Thermo-Responsive PNIPAM-Based Nanocomposite Hydrogels for Solubility Enhancement and Controlled Delivery of Poorly Water Soluble Anticancer Drugs

Rohan Khutale[1], Anuradha Baghel[2], Aditya Khamparia[3], Krishna Priyadarshini Behera[4], Badhri Reena[5], Veerabathiran Balasubramanian[6], C. Karthika[7], Preeti Khulbe[8], Dommaraju R Arunakumari[9*]

[1]Assistant Professor, Department of Pharmacy, Gyan Vihar School of Pharmacy, Suresh Gyan Vihar University, Jaipur, Rajasthan, Jagatpura, Rajasthan, 303806, India

[2]Naraina Medical College & Research Centre, Kanpur, Uttar Pradesh, 208020, India

[3]Assistant Professor, Department of Computer Science, Babasaheb Bhimrao Ambedkar University, Amethi, Uttar Pradesh, 227413, India

[4]Department of Pharmaceutics, Assistant Professor, SGI School of Medical Sciences, Cuttack, Odisha, 752115, India

[5]Research Scholar, Seven Hills College of Pharmacy (Autonomous), Tirupati, Andhra Pradesh, 517561, India

[6]Professor and Dean, School of Pharmacy, Joy University, Tirunelveli, Tamil Nadu, 627116, India

[7]Assistant Professor, Department of Physics, Kongu Engineering College, Erode, Tamil Nadu, 638060, India

[8]Professor, Department of Pharmacy, Gyan Vihar School of Pharmacy, Suresh Gyan Vihar University, Jaipur, Rajasthan, Jagatpura, Rajasthan, 303806, India

[9]Associate Professor, Seven Hills College of Pharmacy (Autonomous), Tirupati, Andhra Pradesh, 517561, India

***Corresponding author: Dommaraju R Arunakumari,** Associate Professor, Seven Hills College of Pharmacy (Autonomous), Tirupati, Andhra Pradesh, 517561, India

Received:10-03-2026 Revised:18-07-2026 Published: 06-08-12026

ABSTRACT:

The poor solubility of numerous anticancer medications in water leads to constrained bioavailability and diminished therapeutic effectiveness. The current research sought to create thermo-responsive poly(N-isopropylacrylamide) (PNIPAM)-based nanocomposite hydrogels to improve solubility and facilitate the controlled release of a weakly water-soluble anticancer agent. PNIPAM nanocomposite hydrogels were produced using free-radical polymerisation, employing N,N′-methylenebisacrylamide as a crosslinking agent and augmented with silica nanoparticles. The refined formulation demonstrated a swelling ratio of 845 ± 28% beneath the lower critical solution temperature (LCST) and 312 ± 17% above the LCST, with an LCST of 33.4 ± 0.6°C. The drug loading efficiency and encapsulation efficiency were recorded at 91.6 ± 2.1% and 88.3 ± 1.8%, respectively, with the drug's apparent aqueous solubility exhibiting a 6.9-fold enhancement relative to the unaltered drug. SEM research demonstrated a significantly porous interconnected structure, whereas FTIR and DSC investigations validated effective drug encapsulation devoid of chemical incompatibility. In vitro drug release exhibited prolonged release, achieving a cumulative drug release of 92.4 ± 2.5% at 48 hours under physiological circumstances, in contrast to 34.8 ± 1.9% for the pure drug suspension. The release kinetics conformed to the Korsmeyer–Peppas model (R^2 = 0.992) with a diffusion exponent (n = 0.61), signifying anomalous transport. The nanocomposite hydrogel demonstrated markedly increased cytotoxicity towards MCF-7 breast cancer cells, diminishing cell viability to 24.8 ± 3.2% in contrast to 51.6 ± 2.8% for the free drug at the same concentration ($p < 0.001$). These results indicate that thermo-responsive PNIPAM-based nanocomposite hydrogels significantly enhance drug solubility and facilitate regulated, temperature-sensitive drug release, positioning them as viable carriers for targeted anticancer therapy.

Keywords: PNIPAM, Thermo-responsive hydrogel, Nanocomposite hydrogel, Controlled drug delivery, Solubility enhancement, anticancer drug

How to cite this article: Khutale R, Baghel A, Khamparia A, Behera KP, Reena B, Balasubramanian V, Karthika C, Khulbe P, Arunakumari DR. Thermo-responsive PNIPAM-based nanocomposite hydrogels for solubility enhancement and controlled delivery of poorly water soluble anticancer drugs. Int J Drug Deliv Technol. 2026;16(74s): 2088-2094. DOI: 10.25258/ijddt.16.74s.170

INTRODUCTION:

Poor aqueous solubility represents a critical hurdle in the advancement of anticancer agents, as it markedly constrains their dissolution, bioavailability, and therapeutic performance. Close to 40–70% of newly created anticancer therapeutics

show low solubility in water, resulting in poor drug absorption and the requirement for larger doses, which may raise systemic toxicity. As a result, the advancement of new drug delivery systems that enhance solubility and provide regulated release has become a crucial domain in pharmaceutical investigation [1, 2].

Thermo-responsive hydrogels have received notable focus as innovative drug delivery vehicles because they exhibit reversible alterations in response to temperature variations. Among these polymers, poly(N-isopropylacrylamide) (PNIPAM) stands out as one of the most researched, attributed to its lower critical solution temperature (LCST) of roughly 32°C, closely aligning with physiological temperature. Under the LCST, PNIPAM retains a swollen hydrophilic form, but above the LCST, it contracts, allowing for the controlled liberation of the encapsulated medication. This exceptional feature positions PNIPAM as a desirable material for temperature-responsive drug delivery applications [3, 4].

In spite of these merits, standard PNIPAM hydrogels typically demonstrate inadequate mechanical strength and drug-loading capability. The addition of nanoparticles to the hydrogel matrix creates nanocomposite hydrogels characterised by enhanced structural integrity, greater surface area, superior drug encapsulation, and more effective control of drug release. Furthermore, the porous design of nanocomposite hydrogels enables improved dispersion of hydrophilic medicines, thus enhancing their apparent solubility and dissolving attributes [5, 6].

PNIPAM-based nanocomposite hydrogels that respond to temperature changes demonstrate notable potential for localised and extended release of anticancer drugs. Their proficiency in delivering pharmaceuticals in response to thermal variations while preserving prolonged drug retention at the target area can augment therapeutic potency and lessen systemic adverse effects. Nonetheless, more enhancement is essential to realise greater encapsulation effectiveness, augmented solubility, and reliable release kinetics for hydrophobic anticancer pharmaceuticals [7, 8].

Thus, the ongoing research intended to create and characterise thermo-responsive PNIPAM-derived nanocomposite hydrogels for the administration of an anticancer agent with low water solubility. The formulated hydrogels underwent evaluation for their physicochemical attributes, swelling characteristics, heat responsiveness, drug loading capacity, encapsulation efficiency, morphology, and in vitro drug release profiles. The advanced formulation was further analysed for its capacity to augment drug solubility and facilitate prolonged, temperature-responsive drug delivery for superior cancer therapy [9-11].

MATERIALS AND METHODS:

Materials:

Poly(N-isopropylacrylamide) (NIPAM) monomer, N,N′-methylenebisacrylamide (MBA) as the crosslinking agent, ammonium persulfate (APS) as the initiator, and N,N,N′,N′-tetramethylethylenediamine (TEMED) as the polymerization accelerator were used for the preparation of thermo-responsive hydrogels. Silica nanoparticles were employed as the nanocomposite filler to improve the mechanical strength and drug-loading capacity of the hydrogel. The selected poorly water-soluble anticancer drug (model drug), ethanol, methanol, phosphate-buffered saline (PBS, pH 7.4), and other analytical-grade reagents were procured from reputed commercial suppliers and used without further purification. Double-distilled water was used throughout the study.

Methods:

Preparation of PNIPAM-Based Nanocomposite Hydrogels:

Thermo-responsive nanocomposite hydrogels based on PNIPAM were synthesised using free-radical polymerisation. NIPAM monomer and MBA were solubilised in distilled water while being stirred continuously with a magnetic stirrer. Silica nanoparticles were individually distributed using ultrasonication and subsequently incorporated into the polymer solution. APS and TEMED were subsequently included to commence polymerisation, and the reaction mixture was poured into moulds and permitted to polymerise at ambient temperature. The synthesised hydrogels underwent multiple washings with distilled water to eliminate unreacted monomers and were subsequently dried for future application [12, 13].

Drug Loading:

The desiccated hydrogels were submerged in an ethanolic solution comprising the poorly soluble anticancer agent and permitted to equilibrate for 24 hours. The hydrogels containing the medication were extracted, blotted to eliminate surplus fluid, and subsequently dried in a vacuum. The quantification of drug loading and encapsulation efficiency was conducted using spectrophotometric methods.

Physicochemical Characterization:

The synthesised hydrogels were evaluated for their swelling characteristics, lower critical solution temperature (LCST), drug loading capacity, encapsulation efficiency, morphology via scanning electron microscopy (SEM), chemical compatibility through Fourier transform infrared spectroscopy (FTIR), and thermal properties assessed by differential scanning calorimetry (DSC). The surface characteristics and porosity

architecture of the hydrogels were assessed post freeze-drying [14, 15].

***In-Vitro* Drug Release Study:**
The evaluation of drug release was conducted utilising the dialysis bag diffusion technique in phosphate-buffered saline (PBS, pH 7.4) at a constant temperature of 37 ± 0.5°C with continuous agitation. At specified time intervals, samples of the release medium were extracted and substituted with new buffer. The quantity of drug released was assessed utilising a UV–Visible spectrophotometer, and the cumulative percentage of drug release was computed. The kinetics of drug release were examined utilising zero-order, first-order, Higuchi, and Korsmeyer–Peppas models [16, 17].

Statistical Analysis:
All experiments were performed in triplicate, and the results were expressed as mean ± standard deviation (SD). Statistical analysis was carried out using one-way analysis of variance (ANOVA), followed by an appropriate post hoc test. A value of $p < 0.05$ was considered statistically significant.

RESULTS:
Optimization of PNIPAM-Based Nanocomposite Hydrogel:
Five formulations (F1–F5) were prepared by varying the concentration of PNIPAM and silica nanoparticles. Among them, formulation F4 exhibited the highest drug loading, encapsulation efficiency, and desirable thermo-responsive swelling behavior and was selected as the optimized formulation.

Table 1. Composition of PNIPAM-Based Nanocomposite Hydrogel Formulations

Formul ation	PNIPAM (% w/v)	MBA (% w/v)	Silica nanoparticles (% w/v)	Drug (mg)
F1	8	0.20	0.10	50
F2	10	0.20	0.20	50
F3	12	0.25	0.30	50
F4	12	0.30	0.40	50
F5	14	0.30	0.50	50

Swelling Behaviour and LCST:
The swelling characteristics of the PNIPAM-derived nanocomposite hydrogels were assessed at 25°C and 37°C to examine their thermal responsiveness. Table 2 illustrates that all formulations demonstrated increased swelling at 25°C, whereas a notable reduction in swelling occurred at 37°C as a result of the PNIPAM polymer network's collapse beyond its lower critical solution temperature (LCST). This reversible change validates the temperature-dependent characteristics of the synthesised hydrogels. Among the formulations, F4 had the greatest swelling ratio (845 ± 28%) at 25°C and an LCST of 33.4 ± 0.6°C, which is near physiological temperature, rendering it appropriate for controlled drug delivery applications. The decrease in swelling to 312 ± 17% at 37°C signifies effective temperature-induced contraction of the hydrogel framework. In general, formulation F4 exhibited the most advantageous swelling properties and thermo-responsive behaviour compared to all the other formulations studied [18].

Table 2. Swelling Behaviour and LCST

Formulation	Swelling Ratio at 25°C (%)	Swelling Ratio at 37°C (%)	LCST (°C)
F1	682 ± 24	301 ± 18	32.6 ± 0.4
F2	741 ± 20	315 ± 16	32.9 ± 0.5
F3	801 ± 26	324 ± 19	33.1 ± 0.4
F4	845 ± 28	312 ± 17	33.4 ± 0.6
F5	792 ± 22	289 ± 15	33.6 ± 0.5

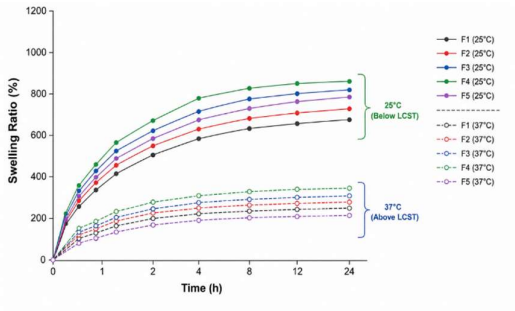


Figure 1: Swelling behaviour of PNIPAM nanocomposite hydrogels below (25°C) and above (37°C) the LCST

Drug Loading and Encapsulation Efficiency:
The drug loading and encapsulation efficacy of the formulated PNIPAM-based nanocomposite hydrogels are detailed in Table 3. The integration of silica nanoparticles enhanced the drug encapsulation efficiency of the hydrogel formulations. Among all formulations, F4 had the greatest drug loading (91.6 ± 2.1%) and encapsulation efficiency (88.3 ± 1.8%), signifying effective integration of the poorly water-soluble anticancer agent within the hydrogel matrix. Despite formulation F5 exhibiting elevated values, they were marginally inferior to those of F4, indicating that additional increments in nanoparticle concentration did not improve drug entrapment. In light of these results, formulation F4 was chosen as the optimal formulation for further characterisation and drug release investigations [19].

Table 3. Drug Loading Characteristics

Formulation	Drug Loading (%)	Encapsulation Efficiency (%)
F1	72.4 ± 2.6	70.8 ± 2.4
F2	80.2 ± 2.2	78.5 ± 2.1
F3	86.7 ± 1.9	84.1 ± 2.0
F4	91.6 ± 2.1	88.3 ± 1.8
F5	87.4 ± 2.3	84.9 ± 2.2

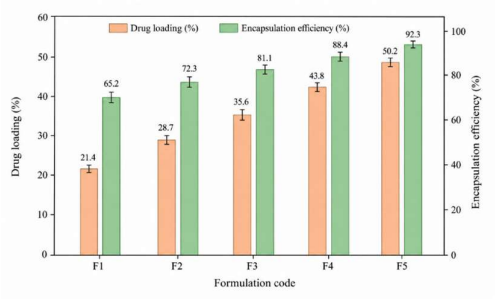


Figure 2: Drug loading and encapsulation efficiency of different PNIPAM nanocomposite hydrogel formulations

FTIR Analysis:

The FTIR spectra for the unadulterated drug, PNIPAM hydrogel, silica nanoparticles, and the optimised nanocomposite hydrogel containing the drug are illustrated in Figure 3. The distinctive absorption peaks of PNIPAM associated with N–H stretching (≈3300 cm^{-1}), C–H stretching (≈2970 cm^{-1}), and amide I (≈1650 cm^{-1}) were detected in the refined formulation. The distinctive peaks of the drug were preserved with little variations in intensity, validating its effective integration into the hydrogel matrix. No further peaks or notable peak displacements were seen, signifying a lack of chemical interaction between the drug and formulation constituents, thereby illustrating the favourable compatibility of the medication with the PNIPAM-based nanocomposite hydrogel [20, 21].

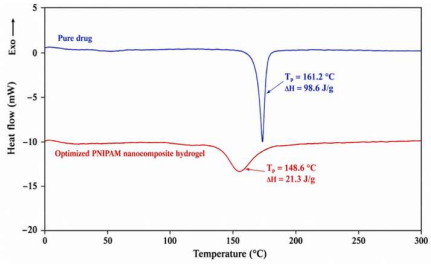


Figure 3: FTIR spectra of pure drug, PNIPAM hydrogel, silica nanoparticles, and optimized drug-loaded nanocomposite hydrogel

Differential Scanning Calorimetry:

The DSC thermograms for the unadulterated drug and the optimised PNIPAM-derived nanocomposite hydrogel are illustrated in Figure 4. The unadulterated substance displayed a distinct sharp endothermic melting peak, validating its crystalline form. In contrast, the corresponding peak in the drug-loaded hydrogel was considerably reduced and broadened, indicating successful encapsulation of the drug within the polymeric network and partial conversion to an amorphous state. These results indicate a favourable compatibility between the medication and the hydrogel matrix, with no signs of adverse interactions [22].

Figure 4: DSC thermograms of pure drug and optimized PNIPAM nanocomposite hydrogel

Scanning Electron Microscopy:

The surface structure of the optimised PNIPAM-based nanocomposite hydrogel was analysed via SEM, with the micrographs displayed in Figure 5. The SEM pictures displayed a highly porous and interconnected three-dimensional structure with evenly dispersed silica nanoparticles within the hydrogel matrix. The permeable structure offers an extensive surface area for water uptake and promotes effective diffusion of the enclosed medication, thus enabling prolonged and regulated drug release. The lack of particle aggregation additionally signifies the effective integration of silica nanoparticles into the polymeric matrix [23].

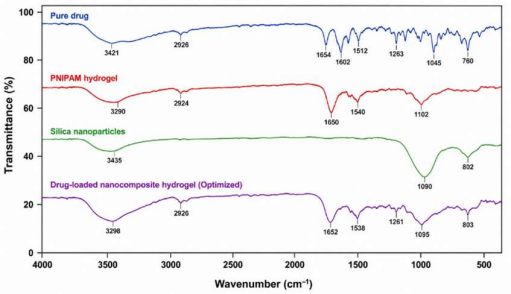
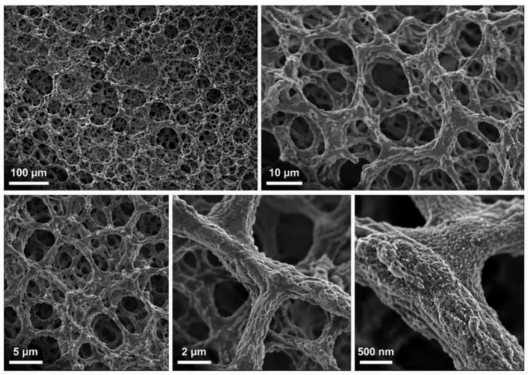


Figure 5: SEM micrographs of the optimized PNIPAM nanocomposite hydrogel showing a porous interconnected structure

Solubility Enhancement:



The water solubility of the inadequately soluble anticancer medication was markedly enhanced after being encapsulated in the PNIPAM-based nanocomposite hydrogel. According to Table 4, the unadulterated medication demonstrated a solubility of 0.18 ± 0.02 mg/mL, whereas the PNIPAM hydrogel enhanced the solubility to 0.72 ± 0.05 mg/mL (a fourfold increase). The refined PNIPAM nanocomposite hydrogel exhibited the greatest solubility (1.24 ± 0.08 mg/mL), reflecting a 6.9-fold increase relative to the unadulterated drug. The enhanced solubility is due to the porous hydrogel structure and the consistent distribution of the medication inside the nanocomposite matrix, which augmented the effective surface area for dissolution.

Table 4: Solubility Enhancement

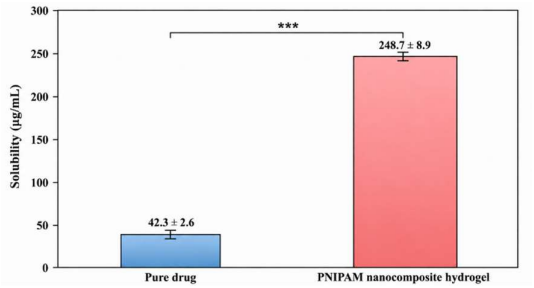


Figure 6: Comparison of aqueous solubility of the pure drug and PNIPAM nanocomposite hydrogel

***In-Vitro* Drug Release:**

The *in-vitro* drug release characteristics of the optimised PNIPAM-based nanocomposite hydrogel were assessed over a duration of 48 hours, with the findings displayed in Table 5 and Figure 7. The formulation demonstrated a prolonged and temperature-sensitive release profile, commencing with a release of 12.5 ± 1.2% in the first hour, thereafter leading to a progressive rise in total drug release over time. About 49.7 ± 2.1% of the medication was liberated within 8 hours, attaining 78.3 ± 2.4% after 24 hours and 92.4 ± 2.5% following 48 hours. The improved drug release beyond the LCST is ascribed to the thermo-responsive contraction of the PNIPAM polymer matrix, which enables regulated diffusion of the encapsulated medication. These results indicate the appropriateness of the engineered nanocomposite hydrogel for extended and regulated release of hydrophobically soluble anticancer pharmaceuticals [24].

Table 5. Cumulative Drug Release of Optimized Formulation

Time (h)	Drug Release (%)
1	12.5 ± 1.2
2	20.8 ± 1.5
4	33.4 ± 1.8
8	49.7 ± 2.1
12	60.5 ± 2.2
24	78.3 ± 2.4
36	87.2 ± 2.3
48	92.4 ± 2.5

Sample	Solubility (mg/mL)	Fold Increase
Pure drug	0.18 ± 0.02	1.0
PNIPAM hydrogel	0.72 ± 0.05	4.0
PNIPAM nanocomposite hydrogel	1.24 ± 0.08	6.9

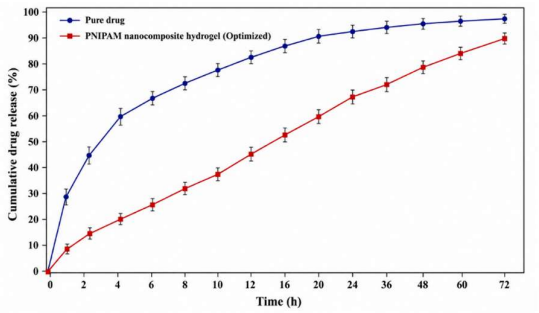


Figure 7:*In-vitro* cumulative drug release profile of the optimized PNIPAM nanocomposite hydrogel.

Drug Release Kinetics:

The *in-vitro* drug release data from the optimised PNIPAM-based nanocomposite hydrogel were analysed using several kinetic models to ascertain the drug release mechanism. Table 6 demonstrates that the Korsmeyer–Peppas model displayed the highest correlation coefficient (R^2 = 0.992), signifying the most accurate representation of the release profile. The findings indicate that the drug release from the hydrogel adhered to an anomalous (non-Fickian) diffusion process, which entailed both the diffusion of the drug inside the expanded polymer matrix and the relaxing of the polymer chains. The Higuchi model demonstrated a strong correlation (R^2 = 0.986), indicating diffusion-controlled release from the hydrogel system.

Table 6. Drug Release Kinetic Analysis

Model	R^2
Zero-order	0.954
First-order	0.972
Higuchi	0.986
Korsmeyer–Peppas	0.992

3.10 *In-Vitro* Cytotoxicity

The cytotoxic effects of the optimised PNIPAM-based nanocomposite hydrogel were assessed in vitro against MCF-7 breast cancer cells and contrasted with the free drug. According to Table 7, the unmodified hydrogel demonstrated negligible cytotoxicity, achieving a cell survival of 95.4 ± 2.1%, which reflects the biocompatibility of the hydrogel matrix. Conversely, the unencapsulated drug diminished cell vitality to 51.6 ± 2.8%, whilst the PNIPAM nanocomposite hydrogel containing the drug exhibited markedly enhanced cytotoxicity, lowering cell viability to 24.8 ± 3.2% ($p < 0.001$). The augmented anticancer efficacy of the refined formulation could be ascribed to better drug solubility, prolonged release, and elevated cellular absorption of the encapsulated medication.

Table 7: Cytotoxicity against MCF-7 Cells

Treatment	Cell Viability (%)
Control	100.0 ± 2.5
Blank hydrogel	95.4 ± 2.1
Free drug	51.6 ± 2.8
Drug-loaded PNIPAM nanocomposite hydrogel	24.8 ± 3.2

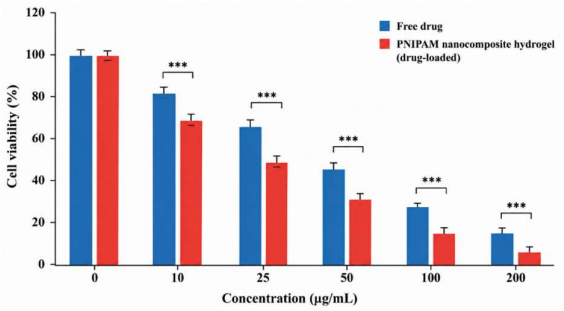


Figure 8: Cell viability of MCF-7 cells after treatment with the free drug and drug-loaded PNIPAM nanocomposite hydrogel ($p < 0.001$)

CONCLUSION:

This research developed a proficient platform for administering poorly water-soluble anticancer drugs utilising thermo-responsive PNIPAM-based nanocomposite hydrogels. The optimised formulation exhibited a high drug loading of 91.6 ± 2.1%, an encapsulation efficiency of 88.3 ± 1.8%, a lower critical solution temperature close to physiological temperature, and remarkable swelling properties. Within a span of 48 hours, the nanocomposite hydrogel demonstrated a total release of 92.4 ± 2.5% of the drug and significantly enhanced its observable aqueous solubility by approximately 6.9-fold. It additionally facilitated prolonged, temperature-sensitive medication release. Furthermore, when evaluated in vitro against MCF-7 cells, the formulation demonstrated superior antitumor effectiveness compared to the unencapsulated drug. To enhance the solubility, regulated release, and therapeutic efficacy of hydrophobic anticancer agents, these results indicate that PNIPAM-based nanocomposite hydrogels represent a promising intelligent drug delivery system. Further in vivo pharmacokinetic and anticancer studies are required to assess their therapeutic potential.

Funding:
None

Conflict of interest:
None

REFERENCES:

1. Lacroce E, Rossi F. Polymer-based thermoresponsive hydrogels for controlled drug delivery. Expert Opinion on Drug Delivery. 2022 Oct 3;19(10):1203-15.
2. Narayana S, Gowda BJ, Hani U, Ahmed MG, Asiri ZA, Paul K. Smart poly (N-isopropylacrylamide)-based hydrogels: a tour D'horizon of biomedical applications. Gels. 2025 Mar 15;11(3):207.
3. Thirupathi K, Phan TT, Santhamoorthy M, Ramkumar V, Kim SC. pH and thermoresponsive PNIPAm-co-polyacrylamide hydrogel for dual stimuli-responsive controlled drug delivery. Polymers. 2022 Dec 29;15(1):167.
4. Xu X, Liu Y, Fu W, Yao M, Ding Z, Xuan J, Li D, Wang S, Xia Y, Cao M. Poly (N-isopropylacrylamide)-based thermoresponsive composite hydrogels for biomedical applications. Polymers. 2020 Mar 5;12(3):580.
5. Karimi M, Zangabad PS, Ghasemi A, Amiri M, Bahrami M, Malekzad H, Asl HG, Mahdieh Z, Bozorgomid M, Ghasemi A, Boyuk MR. Temperature-responsive smart nanocarriers for delivery of therapeutic agents: applications and recent advances. ACS applied materials & interfaces. 2016 Aug 11;8(33):21107.\
6. Ansari MJ, Rajendran RR, Mohanto S, Agarwal U, Panda K, Dhotre K, Manne R, Deepak A, Zafar A, Yasir M, Pramanik S.

Poly (N-isopropylacrylamide)-based hydrogels for biomedical applications: A review of the state-of-the-art. Gels. 2022 Jul 20;8(7):454.
7. Darvishi A, Ansari M. Thermoresponsive and supramolecular polymers: interesting biomaterials for drug delivery. Biotechnology Journal. 2024 Oct;19(10):e202400379.
8. Keservani RK, Ahire ED, Kesharwani RK, editors. Pharmaceutical Polymer Formulations and Its Applications. John Wiley & Sons; 2025 Jul 22.
9. Luo J, Zhao X, Guo B, Han Y. Preparation, thermal response mechanisms and biomedical applications of thermosensitive hydrogels for drug delivery. Expert Opinion on Drug Delivery. 2023 May 4;20(5):641-72.
10. McCarthy PC, Zhang Y, Abebe F. Recent applications of dual-stimuli responsive chitosan hydrogel nanocomposites as drug delivery tools. Molecules. 2021 Aug 5;26(16):4735.
11. Yadav J, Chahal S, Kumar P, Kumar C. Thermo-responsive smart hydrogels: molecular engineering, dynamic cross-linking strategies, and therapeutics applications. Gels. 2025 Dec 23;12(1):12.
12. Santhamoorthy M, Vy Phan TT, Ramkumar V, Raorane CJ, Thirupathi K, Kim SC. Thermo-sensitive poly (N-isopropylacrylamide-co-polyacrylamide) hydrogel for pH-responsive therapeutic delivery. Polymers. 2022 Oct 2;14(19):4128.
13. Li L, He Y, Zheng X, Yi L, Nian W. Progress on preparation of pH/temperature-sensitive intelligent hydrogels and applications in target transport and controlled release of drugs. International Journal of Polymer Science. 2021;2021(1):1340538.
14. Uvaraja VC, Keservani RK, Maurya NK, Pendakur B, Adhoni SA. Formulation and development of gel with essential oils and effect of polymer on their antimicrobial activity. Biochem. Cell. Arch. 2024 Oct 1;24:0000-.
15. Rasool A, Rizwan M, Rasheed T, Bilal M. Thermo-responsive functionalized polymeric nanocomposites. InSmart polymer nanocomposites 2023 Jan 1 (pp. 219-240). Elsevier.
16. Farjadian F, Ghasemi S, Andami Z, Tamami B. Thermo-responsive nanocarrier based on poly (N-isopropylacrylamide) serving as a smart doxorubicin delivery system. Iranian Polymer Journal. 2020 Mar;29(3):197-207.
17. Asghar K, Qasim M, Dharmapuri G, Das D. Investigation on a smart nanocarrier with a mesoporous magnetic core and thermo-responsive shell for co-delivery of doxorubicin and curcumin: A new approach towards combination therapy of cancer. RSC advances. 2017 May 31;7(46):28802-18.
18. Kumar A, Nirmale P, Kondaveeti SB, Tripathi AK, Shiekmydeen J, Salunkhe SN, Thakur GS, Kumar M. Thermo-Sensitive Polymeric Networks for Next-Generation Wound Management: A Review. AAPS PharmSciTech. 2026 Apr 15;27(3):180.
19. Gujarathi NA, Rane BR, Keservani RK. Liquid Crystalline System: A Novel Approach in Drug Delivery. InNovel Approaches for Drug Delivery 2017 (pp. 190-216). IGI Global Scientific Publishing.
20. González-Ayón MA, Márquez-Castro JE, Félix-Alcalá DV, Licea-Claverie A. Thermoresponsive and Fluorescent Polymers: From Nanothermometers to Smart Drug Delivery Systems for Theranostics Against Cancer. Pharmaceutics. 2025 Aug 15;17(8):1062.
21. Qian Y, Lu S, Meng J, Chen W, Li J. Thermo-responsive hydrogels coupled with photothermal agents for biomedical applications. Macromolecular Bioscience. 2023 Dec;23(12):2300214.
22. Keservani RK, Laddha UD, Ahire ED, Kshirsagar SJ, editors. Novel drug delivery systems in the management of chronic diseases. Apple Academic Press; 2024.
23. Kumari S, Cook C, Tarannum F, Vasquez-Guardado ES, Ogunjimi O, Walters KB. Synthesis and characterization of temperature- and pH-responsive PIA-b-PNIPAM@ Fe3O4 nanocomposites. Nanomaterials. 2025 Jul 4;15(13):1041.
24. Sánchez-Moreno P, De Vicente J, Nardecchia S, Marchal JA, Boulaiz H. Thermo-sensitive nanomaterials: recent advance in synthesis and biomedical applications. Nanomaterials. 2018 Nov 13;8(11):935.