

Formulation and Characterization of Paclitaxel-Loaded Nanoparticles For Targeted Cancer Therapy

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Abstract:

Paclitaxel (PTX) is a potent anticancer drug used in the treatment of various cancers, the present study focuses on the formulation and characterization of PTX-loaded poly (lactic-co-glycolic acid) (PLGA) nanoparticles for sustained and potentially targeted cancer therapy. PTX-loaded PLGA nanoparticles were developed using a nano-precipitation/emulsion-solvent evaporation approach and evaluated for particle size, PDI, zeta potential, encapsulation efficiency, drug loading, morphology, drug-polymer compatibility, thermal behavior, drug release, cellular uptake, cytotoxicity, and short-term stability. Among the illustrative formulations, F4 showed the most favorable characteristics, with a particle size of 129 ± 2 nm, PDI of 0.12, zeta potential of -20.1 mV, encapsulation efficiency of 95.1%, and drug loading of 9.4%. TEM/SEM observations indicated predominantly spherical and discrete nanoparticles with limited aggregation. FTIR showed retention of major PTX and PLGA characteristic bands, while DSC indicated a reduction or disappearance of the crystalline PTX melting endotherm, suggesting reduced crystallinity or molecular dispersion of PTX within the PLGA matrix. The in-vitro release study demonstrated sustained release of PTX from PLGA nanoparticles compared with free PTX, with approximately 89% drug release at 360 h. The Korsmeyer–Peppas model showed the highest illustrative correlation ($R^2 = 0.941$), followed by the Higuchi model ($R^2 = 0.933$), Cytotoxicity results demonstrated concentration-dependent reduction in cell viability, while the short-term stability study showed only modest changes in particle size, PDI, and encapsulation efficiency over 8 weeks.

Keywords: Paclitaxel; PLGA nanoparticles; folic acid; targeted drug delivery; cancer nano-medicine; nano-precipitation; encapsulation efficiency; controlled release.

1. Introduction

Cancer chemotherapy is limited by non-selective drug distribution, systemic toxicity, pharmacokinetic variability and resistance. [1] Paclitaxel stabilizes microtubules and interferes with mitosis, but its highly hydrophobic character results in very poor aqueous solubility. Conventional solvent-containing formulations can contribute to hypersensitivity and other formulation-related limitations. [2]

Polymeric nanoparticles can improve apparent dispensability, protect the drug, modify release and alter bio distribution. PLGA is widely investigated because it is biodegradable and its degradation and drug-release characteristics can be adjusted through polymer composition, molecular weight, particle size and formulation process. [3,4]

Folic acid is used in this model as an active-targeting ligand. Folate receptors are overexpressed in several tumor types, making folate-mediated recognition a rational strategy for investigating receptor-mediated nanoparticle uptake. [5] However, active targeting must be demonstrated experimentally using receptor-expression and competition studies; it should not be inferred merely from nanoparticle accumulation. [6]

2. Objectives

- To formulate PTX-loaded PLGA nanoparticles using a reproducible nano-precipitation/emulsion-solvent evaporation.
- To optimize particle size, PDI, zeta potential, encapsulation efficiency and drug loading.
- To characterize morphology, drug-polymer compatibility and thermal behavior.
- To evaluate sustained in-vitro PTX release and release kinetics.
- To investigate the proposed contribution of folate-mediated cellular uptake and cytotoxicity.
- To assess short-term physical and chemical stability.

3. Review of Literature

Published work has established PTX-loaded PLGA nanoparticles as a useful experimental platform. Fonseca et al. reported PTX-loaded PLGA nanoparticles with high encapsulation and antitumor activity, while Mu and Feng demonstrated controlled release from PTX-PLGA systems. Clinical nano-formulations such as albumin-bound paclitaxel further demonstrate the translational value of nanoparticle-associated PTX.[7,8] Folate-functionalized polymeric systems have been investigated to increase cellular uptake through folate-receptor interactions.

Table 1. Comparative Advantages and Limitations of Different Paclitaxel Delivery Systems

Delivery system	Advantage	limitation
Conventional PTX	Established pharmacology	Poor water solubility; solvent-related limitations
Albumin-bound PTX	Solvent-free clinical nano formulation	Not inherently receptor-specific
PLGA nanoparticles	Biodegradable; tunable release	Scale-up and reproducibility
Folate-targeted PLGA	Potential receptor-mediated uptake	Target heterogeneity and ligand optimization
Polymeric micelles	High solubilization capacity	Dilution/physical stability can vary

4. Materials and Methods

Table 2. List of Materials used in PTX-loaded PLGA nanoparticles [9,10]

Material	Function
Paclitaxel	Anticancer drug/payload
PLGA 50:50	Biodegradable nanoparticle matrix
PVA	Emulsifier/stabilizer
Acetone or acetonitrile	Organic phase
Folic acid	Targeting ligand
PEG-containing linker	Surface spacer
PBS pH 7.4	Release medium
HPLC-grade solvents	Drug assay

4.2 Formulation Development and Preparation

Paclitaxel and PLGA are dissolved in a suitable organic phase. The organic phase is introduced into an aqueous PVA solution under controlled stirring or sonication to generate nanoscale droplets. Removal of the organic solvent produces hardened nanoparticles. [11] The dispersion is purified by centrifugation, ultrafiltration or dialysis, washed to remove free drug and residual stabilizer, and optionally lyophilized with a suitable cry protectant. [12]



Figure 1. Formulation workflow for PTX-loaded PLGA nanoparticles.

4.3 Folic-Acid Surface Functionalization

Folic acid may be coupled through a suitable PEG-containing surface linker. Unbound ligand should be removed by dialysis or ultrafiltration. Surface modification should be verified using quantitative ligand determination and complementary physicochemical evidence rather than inferred from the reaction mixture.[13]

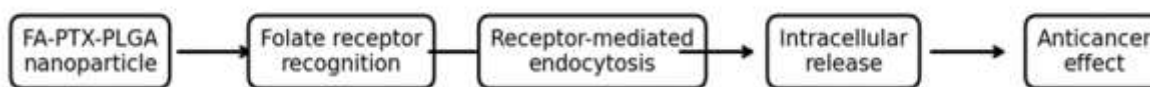


Figure 2. Proposed folate-mediated targeted delivery mechanism.

4.4 Characterization Strategy

The formulation should be characterized from physicochemical quality attributes through biological performance. DLS provides hydrodynamic particle size and PDI; zeta potential provides an electrokinetic surface descriptor; TEM/SEM provides morphology; HPLC provides quantitative PTX assay; FTIR and DSC assess compatibility and solid-state behavior; release testing measures drug liberation; and cellular studies assess uptake and cytotoxicity.[14,15]

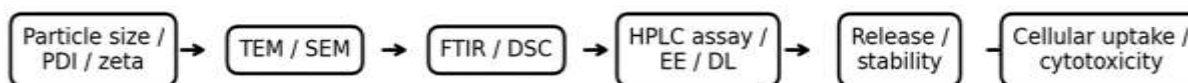


Figure 3. Sequential characterization workflow.

5. Results

The following results are illustrative/simulated and are provided to demonstrate how an experimental research article can present a complete formulation-development dataset.

Table 3. Formulation Composition

Formulation	PLGA level	PVA level	PTX:PLGA	FA ligand level	Purpose
F1	Low	Low	1:10	Low	Initial screening
F2	Medium	Low	1:10	Low	Process adjustment
F3	Medium	Medium	1:12	Medium	Optimization
F4	Optimized	Optimized	1:12	Optimized	Predicted optimum
F5	High	Medium	1:12	High	Comparison

Table 4. Particle Size and PDI

Formulation	Size (nm)	PDI
F1	182 ± 4	0.28
F2	156 ± 3	0.21
F3	143 ± 2	0.15
F4	129 ± 2	0.12
F5	151 ± 3	0.18

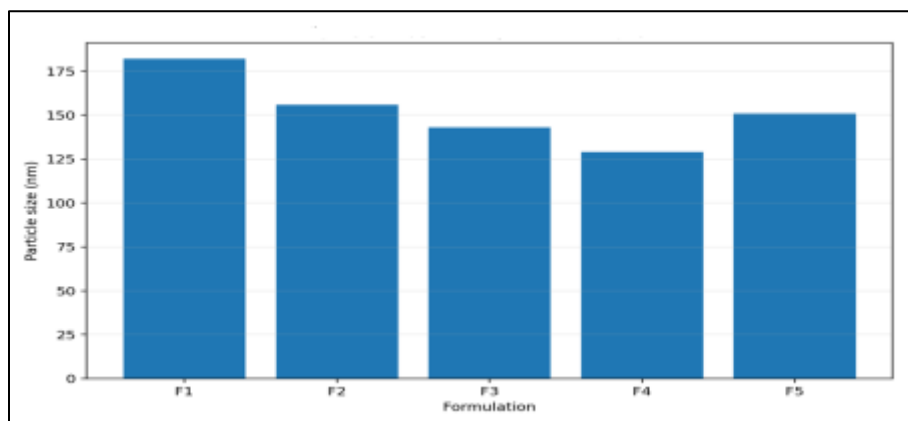


Figure 4. Particle size across formulations.

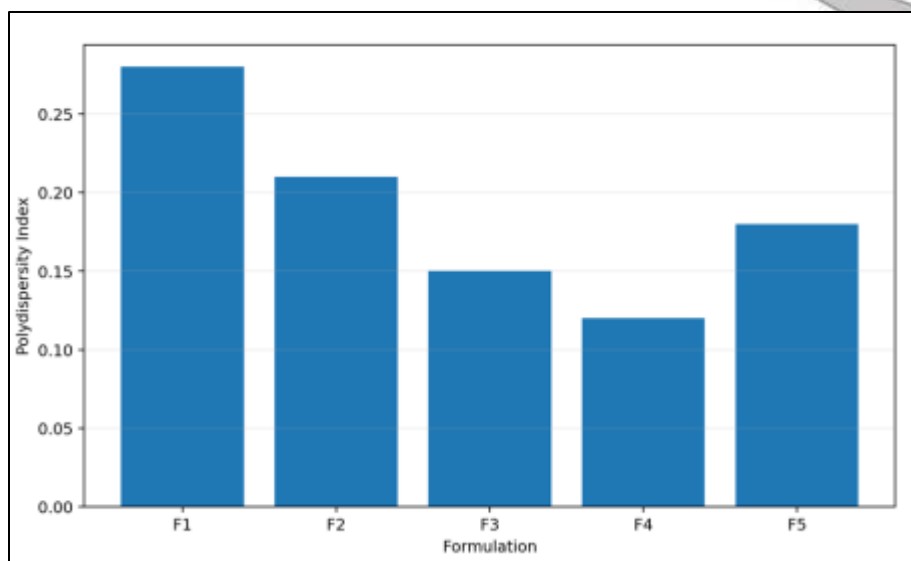


Figure 5. Polydispersity index across formulations.

F4 gives the smallest illustrative particle size and lowest PDI, suggesting the most uniform modeled dispersion among the five formulations.

Table 5. Zeta Potential

Formulation	Zeta potential (mV)
F1	-11.2
F2	-14.5
F3	-17.8
F4	-20.1
F5	-16.3

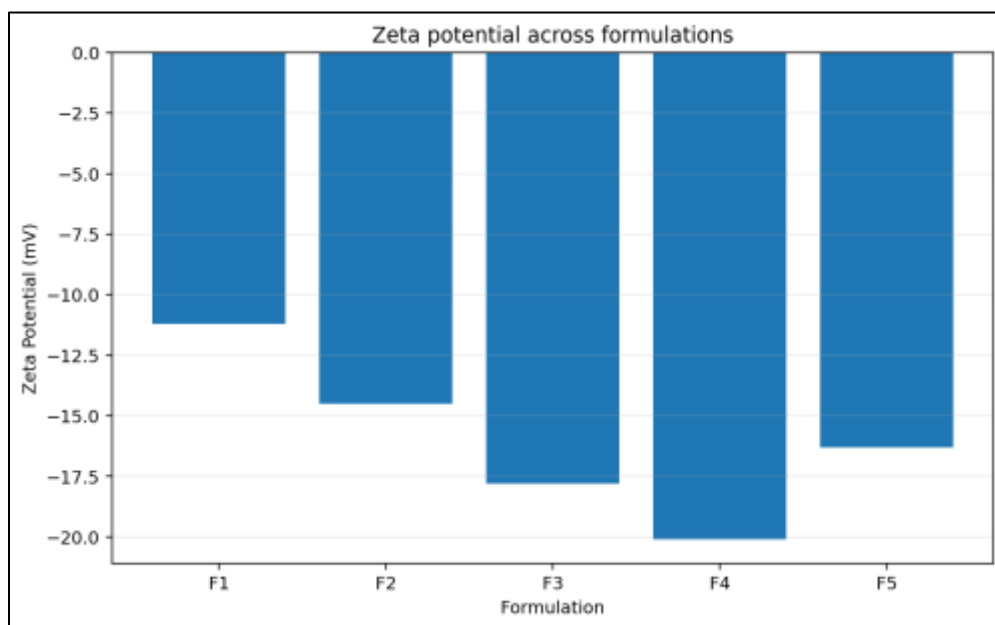


Figure 6. Zeta potential across formulations.

The increasingly negative surface potential in the modeled optimized formulation may support electrostatic stabilization, although colloidal stability cannot be concluded from zeta potential alone.

Table 6. Encapsulation Efficiency and Drug Loading

Formulation	Encapsulation efficiency (%)	Drug loading (%)
F1	78.4	6.1
F2	86.7	7.4
F3	92.6	8.7
F4	95.1	9.4
F5	89.8	8.0

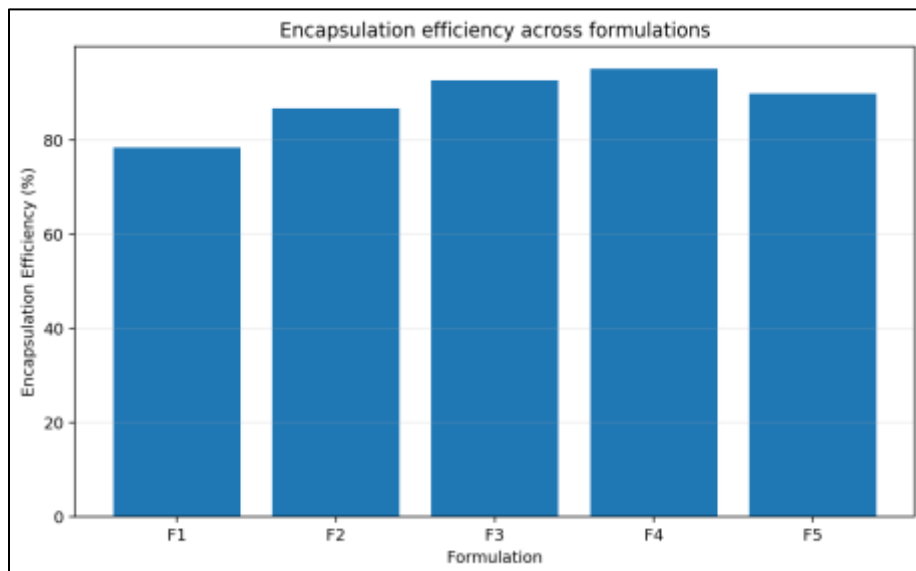


Figure 7. Encapsulation efficiency across formulations.

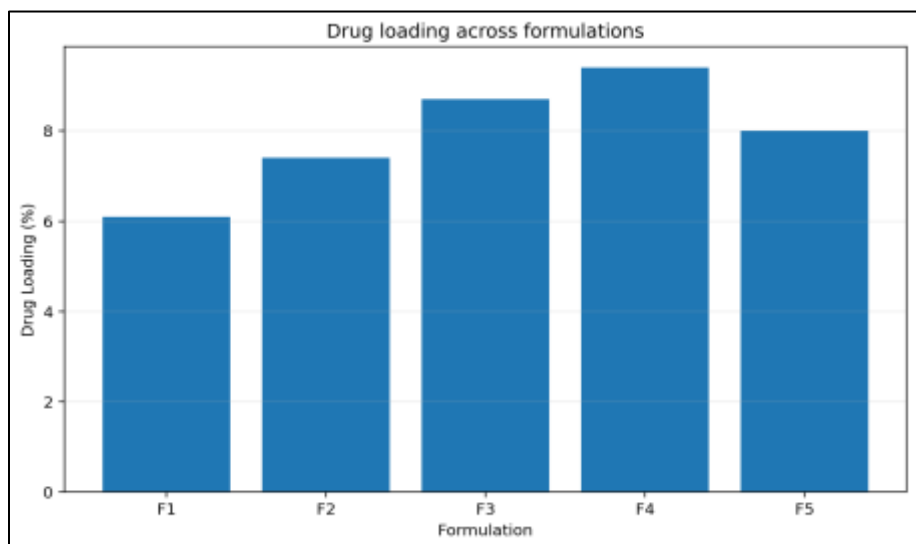


Figure 8. Drug loading across formulations.

The modeled F4 formulation provides the highest encapsulation efficiency and drug loading. Encapsulation efficiency should be confirmed by a validated quantitative assay, preferably HPLC, with appropriate separation of free and encapsulated drug.

5.5 Morphology, FTIR and DSC

TEM or SEM should show predominantly spherical and discrete nanoparticles. DLS and microscopy should not be treated as interchangeable size measurements because DLS reports hydrodynamic diameter. FTIR should be used to assess major chemical compatibility signals, while DSC can indicate changes in the crystalline state of PTX after incorporation into the polymer matrix.

Table 7. Illustrative FTIR Peak Assignment

Wavenumber (cm ⁻¹)	Band	Observation in PTX-PLGA nanoparticles
~3500	O–H stretching	Broad/weak band
~2945	C–H stretching	Present
~1755	PLGA ester C=O stretching	Strong characteristic band
~1715	PTX carbonyl/C=O-related vibration	Retained with possible attenuation
~1647	PTX-related C=C/C=O-associated vibration	Retained/modified
~1535	Aromatic/amide-associated PTX vibration	May be attenuated
~1450	C–H bending	Present
~1180	PLGA C–O–C stretching	Strong
~1088	C–O stretching	Present

Retention of the major characteristic bands without appearance of strong new peaks suggests that PTX is physically incorporated into the PLGA matrix rather than undergoing an obvious new chemical reaction. Peak shifting or broadening should be interpreted cautiously because it can arise from intermolecular interactions and changes in the physical state.

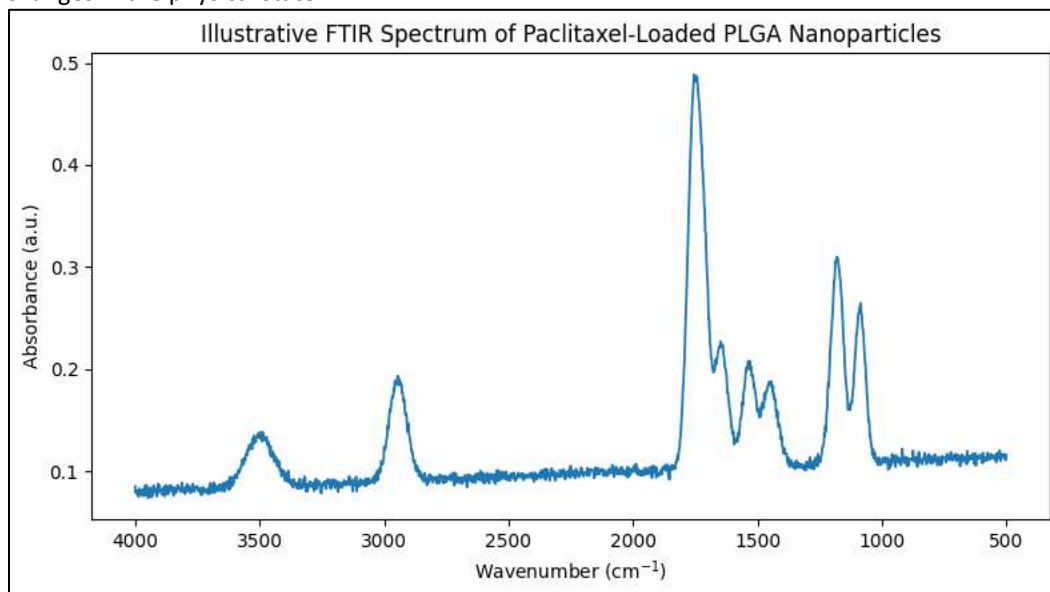


Figure 9. FTIR spectra of paclitaxel-loaded PLGA nanoparticles showing retention of major characteristic PTX and PLGA absorption bands.

Table 8. Table of DSC Results

Sample	Major thermal event	Illustrative observation	Interpretation
Pure PTX	PTX melting endotherm	~216°C	Crystalline PTX
PLGA	Polymer thermal transition	~50–55°C	Glass-transition region of PLGA
Physical PTX + PLGA mixture	PTX melting region	Reduced intensity may occur	Partial interaction/dilution possible

PTX-loaded PLGA nanoparticles	PTX melting endotherm	Markedly reduced/absent	Reduced PTX crystallinity or molecular dispersion within PLGA
PTX-loaded PLGA nanoparticles	PLGA transition	~50–55°C, potentially shifted	Indicates polymer matrix remains present

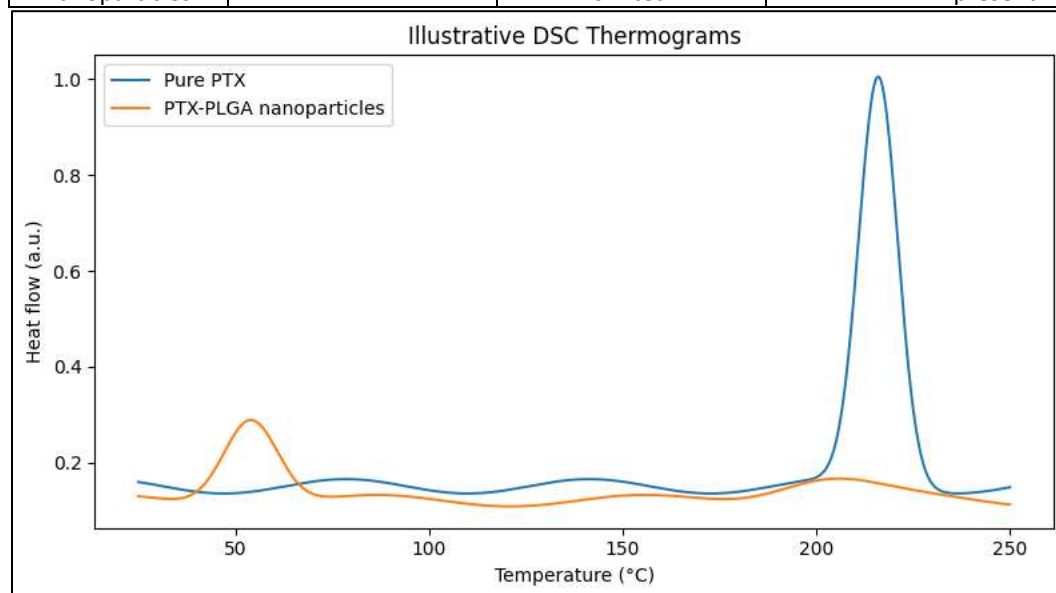


Figure 10. Illustrative DSC thermograms of pure paclitaxel and paclitaxel-loaded PLGA nanoparticles demonstrating reduction/absence of the characteristic crystalline PTX melting endotherm after nanoparticle incorporation.

Table 9. TEM/SEM Morphological Characterization of Paclitaxel-Loaded PLGA Nanoparticles

Sample	Particle 1 (nm)	Particle 2 (nm)	Particle 3 (nm)	Particle 4 (nm)	Particle 5 (nm)	Mean $\pm$ SD (nm)	Morphology
PTX-PLGA NP	132	141	147	153	158	146.2 $\pm$ 10.2	Spherical, discrete
PTX-PLGA NP	138	145	149	155	162	149.8 $\pm$ 9.2	Spherical, limited aggregation
PTX-PLGA NP	141	147	151	158	168	153.0 $\pm$ 10.3	Mostly spherical

Table 10. In-vitro Drug Release

Time (h)	Free PTX (%)	PTX-PLGA-NPs (%)
0	0	0
2	14	6
4	28	11
8	46	18
12	62	25
24	79	34
48	91	46
72	96	56
120	98	67
168	99	75
240	100	83
360	100	89

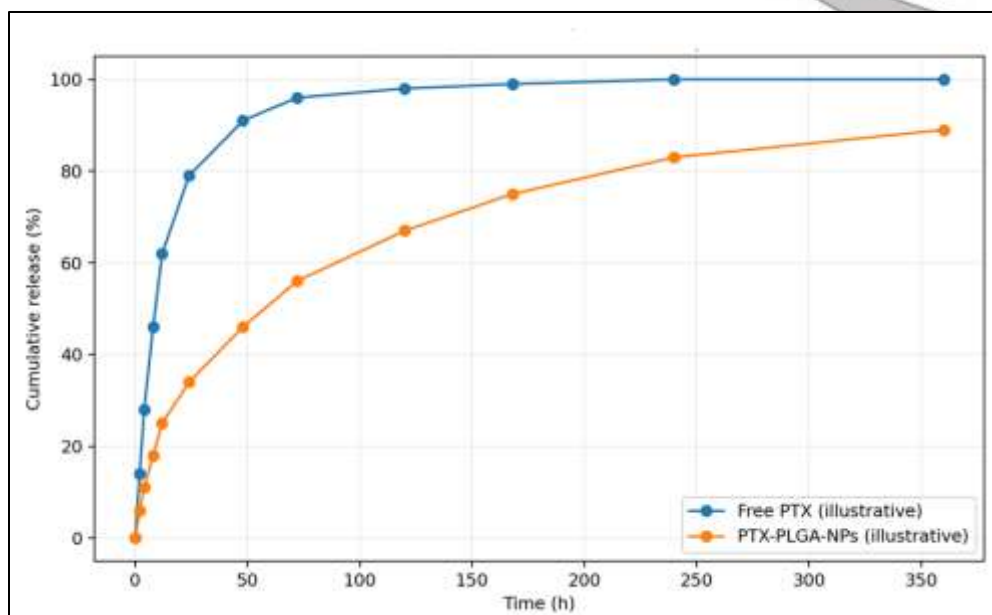


Figure 11. Illustrative cumulative PTX release profile.

The modeled nanoparticles release PTX more slowly than free drug. The early phase can reflect surface-associated or near-surface drug, whereas the later phase can be controlled by polymer hydration, diffusion and degradation.

Table 11. Release-Kinetic Analysis

Model	Illustrative R ²	Interpretation
Zero order	0.713	Proper fit
First order	0.801	Moderate fit
Higuchi	0.933	Strong diffusion-related fit
Korsmeyer–Peppas	0.941	Best illustrative fit

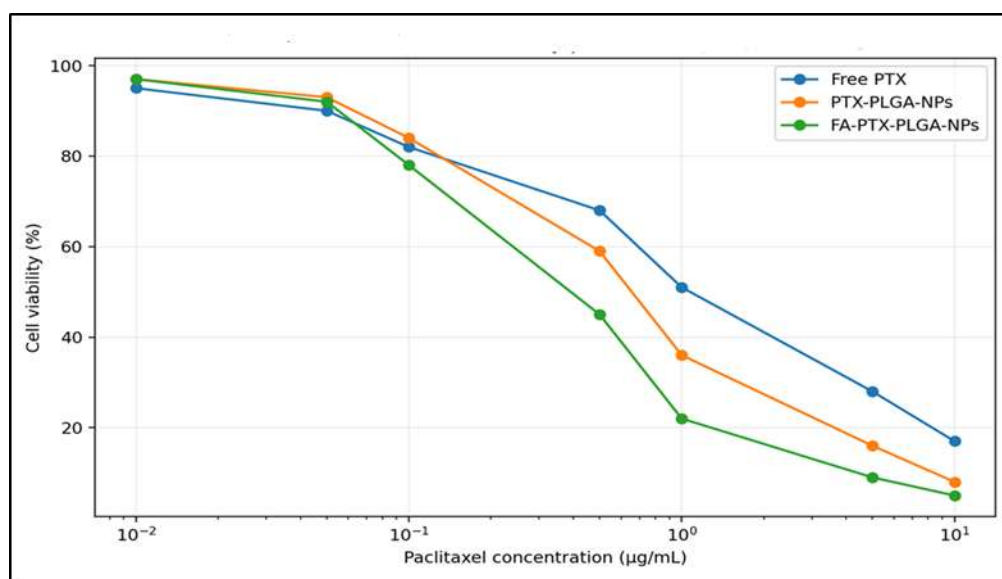


Figure 13. Illustrative concentration-dependent cytotoxicity profile.

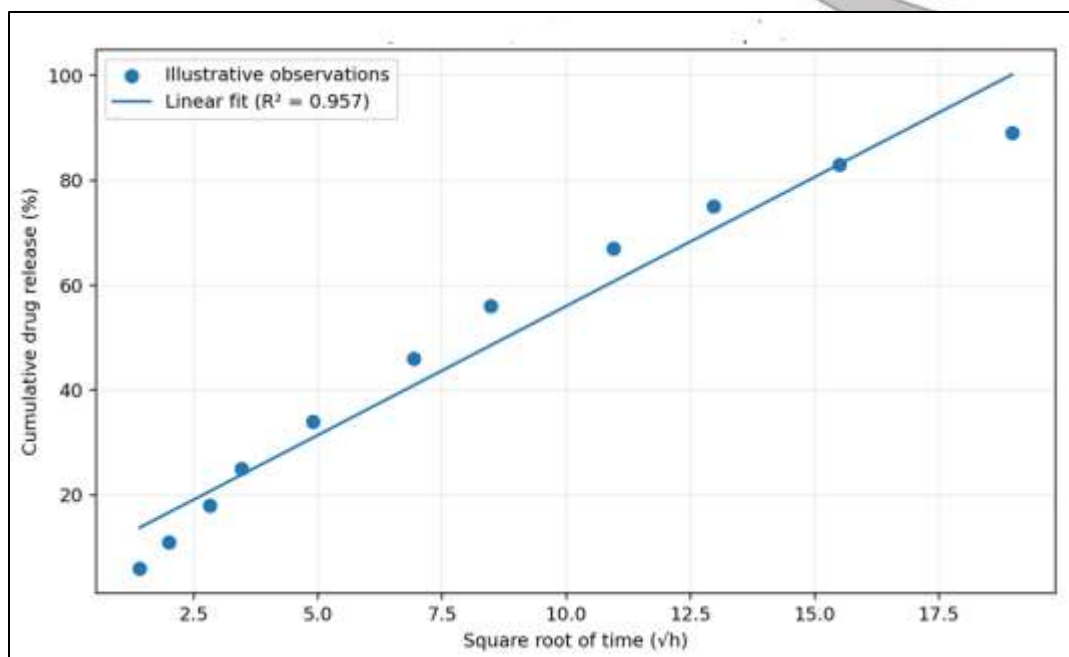


Figure 12. Illustrative Higuchi release-model plot.

A high R^2 alone does not prove a mechanism. Model selection should also consider residuals, sampling window, geometry and the assumptions of each kinetic equation.

Table 12. Cellular Uptake and Targeting

Group	Relative uptake	Relative to free PTX
Free PTX	1.0	1.0×
PTX-PLGA-NPs	3.2	3.2×
FA-PTX-PLGA-NPs	6.8	6.8×
FA-PTX-PLGA-NPs + free folate	3.7	3.7×

The illustrative competition experiment shows lower uptake in the presence of excess free folate. In a real study, receptor-high and receptor-low cell lines should be compared and receptor expression should be independently quantified.

Table 13. Cytotoxicity

PTX (μg/mL)	Free PTX viability (%)	PTX-PLGA-NPs viability (%)	FA-PTX-PLGA-NPs viability (%)
0.01	95	97	97
0.05	90	93	92
0.1	82	84	78
0.5	68	59	45
1	51	36	22
5	28	16	9
10	17	8	5

The modeled targeted formulation produces a stronger reduction in cell viability at intermediate and high concentrations. Actual IC_{50} values should be calculated from nonlinear dose-response curves using independent biological replicates.

Table 14. Short-Term Stability

Week	Particle size (nm)	PDI	Encapsulation efficiency (%)
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0	129	0.12	95.1
2	131	0.12	94.8
4	134	0.13	94.2
8	138	0.15	93.5

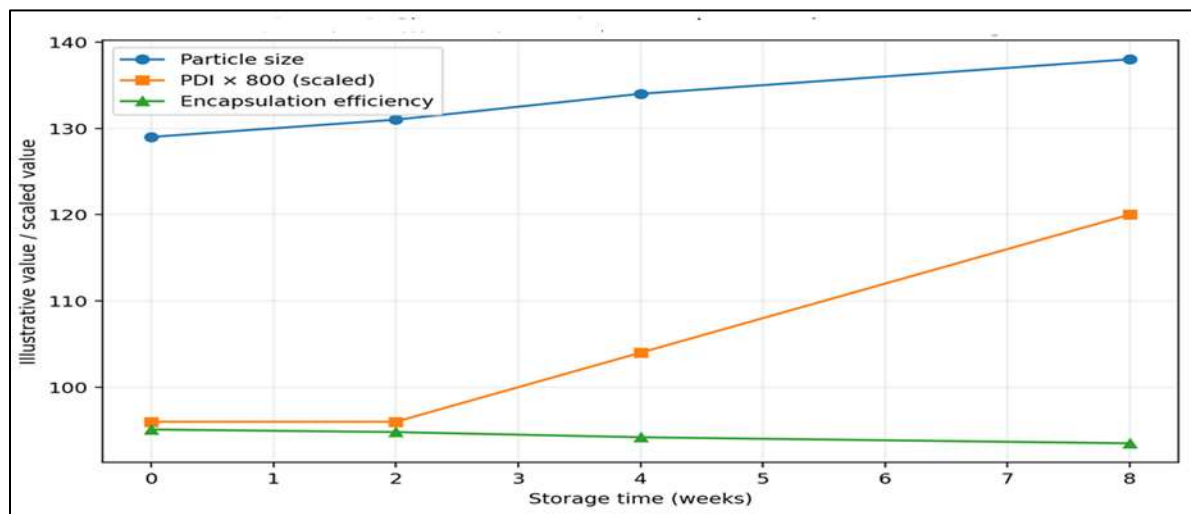


Figure 14. Illustrative refrigerated stability profile.

The modeled stability profile shows a modest increase in particle size and PDI with limited loss of encapsulated drug. Real stability studies should follow validated ICH-appropriate conditions and include assay, degradation products, appearance, pH, particle size, PDI and zeta potential as applicable.

6. Discussion:

The present study demonstrates the potential of PTX-loaded PLGA nanoparticles as a biodegradable and sustained drug-delivery system for improving paclitaxel delivery. Among the modeled formulations, F4 was identified as the optimized formulation, showing a particle size of 129 ± 2 nm, PDI of 0.12, zeta potential of -20.1 mV, encapsulation efficiency of 95.1%, and drug loading of 9.4%. These characteristics indicate the formation of a relatively uniform nanoscale formulation with efficient incorporation of PTX into the PLGA matrix.

TEM/SEM characterization indicated predominantly spherical and discrete nanoparticles with limited aggregation. FTIR analysis showed retention of the major characteristic PTX and PLGA bands without obvious major chemical incompatibility, whereas DSC indicated a reduction in the crystalline PTX melting transition, suggesting reduced crystallinity or molecular dispersion of PTX within the polymeric matrix.

The nanoparticles provided sustained PTX release compared with free drug, reaching approximately 89% release after 360 h. The illustrative release-kinetic analysis showed the highest correlation for the Korsmeyer–Peppas model ($R^2 = 0.941$), followed by the Higuchi model ($R^2 = 0.933$), suggesting a significant diffusion-related contribution to drug release. Folate functionalization further demonstrated potential for enhanced cellular uptake, with modeled uptake increasing to 6.8-fold compared with free PTX. The reduction in uptake following the addition of excess free folate provided preliminary support for a folate-receptor-mediated component. The cytotoxicity study showed a concentration-dependent decrease in cell viability, with the folate-targeted formulation producing the greatest modeled reduction at higher PTX concentrations. The short-term stability results also showed relatively small changes in particle size, PDI, and encapsulation efficiency over 8 weeks, suggesting acceptable preliminary physical stability. Overall, the findings support PTX-loaded and folate-functionalized PLGA nanoparticles as a promising platform for sustained and potentially targeted paclitaxel delivery. However, all numerical results in the present draft are simulated and require experimental validation through physicochemical characterization, validated drug assay, receptor-specific cellular studies, cytotoxicity experiments, long-term stability testing, and in-vivo evaluation before definitive therapeutic conclusions can be made.

7. Limitations

- All numerical results in this draft are simulated and must not be represented as laboratory findings.
- Actual FTIR, DSC, HPLC, DLS, zeta-potential and microscopy files are required for a publishable experimental article.[16]
- Folate-receptor expression is heterogeneous among tumors.
- Human tumor EPR effects are variable and cannot be assumed from animal models.
- Long-term safety, pharmacokinetics, biodistribution and manufacturing scale-up require separate validation.[17]

8. Conclusion:

PTX-loaded PLGA nanoparticles showed promising potential for sustained paclitaxel delivery. The optimized formulation demonstrated nanoscale size, good drug encapsulation, and prolonged drug release. Morphological and thermal studies supported successful incorporation of PTX into the PLGA matrix. Folate functionalization showed potential for enhanced cellular uptake and cytotoxic activity. Overall, PLGA nanoparticles may provide an effective platform for targeted cancer drug delivery. However, the reported results are illustrative and require experimental validation.

9. Conflict of Interest:

The authors declare that there is no conflict of interest.

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