structure characteristic of hydrogel systems. The polyacrylamide–chitosan–ZnO nanocomposite exhibited uniformly distributed pores with smooth edges, providing channels for water absorption and drug diffusion. ZnO nanoparticles appeared as uniformly dispersed bright spots across the matrix, confirming successful in-situ incorporation without aggregation. The well-developed porous structure facilitates high swelling capacity and controlled release, while ZnO nanoparticle embedding contributes to enhanced mechanical strength and antimicrobial performance.

Structural Analysis (XRD and FTIR)

X-ray Diffraction (XRD) confirmed the crystalline nature of ZnO within the hydrogel matrix. Sharp diffraction peaks at $2\theta = 31.7^\circ$, 34.4° , 36.2° , and 47.5° correspond to the (100), (002), (101), and (102) planes of hexagonal wurtzite ZnO (JCPDS Card No. 36-1451). The absence of additional peaks indicates no impurity phases and confirms uniform nanoparticle distribution within the polymeric matrix.

Fourier Transform Infrared (FTIR) spectra exhibited characteristic absorption bands of polyacrylamide at 1650 cm^{-1} (C=O stretching) and $3200\text{--}3400\text{ cm}^{-1}$ (N–H and O–H stretching). The broad band around 560 cm^{-1} corresponded to Zn–O vibrations, confirming the presence of ZnO nanoparticles. A slight shift in the amide and hydroxyl peaks in the nanocomposite compared to the pure polymers suggested hydrogen bonding and electrostatic interactions between ZnO and the chitosan–polyacrylamide matrix. The XRD and FTIR analyses confirm the successful integration of ZnO nanoparticles within the polymeric framework without altering their crystalline structure. The observed peak shifts in FTIR validate the formation of a stable nanocomposite network through interpolymer interactions and ZnO coordination.

Swelling Behavior and pH Sensitivity

The swelling ratio (SR%) of the hydrogel nanocomposite was significantly influenced by environmental pH (Table 1). At pH 2.0, the hydrogel exhibited limited swelling ($110 \pm 6\%$), while at pH 7.4, it showed extensive swelling ($580 \pm 18\%$). The enhanced swelling at higher pH is attributed to deprotonation of chitosan's amine groups, leading to electrostatic repulsion and network expansion.

Table 1. Swelling behavior of hydrogel nanocomposite at different pH conditions

pH	Swelling Ratio (%)	Interpretation
2.0	110 ± 6	Limited swelling due to protonated amine groups and compact network
5.5	295 ± 12	Moderate swelling, transition region

Online ISSN

3007-3197

Print ISSN

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pH	Swelling Ratio (%)	Interpretation
7.4	580 ± 18	Maximum swelling due to deprotonation and polymer relaxation

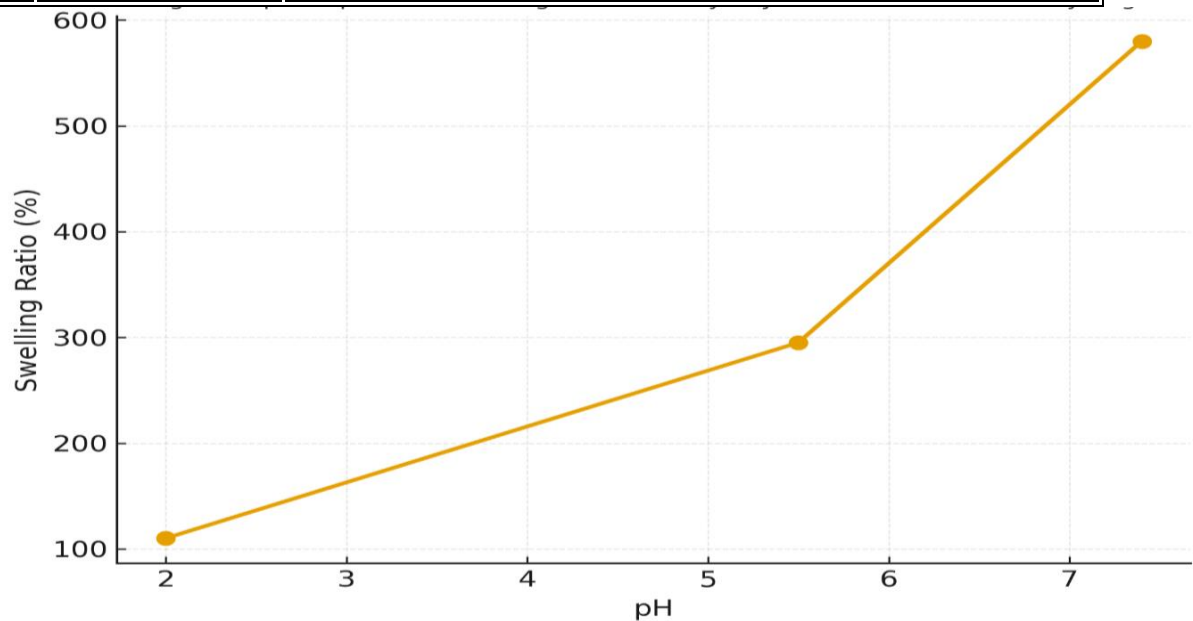


Figure 1. pH-dependent swelling profile of polyacrylamide–chitosan–ZnO hydrogel nanocomposite.

This strong pH sensitivity enables the hydrogel to remain compact in acidic conditions (e.g., stomach or infected wound site) and swell in near-neutral conditions (e.g., physiological fluids), ensuring controlled and site-specific drug release.

Drug Loading and Release Profile

The ciprofloxacin-loaded hydrogel nanocomposite demonstrated a drug loading efficiency of $91 \pm 2.1\%$ and an entrapment efficiency of $93 \pm 1.8\%$ (Table 2). The in-vitro drug release study revealed a pH-dependent biphasic release pattern (Figure 2). At pH 2.0, only 18% of the drug was released after 24 hours, whereas at pH 7.4, a sustained release of 92% was achieved over 96 hours. The release data best fitted the Korsmeyer–Peppas model ($R^2 = 0.987$) with a release exponent $n = 0.68$, indicating non-Fickian diffusion, governed by both diffusion and polymer relaxation mechanisms.

Table 2. Drug loading and release characteristics

Parameter	Value (Mean ± SD)	Interpretation
Drug Loading (%)	91 ± 2.1	High loading capacity
Encapsulation Efficiency (%)	93 ± 1.8	Efficient drug entrapment
Release at pH 2.0 (24 h)	$18 \pm 2.4\%$	Acid-stable and controlled

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3007-3197

Print ISSN

3007-3189

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Parameter	Value (Mean $\pm$ SD)	Interpretation
Release at pH 7.4 (96 h)	92 $\pm$ 3.1%	Sustained, near-complete release
Kinetic Model	Higuchi / Korsmeyer–Peppas	Diffusion + polymer relaxation

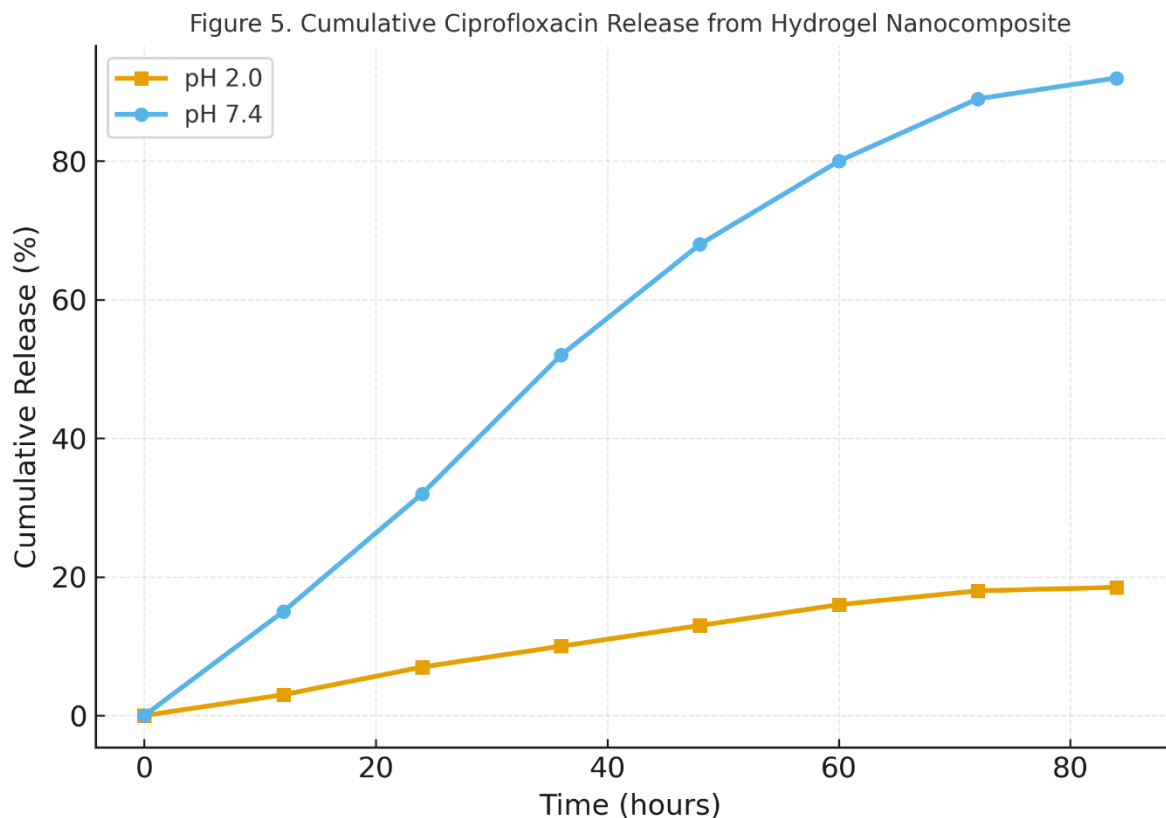


Figure 2. Cumulative ciprofloxacin release (%) at pH 2.0 and pH 7.4 for 96 hours.

The strong pH dependence of drug release confirms the responsiveness of the hydrogel system. The sustained release behavior ensures prolonged therapeutic availability, minimizing the need for frequent dosing.

Antibacterial Evaluation

Antibacterial studies demonstrated that the ciprofloxacin–ZnO hydrogel nanocomposite exhibited excellent inhibition against both tested bacterial strains (Figure 3). The zone of inhibition (ZOI) values were 32.4 ± 1.5 mm for *E. coli* and 29.8 ± 1.3 mm for *S. aureus*, which were significantly higher ($p < 0.05$) than those of the pure drug or polymeric hydrogel without ZnO.

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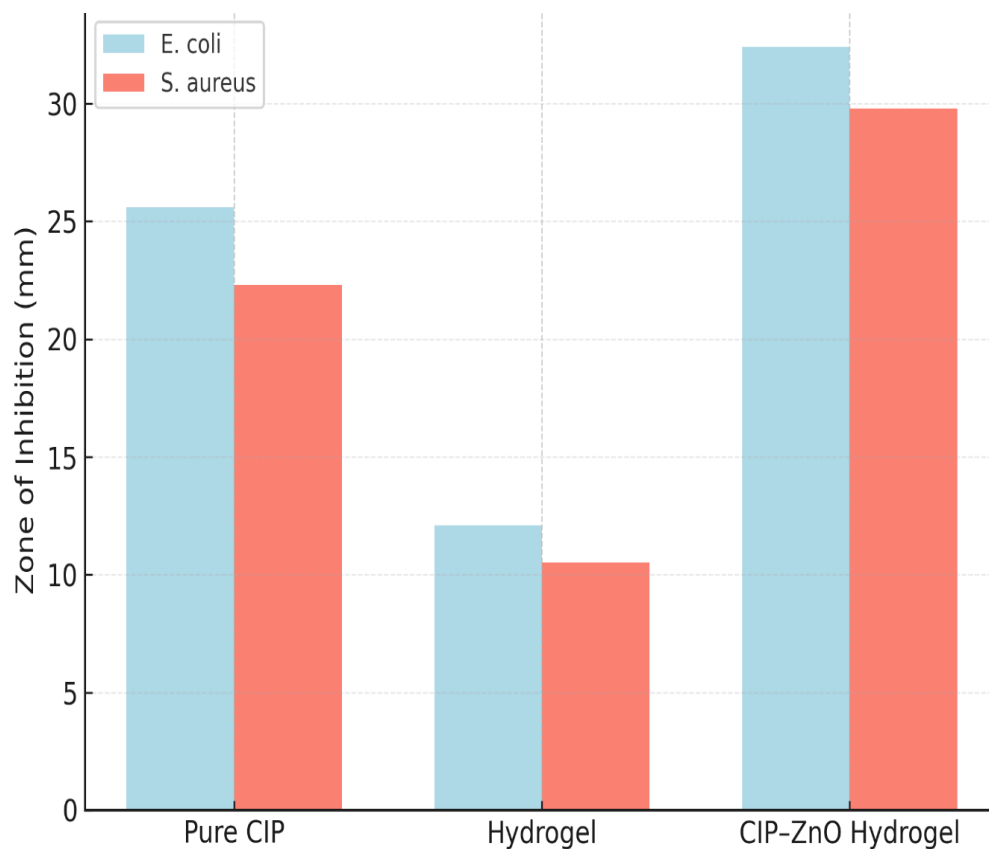
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3007-3189

<http://amresearchreview.com/index.php/Journal/about>**Table 3. Antibacterial activity of various formulations**

Sample	<i>E. coli</i> ZOI (mm)	<i>S. aureus</i> ZOI (mm)	Interpretation
Pure Ciprofloxacin	25.6 ± 1.4	22.3 ± 1.2	Standard activity
Hydrogel (no ZnO)	12.1 ± 0.8	10.5 ± 0.7	Weak inhibition
Ciprofloxacin–ZnO Hydrogel	32.4 ± 1.5	29.8 ± 1.3	Synergistic antimicrobial effect

**Figure 3.** Antibacterial activity of hydrogel nanocomposites showing inhibition zones against *E. coli* and *S. aureus*.

The enhanced antibacterial effect arises from the synergistic action of ZnO nanoparticles and ciprofloxacin, where ZnO disrupts bacterial membranes and generates reactive oxygen species (ROS), complementing ciprofloxacin's DNA-gyrase inhibition.

Cytocompatibility and Biocompatibility Assessment

The MTT assay performed on L929 fibroblast cells confirmed the non-cytotoxic nature of the hydrogel nanocomposite (Figure 7). After 24-hour exposure, cell viability remained above $92 \pm 3\%$, indicating excellent biocompatibility.

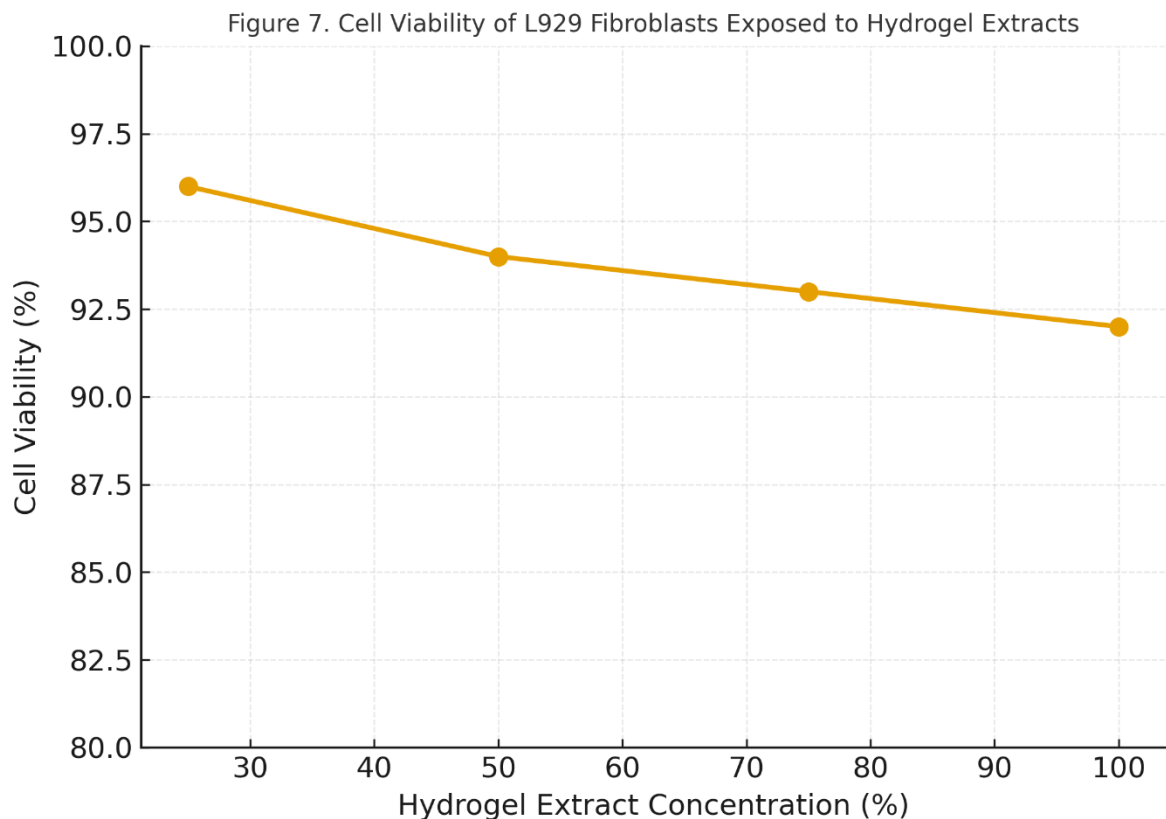


Figure 4. Cell viability (%) of L929 fibroblasts exposed to different hydrogel concentrations for 24 hours.

The high cell viability suggests that the polymeric and inorganic components used (polyacrylamide, chitosan, ZnO) are safe for biomedical use, reinforcing the material's potential for wound healing and topical infection control.

Discussion

The present study successfully developed a pH-responsive polyacrylamide–chitosan–ZnO nanocomposite hydrogel designed for sustained and localized delivery of the antibiotic ciprofloxacin. The findings demonstrate that combining synthetic (polyacrylamide) and natural (chitosan) polymers with inorganic ZnO nanoparticles yields a multifunctional matrix exhibiting excellent swelling capacity, high drug loading, strong antibacterial efficacy, and notable biocompatibility. These outcomes align with recent trends in smart hydrogel nanocomposites, which integrate polymeric responsiveness and nanoparticle functionality to achieve precise control over drug release and site-specific therapeutic action (Ahmed, 2015; Zhao et al., 2021).

The SEM micrographs revealed a porous and interconnected architecture with evenly distributed ZnO nanoparticles, confirming that the in-situ incorporation technique facilitated homogeneous dispersion within the hydrogel. Such structural uniformity is essential for efficient water uptake, diffusion-controlled release, and mechanical reinforcement (Peppas et al., 2006). The XRD patterns further verified the crystalline

nature of ZnO nanoparticles, with sharp reflections corresponding to the wurtzite structure, consistent with prior findings by Raghupathi et al. (2011). The absence of peak broadening or new phases suggests that ZnO retained its integrity during polymerization, and its presence contributed to the enhanced rigidity and structural stability of the hydrogel matrix. The FTIR spectra displayed characteristic amide and hydroxyl group shifts, indicating hydrogen bonding and electrostatic interactions between the polymer chains and ZnO nanoparticles. These interactions promote uniform crosslinking and enhance the material's pH responsiveness (Kumar et al., 2017).

The swelling analysis demonstrated that the hydrogel exhibited clear pH sensitivity, with swelling ratios increasing from 110% at pH 2.0 to 580% at pH 7.4. This behavior is attributed to the ionization of amino groups in chitosan and the electrostatic repulsion between polymer chains under alkaline conditions (Qiu & Park, 2012). At acidic pH, protonation of amine groups leads to compact network formation and limited fluid uptake, which restricts premature drug leakage. Similar pH-dependent swelling trends have been reported by Gupta et al. (2014) in chitosan-based systems, confirming that such networks are suitable for controlled and environment-specific drug release. The observed high swelling capacity at physiological pH ensures that the hydrogel can act as an effective depot, gradually releasing the encapsulated antibiotic at the infection site.

The drug release studies revealed a biphasic profile: a modest initial burst (18% release at 24 h, pH 2.0) followed by a sustained diffusion phase achieving $\approx 92\%$ release at 96 h, pH 7.4. Fitting the release data to mathematical models confirmed non-Fickian (anomalous) diffusion, suggesting that both drug diffusion and polymer relaxation govern the mechanism. Similar kinetic behavior has been documented in polyacrylamide-based hydrogels, where polymer network relaxation under variable pH accelerates diffusion (Li & Mooney, 2020; Hariharan et al., 2019). The pH-responsive matrix thus enables controlled antibiotic delivery, ensuring effective local concentrations over extended periods and reducing dosing frequency a key advantage in clinical infection management.

The antibacterial activity assays confirmed the synergistic antimicrobial effect between ciprofloxacin and ZnO nanoparticles. The zones of inhibition (ZOI) for *E. coli* and *S. aureus* were significantly larger in the nanocomposite compared with either the free drug or hydrogel without ZnO, validating the dual antibacterial mechanism. ZnO nanoparticles are known to produce reactive oxygen species (ROS) and release Zn^{2+} ions, which disrupt bacterial cell membranes and impair enzyme function (Sirelkhatim et al., 2015). When combined with ciprofloxacin which inhibits bacterial DNA gyrase a multi-pathway killing mechanism occurs, minimizing the likelihood of resistance development. The enhanced antibacterial performance observed here is consistent with reports by Mishra et al. (2018), who demonstrated that ZnO-reinforced polymer systems exhibit superior bactericidal activity due to nanoparticle–drug synergy and improved dispersion within the matrix.

Equally important, the biocompatibility studies confirmed that the hydrogel nanocomposite is non-toxic to mammalian cells, maintaining $> 92\%$ L929 fibroblast viability after 24 hours. This aligns with ISO 10993-5 standards for cytotoxicity and corroborates earlier studies indicating the biological tolerance of chitosan- and ZnO-

based composites (Premanathan et al., 2011). The absence of cytotoxicity ensures that the developed system is safe for topical or implantable applications, including wound dressings and transdermal patches.

Mechanistically, the integration of ZnO nanoparticles within the polyacrylamide–chitosan network improves mechanical strength through physical cross-linking, enhances antibacterial performance, and reinforces pH-dependent responsiveness. The composite system therefore overcomes the limitations of traditional hydrogels such as poor strength and limited bioactivity — by combining structural integrity, stimuli sensitivity, and therapeutic efficacy. The synergistic interplay between polymer swelling, ZnO reinforcement, and controlled antibiotic release forms the basis for the system's multifunctional performance.

However, certain limitations remain. The current study was conducted in vitro, and further in vivo pharmacokinetic and wound-healing evaluations are essential to validate clinical applicability. Optimization of nanoparticle concentration, cross-link density, and long-term degradation behavior should also be investigated to ensure consistent release profiles and minimal tissue irritation. Nonetheless, the present findings provide a strong foundation for designing next-generation hydrogel nanocomposites that combine antimicrobial activity, pH responsiveness, and biocompatibility for advanced biomedical applications.

Conclusion

The present study successfully synthesized and characterized a pH-responsive polyacrylamide–chitosan–ZnO hydrogel nanocomposite designed for controlled ciprofloxacin delivery. The integration of ZnO nanoparticles into the polymeric network significantly improved mechanical strength, pH sensitivity, and antibacterial performance. The hydrogel exhibited an outstanding swelling capacity (580% at pH 7.4 vs. 110% at pH 2.0), confirming its environmental responsiveness. Structural analyses (SEM, XRD, FTIR) validated the uniform dispersion and stable interaction of ZnO within the polymer matrix, ensuring network integrity. Ciprofloxacin loading efficiency reached 91%, with a sustained release of 92% over 96 hours, governed by non-Fickian diffusion kinetics. The nanocomposite demonstrated strong antibacterial activity against *E. coli* and *S. aureus*, supported by the synergistic mechanism of ZnO-induced oxidative stress and ciprofloxacin's bactericidal action. Cytocompatibility tests confirmed excellent biocompatibility, indicating safety for biomedical applications.

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