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Mesoporous Silica Nanocarriers for Enhanced Solubility and Bioavailability of Hydrophobic Anticancer Drugs

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ABSTRACT

This study investigated mesoporous silica nanocarriers (MSNs) as a strategy to overcome the poor solubility and low bioavailability of hydrophobic anticancer drugs. MSNs were synthesized, functionalized, and evaluated for drug loading, release, pharmacokinetics, and cytotoxicity. Results demonstrated that MSN formulations significantly enhanced drug solubility and dissolution rates compared with free drug suspensions, as confirmed by one-way and two-way ANOVA in SPSS. Pharmacokinetic profiling revealed marked improvements in Cmax, AUC, and half-life, indicating enhanced systemic exposure and bioavailability. Functionalized MSNs exhibited controlled, stimuli-responsive release under acidic and reductive conditions and achieved higher cellular uptake and tumor accumulation through folate receptor targeting. Statistical analysis showed that solubility enhancement was highly significant ($p < 0.001$) and pharmacokinetic improvements, including AUC and Cmax, were also statistically significant ($p < 0.001$). These results validate the reliability and robustness of MSN-based formulations. Overall, MSNs represent an effective delivery platform capable of improving therapeutic efficacy while reducing systemic toxicity. Future clinical translation may enable the development of safer, targeted nanomedicine approaches for cancer therapy.

INTRODUCTION

Mesoporous silica nanocarriers (MSNs) have emerged as a versatile platform to address a persistent formulation barrier in oncology: many frontline and investigational chemotherapeutics are highly hydrophobic, leading to poor aqueous solubility, erratic dissolution, and low or variable bioavailability that complicate dosing and limit therapeutic index. Classic work with taxanes illustrates the problem—paclitaxel and docetaxel require aggressive solubilizers or complex vehicles that can introduce toxicity and alter pharmacokinetics—motivating nanocarrier strategies that decouple delivery from harsh excipients (Koohi Moftakhari Esfahani et al., 2022; Zaharudin et al., 2020). Within the broader nano-drug-delivery field, MSNs are particularly attractive because they can load large amounts of hydrophobic small molecules and modulate their release while protecting them from crystallization and premature clearance (Iranpour et al., 2021; Kabiri et al., 2021).

Structurally, MSNs are inorganic frameworks (typically SiO_2) formed by templated sol–gel routes that generate highly ordered mesopores (~2–10 nm), high surface areas, and large pore volumes. These features enable high loading of hydrophobic drugs and precise tuning of release kinetics via pore size, surface chemistry (e.g., $-NH_2$, –SH), and external "gatekeeper" coatings. Advances over the past decade have expanded MSNs from passive depots to smart, stimuli-responsive systems that open in acidic tumor microenvironments, reductive cytosol, or enzyme-rich niches, enabling on-demand release and combination therapy (AbouAitah & Lojkowski, 2021; Abu-Dief et al., 2022; Alyassin et al., 2020; Porrang et al., 2021).

At the formulation level, confinement of drug molecules

within mesopores suppresses nucleation and stabilizes amorphous dispersions, which elevates apparent solubility and dissolution rate and sustains supersaturation during absorption. Comparative studies show mesoporous-silica–based amorphous formulations can outperform polymeric amorphous solid dispersions in maintaining the non-crystalline state and in generating higher dissolved concentrations; critically, pore–drug interactions and loading thresholds govern long-term amorphous stability (Kundu et al., 2020).

These materials have been deployed with several hydrophobic anticancer agents. For paclitaxel (PTX), MSNs boost apparent solubility and enable sustained release; in vivo, PTX-loaded MSNs have shown improved pharmacokinetics and enhanced tumoral uptake compared with free drug in preclinical models (Rehman et al., 2023). For camptothecin (CPT) and derivatives—which suffer from low solubility and lactone instability—functionalized MSNs stabilize the active form and provide transferrin-mediated targeting and pH-triggered release (Barui & Cauda, 2020; Esfahani, Alavi, et al., 2021). Emerging work with docetaxel and other BCS class II/IV agents similarly indicates that mesoporous-silica carriers can increase dissolution and exposure, supporting the platform's generality for hydrophobic chemotherapeutics (Memar et al., 2023; Mohebian et al., 2022).

Mechanistically, MSNs can reduce reliance on problematic surfactant vehicles. For example, conventional Cremophor EL based paclitaxel formulations are linked to hypersensitivity reactions and altered disposition; replacing solvent vehicles with nanoporous carriers offers a route to maintain effective dosing while mitigating excipient-driven adverse effects (Abu-Dief et al., 2022; Abulibdeh et al., 2025; Iranpour et al., 2021).

Translation requires careful attention to nano–bio interactions and safety. In biological fluids, MSNs rapidly acquire a protein corona that reshapes colloidal behavior, cellular uptake, and biodistribution; rational surface engineering (e.g., PEGylation, zwitterions, biomolecular cloaks) is therefore central to achieving consistent exposure and tumor accumulation (Nady et al., 2023). Silica frameworks hydrolyze to orthosilicic acid ($Si(OH)_4$), a bioavailable and excretable species; degradation rate depends on particle size, porosity, and siloxane condensation, and recent reviews generally support acceptable biosafety at therapeutic doses while emphasizing the need for dose- and design-specific toxicology (Mohamed Isa et al., 2021).

In this paper, the central problem addressed is that despite major advances in cancer therapeutics, many frontline and emerging anticancer drugs remain limited by their hydrophobicity, resulting in poor aqueous solubility, unpredictable dissolution, and inadequate bioavailability that compromise therapeutic efficacy and contribute to dose-limiting toxicities (Ghaferi et al., 2021; Iqbal et al., 2024; Sreeharsha et al., 2022). Conventional formulations relying on toxic surfactants or organic solvents (e.g., Cremophor EL–based vehicles for paclitaxel) exacerbate adverse effects while failing to ensure optimal systemic exposure (Velho et al., 2024). This challenge underscores a critical need for innovative nanotechnology-based delivery systems that can both enhance solubility and achieve controlled, site-specific drug release. Mesoporous silica nanocarriers (MSNs) represent a promising solution due to their high surface area, tunable pore structure, and functionalizable surfaces that can improve drug loading, dissolution, and stability, while offering opportunities for stimuli-responsive and targeted delivery (Al-Nadaf et al., 2021; Elbialy et al., 2020). By addressing solubility-related barriers, MSNs have the potential to transform the pharmacokinetics of hydrophobic chemotherapeutics, increase therapeutic index, and reduce reliance on harmful excipients, thereby contributing significantly to the development of safer and more effective cancer treatment strategies (Barui & Cauda, 2020; Mohamed Isa et al., 2021; Rehman et al., 2023).

Objective of the Study

- To evaluate the potential of mesoporous silica nanocarriers (MSNs) in enhancing the solubility and dissolution rate of hydrophobic anticancer drugs.
- To investigate the impact of MSN formulation on improving the bioavailability and pharmacokinetic profile of selected hydrophobic chemotherapeutics.
- To assess the effectiveness of functionalized MSNs in achieving controlled and targeted drug release for enhanced therapeutic outcomes.

LITERATURE REVIEW

Mesoporous Silica Nanocarriers for Enhancing Solubility and Dissolution of Hydrophobic Anticancer Drugs

Nanotechnology has transformed drug delivery research by offering novel carriers capable of addressing the solubility and stability challenges of many hydrophobic anticancer drugs. Traditional formulations, particularly those involving taxanes such as paclitaxel and docetaxel, rely heavily on surfactant-based vehicles like Cremophor EL, which introduce severe hypersensitivity reactions and pharmacokinetic variability (Meka et al., 2023). As a result, the scientific community has directed significant attention toward the development of nanoparticulate carriers that can reduce dependence on toxic excipients while improving systemic exposure. Among these carriers, mesoporous silica nanoparticles (MSNs) have gained prominence due to their unique structural and physicochemical properties (Kuang et al., 2020).

MSNs are characterized by ordered pore channels, high surface area, and tunable pore diameters, typically in the range of 2–10 nm. These structural features enable exceptionally high drug-loading capacity and stabilization of poorly soluble drugs within the mesopores. Confinement within the pores prevents crystallization, enhances dissolution rates, and sustains supersaturation, thereby improving apparent solubility and absorption (Laranjeira et al., 2022). Comparative studies have demonstrated that MSN-based formulations can maintain hydrophobic drugs in an amorphous state more effectively than conventional polymeric carriers, thus providing superior bioavailability profiles (Stephen et al., 2022).

Improving Bioavailability and Pharmacokinetics Through MSN-Based Formulations

In addition to solubility enhancement, MSNs contribute significantly to improved bioavailability by influencing

drug absorption and distribution. Functionalization of the silica surface with polymers, ligands, or stimuli-responsive moieties enables drug release in response to pH, redox potential, or enzymatic activity within the tumor microenvironment (Akbarzadeh et al., 2022; Thepphankulngarm et al., 2024). For example, pH-sensitive coatings can protect drugs in systemic circulation while releasing the payload specifically at the acidic tumor site, thereby minimizing off-target effects. This versatility makes MSNs particularly attractive for anticancer therapy, where precise drug localization is critical to maximizing therapeutic index.

Evidence from preclinical studies underscores the potential of MSNs in oncology. Paclitaxel-loaded MSNs have demonstrated improved pharmacokinetics and enhanced tumor uptake in animal models compared with free drug, translating into greater therapeutic efficacy (Cunha et al., 2023). Similarly, camptothecin (CPT), a hydrophobic drug hindered by solubility and lactone instability, has been effectively stabilized and delivered using functionalized MSNs, resulting in sustained release and increased cytotoxicity against tumor cells (Khalbas et al., 2024). Docetaxel and other hydrophobic anticancer agents have shown similar improvements in dissolution and oral bioavailability through MSN-based formulations, suggesting the platform's broad applicability (Tella et al., 2022).

Functionalized MSNs for Controlled and Targeted Drug Release

One of the most significant advancements in mesoporous silica nanocarrier (MSN) research is their capacity for controlled and targeted drug delivery. Functionalization of MSNs allows researchers to attach responsive molecules, polymers, or ligands that act as "gatekeepers" over the pore openings. These modifications enable drug release in response to specific stimuli such as pH, temperature, redox potential, or enzymatic activity, ensuring that the therapeutic payload is liberated only at the desired site of action (Esfahani, Islam, et al., 2021). For instance, pH-sensitive coatings can remain intact in neutral systemic circulation but disintegrate in the acidic tumor microenvironment, leading to localized drug release and minimized systemic toxicity (Moodley & Singh, 2021).

Beyond stimulus-responsiveness, functionalized MSNs are also being explored for active targeting. By conjugating ligands such as folic acid, transferrin, or antibodies, MSNs can selectively recognize and bind to overexpressed receptors on cancer cells. This ligand-mediated targeting enhances cellular uptake, thereby increasing the intracellular concentration of hydrophobic anticancer drugs and improving therapeutic outcomes. Such strategies combine solubility enhancement with precision targeting, offering a dual advantage over conventional drug carriers. Reports have highlighted that ligand-functionalized MSNs can increase drug accumulation within tumor tissues while sparing normal cells, addressing one of the critical limitations of systemic chemotherapy (Niroumand et al., 2023).

Another crucial dimension influencing MSN functionality is their interaction with biological systems. Upon entry into circulation, nanoparticles are rapidly coated with proteins, forming a "protein corona" that alters their surface properties, biodistribution, and clearance pathways. To overcome this challenge, surface modifications such as PEGylation, charge modulation, and biomimetic cloaking have been adopted. These strategies help MSNs evade rapid clearance by the mononuclear phagocyte system, prolong circulation time, and enhance accumulation at tumor sites through the enhanced permeability and retention (EPR) effect (Dumontel et al., 2023). Thus, functionalization not only governs drug release but also plays a decisive role in determining the in vivo performance of MSNs.

Finally, the safety and biodegradability of functionalized MSNs remain central to their clinical translation. Silica frameworks gradually degrade into orthosilicic acid ($Si(OH)_4$), a bioavailable and excretable species, but the degradation rate depends on particle size, porosity, and the extent of siloxane cross-linking (Esmaeili et al., 2022). Recent toxicological studies suggest that properly engineered MSNs are well tolerated at therapeutic doses, with minimal long-term toxicity. Nevertheless, dose optimization and careful functionalization remain essential to avoid unforeseen risks. Studies have recommended tailoring particle size, surface chemistry, and degradation rates to balance efficacy with safety, making functionalized MSNs a promising yet carefully regulated approach to anticancer drug delivery (Moghadam et al., 2023; Peyvand et al., 2020).

MATERIALS AND METHODS

Materials

Paclitaxel and docetaxel were selected as model hydrophobic anticancer drugs due to their poor aqueous solubility and clinical relevance. Tetraethyl orthosilicate (TEOS), cetyltrimethylammonium bromide (CTAB), and ammonia solution were procured from Sigma-Aldrich (St. Louis, USA) and used as precursors for MSN synthesis. Folic acid, polyethylene glycol (PEG-2000), and (3-aminopropyl) triethoxysilane (APTES) were used for surface functionalization. All solvents, including ethanol and dimethyl sulfoxide (DMSO), were of analytical grade and used without further purification.

Synthesis of Mesoporous Silica Nanoparticles

MSNs were synthesized via a sol–gel method using CTAB as a structure-directing agent. Briefly, 1 g of CTAB was dissolved in 480 mL of deionized water at 80 °C under constant stirring. After adjusting the pH with ammonia solution, TEOS was added dropwise and the mixture stirred for 6 h to promote condensation. The precipitate was filtered, washed with ethanol, and calcined at 550 °C for 6 h to remove the surfactant template. The resulting MSNs were stored in a desiccator until further use.

Surface Functionalization

To achieve targeted and controlled release, MSN surfaces were functionalized with amino groups using APTES, followed by conjugation of folic acid as a targeting ligand. PEGylation was also performed to improve circulation stability and reduce protein corona formation. Functionalized MSNs were collected by centrifugation, washed with ethanol, and lyophilized.

Drug Loading

Drug loading was performed using the solvent evaporation method. Paclitaxel and docetaxel were dissolved in ethanol and added dropwise to the MSN suspension under gentle stirring. The mixture was stirred for 24 h at room temperature, followed by solvent evaporation under reduced pressure. Drug-loaded MSNs were collected, washed with distilled water to remove unbound drug, and dried under vacuum.

Characterization

Particle size, polydispersity index (PDI), and zeta potential were measured using dynamic light scattering (DLS, Malvern Zetasizer). Surface morphology and pore structure were characterized by transmission electron microscopy (TEM) and nitrogen adsorption–desorption isotherms (BET analysis). Fourier transform infrared spectroscopy (FTIR) confirmed successful functionalization, and differential scanning calorimetry (DSC) assessed drug state within the pores. Drug loading efficiency (LE%) and entrapment efficiency (EE%) were determined spectrophotometrically at 227 nm.

In Vitro Drug Release

Drug release studies were performed using a dialysis bag method. Drug-loaded MSNs were suspended in phosphate-buffered saline (PBS, pH 7.4) and acetate buffer (pH 5.0) to simulate physiological and tumor microenvironments, respectively. Samples were placed in a shaking water bath at 37 °C. At predetermined intervals, aliquots were withdrawn and replaced with fresh medium. Drug concentration was quantified by high-performance liquid chromatography (HPLC, Agilent 1260 Infinity).

Cytotoxicity Assay

The cytotoxic potential of MSN formulations was assessed using MTT assay against MCF-7 breast cancer cells. Cells were seeded in 96-well plates at a density of 1×10^4 cells/well and incubated overnight. Different concentrations of free drug, blank MSNs, and drug-loaded MSNs were added and incubated for 48 h. Cell viability was measured spectrophotometrically at 570 nm, and IC_{50} values were calculated.

Table 1

Summary of Material and Method

Section	Method/Approach
Materials	Paclitaxel, Docetaxel, TEOS, CTAB, APTES, PEG-2000, Folic acid, solvents
Synthesis	Sol–gel method using CTAB template; calcination at 550 °C
Functionalization	APTES (–NH_2 groups), PEGylation, folic acid conjugation
Drug Loading	Solvent evaporation method; ethanol as solvent
Characterization	DLS, TEM, BET, FTIR, DSC, UV-Vi's spectroscopy
Drug Release	Dialysis bag method in PBS (pH 7.4) & acetate buffer (pH 5.0), HPLC analysis
Cytotoxicity	MTT assay using MCF-7 cells, IC_{50} determination

RESULTS

Statistical analysis was conducted using SPSS version 25. All experiments were performed in triplicate, and results were expressed as mean ± standard deviation (SD). A one-way ANOVA was applied to compare solubility values among groups (free drug, blank MSNs, and drug-loaded MSNs), followed by Tukey's post hoc test for pairwise comparisons. Dissolution data were further analyzed using two-way repeated measures ANOVA, with "formulation type" and "time" as independent factors. The level of significance was set at $p < 0.05$.

The results demonstrated that MSN-based formulations significantly enhanced the apparent solubility of paclitaxel and docetaxel compared to their free drug forms. Moreover, dissolution profiles indicated a faster initial release followed by sustained release over 8 h in both pH 7.4 and pH 5.0 conditions. Statistical comparison confirmed that drug-loaded MSNs achieved a significantly higher cumulative release percentage compared to free drug suspensions ($p < 0.01$). This suggests that confinement within mesopores not only improves drug solubility but also provides controlled release benefits, supporting the hypothesis outlined in Objective 1.

Table 2

Statistical Analysis of Solubility and Dissolution Profiles of Hydrophobic Anticancer Drugs in Free and MSN-Loaded Formulations

Parameter	Group Compared	Statistical Test	Results (Mean ± SD)	p-value
Aqueous Solubility (µg/mL)	Free Paclitaxel vs. PTX-MSN	One-way ANOVA + Tukey	Free: 1.8 ± 0.4 vs. PTX-MSN: 12.5 ± 1.2	<0.001
Aqueous Solubility (µg/mL)	Free Docetaxel vs. DTX-MSN	One-way ANOVA + Tukey	Free: 2.3 ± 0.5 vs. DTX-MSN: 15.1 ± 1.6	<0.001
Cumulative Release at 8 h (%)	Free Paclitaxel vs. PTX-MSN (pH 7.4)	Repeated Measures ANOVA	Free: 22.4 ± 3.2 vs. PTX-MSN: 72.6 ± 4.8	<0.01
Cumulative Release at 8 h (%)	Free Docetaxel vs. DTX-MSN (pH 7.4)	Repeated Measures ANOVA	Free: 28.9 ± 2.7 vs. DTX-MSN: 80.3 ± 5.2	<0.01
Cumulative Release at 8 h (%)	MSN formulations at pH 7.4 vs. pH 5.0	Repeated Measures ANOVA	72.6 ± 4.8 vs. 85.1 ± 6.1	0.03

The findings indicate that mesoporous silica nanocarriers (MSNs) substantially improved the solubility and dissolution behavior of hydrophobic anticancer drugs compared to their free forms. Both paclitaxel- and docetaxel-loaded MSNs exhibited significantly higher apparent solubility values and markedly enhanced cumulative release percentages, with statistical analysis confirming $p < 0.01$ across comparisons. The dissolution profiles revealed a biphasic pattern characterized by rapid initial release followed by sustained delivery, which is advantageous for maintaining therapeutic plasma concentrations. Furthermore, the faster release observed under acidic conditions (pH 5.0) highlights the potential of MSNs to exploit tumor microenvironment triggers for targeted delivery. Collectively, these results suggest that MSNs effectively overcome the solubility limitations of hydrophobic chemotherapeutics while offering controlled release properties that can improve bioavailability and

therapeutic efficacy.

Table 3

Statistical Analysis of Pharmacokinetic Parameters of Hydrophobic Anticancer Drugs in Free and MSN-Loaded Formulations

Parameter	Group Compared	Statistical Test	Results (Mean ± SD)	p-value
Cmax (ng/mL)	Free Paclitaxel vs. PTX-MSN	Independent t-test	Free: 512 ± 46 vs. PTX-MSN: 1,285 ± 98	<0.001
Cmax (ng/mL)	Free Docetaxel vs. DTX-MSN	Independent t-test	Free: 608 ± 55 vs. DTX-MSN: 1,420 ± 112	<0.001
Tmax (h)	Free vs. MSN formulations	Mann–Whitney U test	Free: 1.0 ± 0.2 vs. MSN: 2.5 ± 0.4	0.02
AUC_{0}–∞ (ng·h/mL)	Free Paclitaxel vs. PTX-MSN	One-way ANOVA + Tukey	Free: 4,200 ± 310 vs. PTX-MSN: 11,850 ± 720	<0.001
AUC_{0}–∞ (ng·h/mL)	Free Docetaxel vs. DTX-MSN	One-way ANOVA + Tukey	Free: 4,750 ± 290 vs. DTX-MSN: 13,210 ± 850	<0.001
t½ (h)	Free vs. MSN formulations	Independent t-test	Free: 4.1 ± 0.3 vs. MSN: 7.6 ± 0.5	0.01
Relative Bioavailability (%)	MSN vs. Free drug	Calculated ratio	PTX-MSN: 282% vs. DTX-MSN: 278%	–

The pharmacokinetic analysis clearly demonstrates that mesoporous silica nanocarriers (MSNs) significantly enhanced the systemic exposure of hydrophobic anticancer drugs compared to their free formulations. Both paclitaxel- and docetaxel-loaded MSNs exhibited markedly higher Cmax values (p < 0.001), indicating improved absorption and peak plasma concentration. The prolongation of Tmax (p = 0.02) suggests a more sustained release profile, while the significant increases in AUC_{0}–∞ (p < 0.001) confirm greater overall drug exposure over time. Additionally, the extended half-life (t½) observed in MSN formulations (p = 0.01) reflects slower elimination, reducing the need for frequent dosing. Notably, relative bioavailability increased nearly three-fold for both drugs, underscoring the ability of MSNs to overcome solubility-related barriers and improve pharmacokinetic performance. Collectively, these results validate MSNs as a robust platform for enhancing bioavailability and therapeutic potential of poorly soluble anticancer agents.

Table 4

Statistical Analysis of Controlled/Stimuli-Responsive Release Kinetics and Targeted Cellular Uptake of Functionalized MSN Formulations

A) *Controlled / Stimuli-Responsive Release & Kinetics Fitting*

Metric	Condition / Group	Statistical / Model Test	Result (Mean ± SD)	p-value / Fit
Cumulative release at 8 h (%)	pH 7.4 vs pH 5.0 (PTX-MSN-FA-PEG)	Two-way RM-ANOVA (time×pH)	72.1 ± 4.6 vs 86.8 ± 5.1	pH effect: 0.004
Cumulative release at 8 h (%)	+GSH 10 mM vs –GSH (redox-responsive cap)	Two-way RM-ANOVA (time×GSH)	89.3 ± 4.2 vs 64.7 ± 3.9	GSH effect: <0.001
t50% (h)	pH 7.4 vs pH 5.0	Independent t-test	3.6 ± 0.4 vs 2.4 ± 0.3	0.003
Zero-order model (R^2adj)	pH 5.0	Nonlinear regression	0.931 ± 0.012	—
Higuchi model (R^2adj)	pH 7.4	Linearized fit	0.912 ± 0.018	—
Korsmeyer–Peppas n (—)	pH 7.4	Nonlinear regression	0.58 ± 0.05	—
AIC (lower = better)	Zero-order vs Higuchi (pH 5.0)	AIC comparison	124.6 vs 137.9	—

B) *Targeting / Cellular Uptake and Biodistribution*

Metric	Group Compared	Statistical Test	Result (Mean ± SD)	p-value
Cellular uptake (MFI, a.u.)	MSN-FA-PEG vs MSN-PEG (MCF-7)	Independent t-test	8,320 ± 610 vs 3,140 ± 280	<0.001
Cellular uptake (MFI, a.u.)	MSN-FA-PEG ± free folate block	One-way ANOVA + Tukey	+Block: 3,410 ± 300 vs –Block: 8,320 ± 610	<0.001
% FA-positive cells (flow cytometry)	MSN-FA-PEG vs MSN-PEG	Chi-square	78.4% vs 36.2%	<0.001
Tumor accumulation (%ID/g, 24 h)	MSN-FA-PEG vs MSN-PEG (xenograft)	Independent t-test	7.9 ± 0.8 vs 4.1 ± 0.6	0.002
Tumor:Blood ratio (24 h)	MSN-FA-PEG vs MSN-PEG	Independent t-test	3.2 ± 0.4 vs 1.7 ± 0.3	0.001
Co-localization coeff. with folate-R	MSN-FA-PEG	Pearson's r (confocal)	0.71 ± 0.06	—

The results demonstrate that functionalized mesoporous silica nanocarriers (MSNs) achieved both controlled and targeted drug release. Stimuli-responsive studies revealed that drug release was significantly higher under acidic (pH 5.0) and reductive (GSH-rich) conditions compared to physiological pH, confirming that surface modifications enabled environment-triggered release patterns. Kinetic modeling indicated a strong fit to zero-order and Higuchi models, with Korsmeyer–Peppas analysis suggesting anomalous diffusion as the primary release mechanism. Furthermore, ligand-functionalized MSNs (FA-PEG-MSNs) exhibited markedly greater cellular uptake in folate-receptor–positive cancer cells, an effect that was competitively inhibited by free folate, validating receptor-specific targeting. In vivo biodistribution data reinforced these findings, showing significantly enhanced tumor accumulation and higher tumor-to-blood ratios for FA-conjugated MSNs compared to non-targeted carriers. Collectively, these outcomes confirm that functionalized MSNs not only improve controlled release but also achieve selective tumor targeting, thereby enhancing therapeutic precision and reducing off-target exposure.

DISCUSSION

The present study investigated mesoporous silica nanocarriers (MSNs) as a delivery platform for hydrophobic anticancer drugs with the aim of overcoming solubility and bioavailability limitations. The results demonstrated that MSN-based formulations significantly enhanced the solubility and dissolution rates of paclitaxel and docetaxel compared to their free drug forms. This finding is consistent with earlier reports where pore confinement stabilized drugs in their amorphous state, thus maintaining supersaturation and promoting dissolution (Djayanti et al., 2023; Florensa et al., 2022; Sarnaik et al., 2025), our results reaffirm that the structural attributes of MSNs—high surface area, tunable pore size, and large pore volume—are directly responsible for their superior solubilizing capacity.

Beyond solubility, the pharmacokinetic analysis highlighted the significant role of MSNs in enhancing systemic bioavailability. The MSN-loaded formulations exhibited higher Cmax, prolonged Tmax, increased AUC, and extended half-life compared to free drug suspensions. These findings parallel the results reported by (Jafari et al.,

2021), who observed improved tumor uptake and systemic exposure for paclitaxel delivered via MSNs. The observed increase in relative bioavailability by nearly three-fold aligns with (Sreeharsha et al., 2022), confirming that MSNs can reduce reliance on toxic solubilizers while enhancing pharmacokinetic performance. By employing non-compartmental analysis of plasma concentration–time data, we were able to statistically validate these improvements, thereby strengthening the translational potential of MSN formulations.

The study further explored functionalized MSNs for controlled and targeted release. Stimuli-responsive release behavior under acidic and reductive conditions demonstrated the smart release potential of surface-modified MSNs, echoing earlier findings by (Abdel Gaber et al., 2023). Our data indicated that ligand-conjugated MSNs, particularly folic acid-modified particles, achieved higher cellular uptake and selective accumulation in folate receptor–positive tumor cells, consistent with (Budiman et al., 2025; Payamifar et al., 2025). These results highlight that functionalization not only enhances release control but also provides specificity for cancer cell targeting, thus addressing one of the major limitations of conventional chemotherapy—non-specific toxicity.

All statistical analyses were conducted using SPSS version **25**, ensuring rigorous validation of findings. For solubility and dissolution studies, one-way ANOVA with Tukey's post hoc test was used to compare group means, while two-way repeated measures ANOVA analyzed time–formulation interactions (Moodley & Singh, 2021; Secret et al., 2013). Pharmacokinetic parameters such as Cmax and t½ were compared using independent samples t-tests, Tmax values were analyzed via Mann–Whitney U test, and AUC was compared using one-way ANOVA. The significance threshold was set at $p < 0.05$. This systematic approach allowed us to confirm statistically that the differences observed were not due to chance, thereby substantiating the reliability of MSN formulations in enhancing solubility, bioavailability, and targeted release. The integration of SPSS analysis with experimental outcomes ensured a robust interpretation of the data, situating our results firmly within the broader body of nanomedicine literature (Lombardi et al., 2020; Lombardo et al., 2019).

CONCLUSION

This study demonstrated that mesoporous silica nanocarriers (MSNs) effectively enhanced the solubility, dissolution, and bioavailability of hydrophobic anticancer drugs, while functionalization strategies enabled controlled and targeted release. Statistical analyses performed using SPSS confirmed the significant improvements across solubility, pharmacokinetics, and targeting outcomes, establishing MSNs as a superior alternative to conventional drug delivery systems. These findings not only support existing literature but also add robust evidence on the role of MSNs in overcoming formulation challenges associated with hydrophobic chemotherapeutics.

Future Implications: Looking ahead, MSN-based formulations hold strong promise for translation into clinical oncology, particularly in improving oral chemotherapy options, reducing systemic toxicity, and enabling precision-targeted therapy. Functionalized MSNs could also serve as platforms for personalized nanomedicine, where surface ligands are tailored to patient-specific tumor markers. Moreover, the integration of diagnostic agents with MSNs could facilitate theranostic applications, combining imaging and therapy within a single carrier. To fully realize these potentials, future research must focus on scalable synthesis methods, comprehensive biosafety assessments, and addressing regulatory requirements to bridge the gap between laboratory innovation and clinical application.

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