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A Comparative Review of Nanoclay, Mesoporous Silica, and Carbon-Based Nanocarriers for Drug Delivery

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Abstract

This review presents a comparative analysis of three major classes of inorganic nanocarriers nanoclays, mesoporous silica nanoparticles, and carbon-based nanomaterials with emphasis on their structural and physical properties, drug release mechanisms, biocompatibility and toxicity, specific applications, and key surface modifications. Nanoclays offer natural abundance, high cation-exchange capacity, and versatile interlayer chemistry that enable sustained ion-exchange-driven release. Mesoporous silica nanoparticles are distinguished by their high surface area, ordered pore networks, and selectively functionalizable external and internal surfaces, supporting exceptionally high drug loading and stimuli-responsive release systems. Carbon-based carriers, including carbon nanotubes and graphene-family materials, combine large specific surface areas with photothermal capacity and dual drug- and gene-delivery potential, yet exhibit the most contested toxicity profile, largely governed by functionalization, purity, and exposure route. Across all three families, surface chemistry exemplified by PEGylation determines dispersion stability, biocompatibility, and circulation behavior. The three platforms are best viewed as complementary rather than competing, with future progress depending on standardized toxicological evaluation and continued refinement of surface engineering to translate these nanocarriers toward clinical applications in cancer therapy, gene therapy, and controlled drug delivery.

Keywords: Nanocarriers, Nanoclay, Mesoporous silica, Carbon nanotubes (CNT), Drug delivery.

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Introduction

Nanocarriers are colloidal drug carrier systems with submicron particle sizes, typically less than 500 nm, that have been studied extensively over the past few decades for their promising results in drug delivery (Unnikrishnan, Joy, Megha, Kolanthai, & Senthilkumar, 2023, p. 158). Owing to their high surface area-to-volume ratio, nanocarriers can alter the fundamental properties and bioactivity of loaded drugs (Unnikrishnan, Joy, Megha, Kolanthai, & Senthilkumar, 2023, p. 158). Drug design at the nanoscale is currently the most advanced technology in nanoparticle applications because it allows modification of properties such as solubility, drug release profiles, diffusivity, bioavailability, and immunogenicity, leading to improved biodistribution, lower toxicity, fewer side effects, and an extended drug life cycle (Patra, et al., 2018, p. 74). The principal goals in designing nanocarriers are to control particle size, surface properties, and the release of pharmacologically active agents so as to achieve site-specific action at the therapeutically optimal rate and dose regimen (Jahanshahi & Babaei, 2008, p. 4927). Nanocarrier platforms span liposomes, polymeric nanoparticles, dendrimers, micelles, and inorganic nanoparticles, which enclose drugs, genes, or imaging agents, safeguarding them from degradation, enabling regulated release, and facilitating transport to specific sites of action (Kardani, 2024, p. 2). These systems combine nanoscale size, controlled release kinetics, biocompatibility, targeted delivery capability, and long-term stability, with polymeric carriers such as PLGA able to provide prolonged release that maintains therapeutic drug levels in the body over extended periods (Chehelgerdi, et al., 2023, p. 185). In comparison with conventional delivery systems, nanoformulation of drugs offers several distinct advantages (Farjadian, et al., 2018, p. 94). Nanocarriers deliver pharmaceutical agents more precisely to the targeted tissue, reducing the overall dose and potentially toxic side effects; the enhanced permeability and retention effect enables passive targeting and accumulation of nanosized drugs at malignant tumors and other pathological sites; nanosized formulations yield increased active concentration and bioavailability relative to conventional microsized formulations; and drug release can occur at a constant rate over the desired timescale (Farjadian, et al., 2018, p. 94). Because of their small size, nanoparticles can extravasate through the endothelium in inflammatory sites, the epithelium, and tumors, allowing efficient cellular uptake and selective drug accumulation at target sites, and they are better suited for intravenous delivery than microparticles larger than 1 μm (Singh

& Lillard, 2009, p. 216). Nanocarriers also protect therapeutic agents against enzymatic degradation and can improve bioavailability, sustain drug release, and solubilize drugs for systemic delivery (Singh & Lillard, 2009, p. 216). By contrast, conventional drug delivery systems often rely on bulkier carriers or routes that lack specificity, resulting in lower drug efficacy, higher required doses, and increased potential for adverse effects (Kardani, 2024, p. 2). Compared with conventional chemotherapeutic agents, nanoscale carriers improve treatment efficacy while avoiding toxicity in normal cells through highly selective tumor accumulation via the EPR effect and active cellular uptake (Senapati, Mahanta, Kumar, & Maiti, 2018, p. 7), and specific targeting and controlled release significantly reduce side effects, which also improve bioavailability and the uptake of poorly soluble drugs (Sim & Wong, 2021, p. 45). Nevertheless, concerns remain over the lack of biodegradation, poor bioavailability, instability in the circulation, inadequate tissue distribution, and potential toxicity of nanocarriers, especially for long-term administration (Senapati, Mahanta, Kumar, & Maiti, 2018, p. 7).

Structural and Physical Properties

The structural and physical properties of nanocarrier materials govern drug-loading capacity, release kinetics, and interactions with biological systems. Nanoclays are layered aluminosilicate nanoparticles whose lamellar structure, high specific surface area, diverse ion-exchange capacity, and tunable surface chemistry make them attractive pharmaceutical carriers (Khatoon, Chu, & Zhou, 2020). The dual charge characteristic of these nanolayered silicates allows neutral biomolecules to bind via hydrogen bonding and cationic therapeutics via ionic exchange, with intercalation of guest molecules into the interlayer galleries controlling loading and sustained release (Gaharwar, et al., 2019, p. 22). Montmorillonite, the most studied nanoclay, exhibits particularly rich intercalation chemistry that enables organoclay formation for enhanced drug loading and release (Uddin, 2018, p. 7). Mesoporous silica nanoparticles possess an ordered porous network with homogeneous pore sizes, high pore volume, and a silanol-containing surface amenable to functionalization (Vallet-Regí, Schüth, Lozano, Colilla, & Manzano, 2022, p. 5367). Their pore size and volume can be precisely tuned during synthesis to encapsulate small molecules, macromolecules, and imaging agents, while the porous structure acts as a reservoir enabling controlled release over extended periods (Pande, Kothawade, Kuskar, Bole, & Chakole, 2023, p. 3); the stability of the framework derives from Si–O bonds within the silica structure (Yan, et al., 2024, p. 3553). Among carbon-based carriers, carbon nanotubes and graphene are low-dimensional sp^2 carbon nanomaterials with unique physical and chemical properties (**Fig. 1**) (Liu, Robinson, Tabakman, Yang, & Dai, 2011).

Carbon nanotubes offer a high aspect ratio and large surface area providing multiple attachment sites for drug targeting (Kakran & Li, 2012), whereas the single-layer graphene sheet affords a large surface area, excellent thermal conductivity, high mechanical and elastic strength, and two accessible faces for drug binding (Debnath & Srivastava, 2021, p. 3). Both classes can be functionalized covalently or non-covalently, and their tunable pore structure permits reasonable control over drug release (Zeinali, Zaeifi, Zolfaghari-Moghaddam, Paul, & Biazar, 2025, p. 12236).

Nanoclay

Nanoclays are naturally occurring, layered aluminosilicate minerals whose structure dictates their physicochemical behavior (Biswas, et al., 2019, p. 3745). Produced by exfoliating natural clays, nanoclays vary in particle size from a few stacked layers to much larger stacks depending on the exfoliation conditions, and the degree of stacking strongly influences all their basic characteristics (Mintova, Jaber, & Valtchev, 2015, p. 7221). Among the most important properties of clay minerals is the cation exchange capacity the total amount of cations available for exchange at a given pH, commonly expressed as meq/100 g of calcined clay (Mintova, Jaber, & Valtchev, 2015, p. 7221). In smectites such as montmorillonite, the layer charge originates from the substitution of dioctahedral Al^{3+} by Mg^{2+} (Valdés, et al., 2017, p. 2). This lamellar architecture confers high specific surface area, sorptive and ion-exchange capacities, rheological properties, chemical inertness, and low toxicity, all of which justify their use in pharmaceutical formulations (Valdés, et al., 2017, p. 2). Nanoclays also exhibit high retention capacities and swelling behavior, along with a strong affinity for biopolymers through exfoliation or intercalation, enabling them to act as carriers that modify the rate and timing of drug release, increase drug stability, and improve dissolution profiles (Mousa, Evans, Oreffo, & Dawson, 2018, p. 205).

Mesoporous silica

Mesoporous silica nanoparticles are ordered porous materials whose structural and physical features underpin their performance as drug nanocarriers (Vallet-Regí, Schüth, Lozano, Colilla, & Manzano, 2022, p. 5383). The M41S family of mesoporous silicas, for instance, is characterized by an abundance of silanol groups (Si–OH) located on both the internal pore walls and the external surface, which facilitate surface functionalization for specific bioapplications, while their mesophase arrangement, pore size, particle morphology, and dimensions can be readily adjusted by varying the synthesis conditions (Xu, Li, Shi, & Liu, 2023). Nanoporous silica presents two functional surfaces the cylindrical pore surfaces and the exterior particle

surfaces both heavily covered with silanol groups that serve as reactive sites for functionalization (Baig, Kammakakam, & Falath, 2021). Thanks to their large surface area and pore volume, MSNs can serve as efficient carriers for various therapeutic agents, and their functionalization with molecular, supramolecular, or polymeric moieties renders the delivery process highly controllable (Li, Barnes, Bosoy, Stoddart, & Zink, 2012). Ultimately, the nanomaterial design surface engineering, framework hybridization, and particle morphology governs both physicochemical properties and biosafety, determining the ability to load and controllably deliver drugs in response to internal stimuli such as pH, redox, and enzymes, or external stimuli such as light, magnetic fields, and ultrasound (Croissant, Fatieiev, Almalik, & Khashab, 2017).

Carbon-Based Nanocarriers

Carbon-based nanocarriers including carbon nanotubes, graphene, fullerenes, and nanodiamonds are low-dimensional carbon nanomaterials endowed with unique physical and chemical properties that make them attractive drug delivery vehicles (Wang, Hu, Xu, & Zhao, 2014, p. 1). CNTs in particular combine exceptional mechanical strength with excellent thermal and electrical conductivity, properties that have driven their use across nanoelectronics, materials science, and biomedicine (Karimi, et al., 2015). At the molecular level, however, the entirely sp^2-hybridized carbon composition renders pristine CNTs extremely hydrophobic and highly prone to aggregation, leaving them largely incompatible with biological systems; consequently, most drug-delivery efforts center on chemical functionalization, which serves the twin objectives of providing water solubility and reducing aggregation while furnishing functional groups for attaching biological cargo (Karimi, et al., 2015). The intrinsic stability and structural flexibility of CNTs may prolong the circulation time and bioavailability of conjugated drug molecules (Chen, et al., 2008). Furthermore, CNTs interact with biomacromolecules such as proteins and DNA by physical adsorption, and their extensive symmetric carbon bonds produce characteristic Raman signatures used to probe structural features, while covalent and non-covalent modification schemes enable conjugation of therapeutic molecules and targeting moieties (Cha, Shin, Annabi, Dokmeci, & Khademhosseini, 2013).

Drug Loading and Release Mechanism

Drug loading and release in nanocarrier systems are governed by the structural features of the carrier and the physicochemical properties of the payload. The surface chemistry of nanoclays is versatile enough for targeted modifications that control loading and release properties, while synthetic mesoporous materials offer finely controlled size features, and both can be functionalized into organic–inorganic architectures with stimuli-responsive behavior (Cavallaro, Lazzara, & Fakhrullin, 2018). Nanoclays typically load drugs through intercalation into their layered structure cationic exchange into the interlayer space of Laponite and montmorillonite, or surface adsorption onto tubular halloysite with salt concentration and pH modulating nanoclay–drug interactions and hence release kinetics (Khachani, et al., 2022). In mesoporous silica, cargo is loaded through weak non-covalent interactions such as hydrogen bonding, physical adsorption, electrostatic interaction, and aromatic stacking, and pore size together with surface functionalization tunes release from burst to long-term sustained profiles (Luther, et al., 2020, p. 195). Carbon-based carriers bind aromatic drugs by π–π stacking on their sp^2 surfaces, with loading and release controllable through pH and nanotube diameter (Liu, Sun, Nakayama-Ratchford, & Dai, 2007); graphene and its oxide load poorly soluble drugs similarly via π–π, electrostatic, and hydrophobic interactions (Shareena, McShan, Dasmahapatra, & Tchounwou, 2018, p. 59). In vitro release from such carriers is often described by Higuchi and Korsmeyer–Peppas kinetic models (Bediako, et al., 2018), and stimuli-responsive designs afford spatiotemporal control of release in response to pH, enzymes, light, temperature, or magnetic fields (**Fig. 2**) (Khaki, Ekhlasi, Shahryari, Nazarpak, & Nouri, 2026).

Drug release from nanoclay carriers is governed primarily by cation-exchange equilibria between the clay and the surrounding biological medium (Paravastu, Yarraguntla, & Suvvari, 2019, p. 98). Three principal mechanisms have been described for drug intercalation into montmorillonite: adsorption of the drug onto the free clay surface, replacement of interlayer sodium by the drug, and ionic bonding between the drug and clay hydroxyl groups coordinated to Al^{3+} and Mg^{2+} (Paravastu, Yarraguntla, & Suvvari, 2019, p. 98). In biological fluids, counterions displace the cationic drug from the clay substrate, releasing free drug molecules for absorption while the unloaded submicron particles are eliminated from the body (Paravastu, Yarraguntla, & Suvvari, 2019, p. 98). Because the interlayer cations of montmorillonite are non-structural, they are readily exchanged by positively charged drug molecules, and the resulting strong electrostatic interactions confer the characteristic controlled-release properties; anionic or neutral drugs held by weaker physical adsorption or ion-dipole interactions are typically released faster (Dening, Rao, Thomas, & Prestidge, 2015, p. 35). Release rates can also be tuned externally coating the clay with a large cationic polymer such as Eudragit® E-100 accelerates drug delivery, illustrating the controllable-release feature of nanoclay platforms (Zoveidavianpoor, 2018, p. 188).

Drug release from mesoporous silica nanoparticles depends on how the cargo is loaded and how the pore system is engineered. Drugs can be loaded in situ during the synthesis route or by post-sorption through physisorption or chemisorption (Manzano & Vallet-Regí, 2019, p. 14). Because their structure, morphology, size, and surface properties are readily tunable, MSNs can be tailored specifically for drug loading, controlled drug release and delivery, and multifunctionalization (He & Shi, Mesoporous silica nanoparticle based nano drug delivery systems: synthesis, controlled drug release and delivery, pharmacokinetics and biocompatibility, 2011). Their external and internal surfaces can be selectively functionalized with multiple organic and inorganic groups, forming the basis of nanodevices for the controlled release of drugs and genes into living cells (Trewyn, Slowing, Giri, Chen, & Lin, 2007). Release is typically governed either by strong electrostatic adsorption of the payload compared with FDA-approved Doxil, the doxorubicin capacity of mesoporous silica nanoparticles can be nearly 1,000 times greater, owing to the high surface area and attractive electrostatic interactions or by sealing the pores after loading with caps, supramolecular nanovalves, polymer coatings, or supported lipid bilayers, which enable controlled release in response to stimuli such as pH change, enzymatic ligand cleavage, light, and externally applied magnetic fields (Tarn, et al., 2013, p. 797).

Drug release from carbon-based nanocarriers is governed by their sp^2 carbon surfaces and by surface modification strategies (Liu, Robinson, Tabakman, Yang, & Dai, 2011). Because carbon nanotubes and fullerenes are intrinsically hydrophobic, their surfaces are typically treated by oxidation, carboxylation, or amidation, or conjugated with functional molecules, to prevent aggregation and opsonization while enabling payload attachment (Lee & Yeo, 2014, p. 86). Graphene-based carriers combine a large specific surface area with the ability to prevent premature drug release in target cells, although agglomeration in aqueous media remains a concern; release from ibuprofen-loaded graphene oxide–bacterial cellulose composites followed a non-Fickian diffusion mechanism (Ateş, Köytepe, Ulu, Gürses, & Thakur, 2020, p. 9337). Release from carbon carriers is characteristically pH- and redox-responsive: PEGylated multi-walled carbon nanotubes conjugated with doxorubicin released 57% of the drug at lower pH within 24 h (Navya, et al., 2019, p. 35), and polymer-grafted graphene oxide favored doxorubicin release in acidic environments as surface hydrophilicity increased and hydrogen bonding between drug and carrier weakened, while PMMA-coated graphene oxide nanoparticles accelerated doxorubicin release in tumor tissue in response to glutathione (Maiti, Tong, Mou, & Yang, 2019, p. 7). Carbon nanospheres likewise provided high loading capacity with sustained release under the acidic conditions of the tumor microenvironment (Navya, et al., 2019, p. 35).

Biocompatibility and Toxicity

Biocompatibility and toxicity are decisive factors determining whether nanocarrier systems can advance toward clinical application, since approval of nanoparticle-based formulations depends strongly on their biological safety and biocompatibility in addition to therapeutic efficacy (Pandey, Vidić, Mukherjee, & Chang, 2023). However, the complex and numerous interactions between nanomaterials and biological systems mean there is no universal toxicity mechanism or assessment method, with factors such as size, morphology, surface charge, solubility, pH, and mode of exposure all influencing nanotoxicity (**Fig. 3**) (Mahamuni-Badiger & Dhanavade, 2023).

In vivo studies of mesoporous silica nanoparticles show they distribute mainly in the liver, spleen, and lungs (over 80% after intravenous administration), with clearance kinetics dependent on particle shape, yet hematology, serum biochemistry, and histopathology results indicate no significant toxicity (Huang, et al., 2011); neither MSNs nor PEGylated MSNs caused tissue toxicity after one month in mice (He, Zhang, Gao, Li, & Shi, 2010). Earlier investigations, however, reported that intravenous or intraperitoneal injection of mesoporous silica particles in mice resulted in death, possibly due to pulmonary thrombosis, underscoring the importance of administration route (Napierska, Thomassen, Lison, Martens, & Hoet, 2010). For nanoclay carriers, organically modified aminoclay nanoparticles distributed rapidly into various organs but cleared quickly without long-term accumulation, indicating low risk of tissue retention (Yang, et al., 2014). Carbon-based carriers present more conflicting evidence some *in vitro* and *in vivo* studies showed no particular risks, while others indicated that graphene-family nanomaterials might become health hazards (Bianco, 2013) and graphene is listed among hazardous materials by the European Scientific Committee on Emerging and Newly Identified Health Risks, with a simple cytotoxicity test considered insufficient to establish biocompatibility (Syama & Mohanan, 2019).

The expanding industrial and biomedical use of nanoclays and nanoclay-doped polymer composites raises the risk of human exposure, making toxicological evaluation of these materials increasingly important (Naumenko & Fakhrullin, 2016). Most studies to date indicate that nanoclays are relatively biocompatible: halloysite nanotubes maintained cell viability above 60% in HUVECs and MCF-7 cells at concentrations of 2.5–200 μg/mL over 72 h, did not significantly alter zebrafish embryo survival at 0.25–10 mg/mL, and were excreted through the gastrointestinal tract (Long, et al., 2018). Macrophage studies likewise found no

cytotoxic damage, with only slight, transient proinflammatory cytokine production at 100 µg/mL followed by an anti-inflammatory response (Toledano-Magaña, et al., 2021). *In vivo*, oral doses of 5 mg/kg caused no adverse effects in mice, whereas 50 mg/kg elicited reversible inflammation of the small intestine (Setter & Segal, 2020), and doses up to 25 mg/kg by various administration routes, together with 8-month chronic exposure, appeared safe (Toledano-Magaña, et al., 2021). Importantly, surface modification modulates toxicity, since nanoclays functionalized with bio-reactive organic modifiers reduced cell numbers and induced more elongated morphologies relative to pristine clay (Wagner, et al., 2017). Nevertheless, a clear cytotoxic effect emerges at the highest concentrations tested (1000 µg/mL), and because halloysite properties are origin-dependent, toxicity studies must be coupled with thorough physicochemical characterization (Setter & Segal, 2020).

The biocompatibility of mesoporous silica nanoparticles is largely defined by their hemolytic activity and their degradability and clearance from the body, since approved pharmaceutical products must not accumulate to prevent unpredictable side effects (Croissant, Fatieiev, & Khashab, Degradability and Clearance of Silicon, Organosilica, Silsesquioxane, Silica Mixed Oxide, and Mesoporous Silica Nanoparticles, 2017). Hemolysis studies with red blood cells show that MSNs exhibit low hemolytic activity compared with amorphous silica (Slowing, Wu, Vivero-Escoto, & Lin, 2008), but the response is concentration- and size-dependent, with hemolysis arising only when the particles possess long-range ordered pore structure and increasing as pore integrity is compromised, although a polyethylene glycol coating can eliminate hemolysis entirely (Lin & Haynes, 2010). Size effects are also evident at the cellular level: small MCM-41-type particles (~100 nm) adsorb to red blood cell surfaces without disturbing the membrane, whereas large SBA-15-type particles (~600 nm) induce strong local membrane deformation leading to spiculation, internalization, and eventual hemolysis (Zhao, et al., 2011). In vivo, rats injected with mesoporous silicates showed no overt toxicity, and showed good biocompatibility on histology at all time points over a 3-month period (Hudson, Padera, Langer, & Kohane, 2008, p. 4045).

The toxicity of carbon-based nanocarriers remains one of the most debated issues in nanomedicine, with controversial and sometimes contradictory data restricting their biomedical application (Chetyrkina, Fedorov, & Nasibulin, 2022). These disparities are attributed to impurities, amorphous carbon, surface charge, shape, length, agglomeration, and layer numbers, as well as the exposure route, with underlying toxicity mechanisms including oxidative stress, inflammatory responses, DNA damage, granuloma formation, and interstitial fibrosis (Liu, Zhao, Sun, & Chen, 2012). In vivo findings depend strongly on surface modification: raw carbon nanotubes proved toxic to mice after inhalation and unfunctionalized long MWNTs may pose a carcinogenic risk, whereas well-functionalized CNTs with biocompatible surface coatings were nontoxic in vitro and in vivo (Liu, Tabakman, Welsher, & Dai, 2009). Likewise, subcutaneously implanted MWCNTs showed histological reactions very similar to those of carbon black, indicating good tissue compatibility (Saito, et al., 2014). Graphene-family nanomaterials exhibit dose-dependent toxicity toward mammalian cells such as lung fibroblasts, epithelial and alveolar cells, neuronal cells, and red blood cells; graphene oxide administered at a low dose showed no obvious toxicity in mice, but high doses produced chronic toxicity with granuloma formation in the lungs, kidneys, liver, and spleen (Jastrzębska, Kurtycz, & Olszyna, 2012). Pristine graphene, graphene oxide, and reduced graphene oxide all elicit toxic effects in vitro and in vivo, although surface modifications can significantly reduce their toxic interactions with living systems (Guo & Mei, 2014). Methodological caveats compound the picture the MTT assay can generate false positive toxicity signals for graphene-family materials owing to their spontaneous reduction of the tetrazolium dye (Jastrzębska, Kurtycz, & Olszyna, 2012).

Specific Applications

The translation of nanocarrier platforms into the clinic has concentrated on three principal applications cancer therapy, gene therapy, and drug delivery building on the tunable surface chemistry, high loading capacity, and targeting capability of mesoporous silica, carbon-based nanomaterials, and clays. Mesoporous silica nanoparticles have been demonstrated as drug-delivery vehicles, gene-transfection reagents, and cell markers, and conjugation with ligands such as folic acid directs them to cancer cells, while nanovalve- and nanoimpeller-equipped MSNs enable controllable delivery (Lü, Liong, Li, Zink, & Tamanoi, 2010, p. 1795). MSN-based systems further exhibit high loading capacity for poorly soluble drugs, anticancer agents, and therapeutic genes (Zhou, et al., 2018).

Indeed, their use has been described as "using one stone to kill three birds" for cancer theranostics and drug and gene delivery (Kesse, et al., 2019). For gene therapy specifically, the strong silica framework shields fragile nucleic acids from nuclease digestion in serum, and charge-modifying coatings such as ZIF-8 films enhance siRNA loading for combinatorial chemo–gene therapy (Huang, et al., 2020, p. 21). Among carbon-based carriers, graphene, fullerenes, carbon nanotubes, carbon nanohorns, carbon quantum dots, and graphyne have all been investigated for cancer treatment (Cheng,

Li, Dey, & Chen, 2021, p. 94), and graphene derivatives can transport both therapeutic medicines and nucleic acid sequences, driving progress in gene and drug delivery composites (Moghadam, Avatefi, Karimi, & Mahmoudifard, 2023). Nanoclays have likewise been formulated as temperature-responsive nanocarriers for controlled anticancer drug release (Hemmatpour, et al., 2023, p. 2402).

Specific Modifications and Advantages

The performance of all three nanocarrier families is ultimately governed by their surface chemistry, which can be engineered to optimize stability, biocompatibility, targeting, and release control (Friedl, Nele, Rosa, & Bernkop-Schnürch, 2021, p. 1). For nanoclays, the interlayer cations and these groups serve as versatile modification sites: chemical modification via intercalation of ions into the interlayer space or surface functionalization is a direct strategy to tune nanoclays for drug loading and release (Khatoon, Chu, & Zhou, 2020), and converting surface hydroxyl groups to amines with 3-aminopropyldimethylethoxysilane followed by NHS-EDC conjugation limits the pH sensitivity of the nanoclay–drug complex while increasing its stability and preventing off-target release (Gaharwar, et al., 2019, p. 24). Likewise, incorporating a small fraction of clay nanoplatelets into a polymer network improves mechanical properties, swelling capacity, film-forming capability, rheological properties, and bioadhesion without sacrificing matrix processability (Mousa, Evans, Oreffo, & Dawson, 2018, p. 205). Mesoporous silica offers selective functionalization of the external surface and mesopore walls before or after surfactant extraction enabling controlled modulation of the charge and release kinetics of loaded drugs (Vallet-Regí, Schüth, Lozano, Colilla, & Manzano, 2022, p. 5384); modification with supramolecular assemblies and metal species further unlocks stimuli-responsive (light, ultrasound, magnetic) delivery (Kankala, et al., 2020), while magnetic and luminescent functionalization integrates targeting and tracking abilities into a single platform (Yang, Gai, & Lin, 2012). For carbon-based carriers, PEGylation is the most widely used strategy, as PEG brushes create steric hindrance that prevents protein adsorption and corona formation (Zou, Nishina, & Bianco, 2024, p. 118665); amine-terminated PEG functionalization stabilizes carbon nanotube dispersions in biological media and reduces deleterious effects on cultured cells (Heister, et al., 2010, p. 2616), and PEG coatings broadly improve biocompatibility, avoid aggregation, and prolong blood circulation time (Chen, et al., 2018, p. 9).

Conclusion

This comparative analysis demonstrates that nanoclay, mesoporous silica, and carbon-based nanocarriers each offer distinct structural, functional, and biological profiles that position them for complementary roles in nanomedicine. Nanoclay platforms, exemplified by montmorillonite and halloysite nanotubes, are distinguished by their natural abundance, high cation-exchange capacity, and versatile interlayer chemistry, which enable robust drug intercalation and sustained release through ion-exchange mechanisms. Their generally favorable biocompatibility and rapid clearance profiles make them attractive low-cost candidates for oral and topical delivery, though origin-dependent variability and concentration-dependent cytotoxicity warrant careful physicochemical characterization.

Mesoporous silica nanoparticles stand out for their exceptional structural tunability high surface area, ordered pore networks, and selective functionalization of external and internal surfaces which supports exceptionally high drug loading capacities and precisely engineered, stimuli-responsive release systems such as nanovalves and capped pores. Their well-documented biodistribution, shape- and size-dependent clearance, and hemocompatibility considerations have been extensively investigated, making them one of the most thoroughly characterized inorganic nanocarrier systems for cancer theranostics and combined chemo–gene therapy.

Carbon-based nanocarriers, including carbon nanotubes, graphene family materials, and fullerenes, offer unique advantages in photothermal conversion, large specific surface area, and the ability to transport both therapeutic drugs and nucleic acids. However, their application remains constrained by the most contested toxicity profile of the three families, with outcomes strongly dependent on surface functionalization, purity, dimensions, and exposure route; surface modification strategies such as PEGylation have proven essential to improving their dispersion stability, biocompatibility, and circulation time.

Taken together, the three families should not be viewed as competing but as complementary platforms, each with characteristic strengths and limitations. The shared lesson across all three is that surface chemistry, rather than core composition alone, dictates therapeutic performance and biological safety. Future progress will depend on continued refinement of surface functionalization, standardized and systematic toxicological evaluation, and translation of the most promising modified nanocarriers toward clinical application, where their combined capabilities in controlled drug delivery, gene therapy, and cancer treatment can be fully realized.

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Figures

Fig. 1:
A schematic illustration of various approaches to CNT-based drug delivery and cancer therapy (16).

Fig. 2:
Comparative criteria for evaluating the structure, performance, and biocompatibility of nanoclay, mesoporous silica, and carbon-based nanocarriers (38).

Fig. 3:
Comparative characteristics, delivery performance, stability, functionalization potential, and biocompatibility of nanoclay, mesoporous silica, and carbon-based nanocarriers (51).

Fig. 4:
Schematic illustration of the synthesis of mesoporous silica nanoparticles (75).