International Journal of Pharmaceutical Drug Design (IJPDD)
Website: https://ijpdd.org/
ISSN: 2584-2897
Vol. 2, Issue 12, December, 2025
Page No.: 40-44

Review

Mesoporous Silica Nanoparticles as Advanced Drug Delivery Platforms: A Comprehensive Review

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DOI: *10.62896/ijpdd.2.12.03*

Conflict of interest: *NIL*

Article History
Received: 12/11/2025
Accepted: 14/12/2025
Published: 15/12/2025

Abstract:
Mesoporous silica nanoparticles (MSNs) have emerged as one of the most promising nanocarriers in advanced drug delivery systems due to their highly ordered pore structure, large surface area, tunable pore size, and exceptional biocompatibility. Drug delivery aims to transport therapeutic compounds efficiently to targeted tissues, improving pharmacokinetics and pharmacodynamics while minimizing adverse effects. Over the past two decades, MSNs have gained significant attention for their customizable architecture, surface modification capacity, and ability to enhance the stability, solubility, and controlled release of various drugs (1,6). The development of surfactant-templated mesoporous silica in 1992 marked a major breakthrough, followed by the introduction of MSNs for drug delivery in 1998 through pioneering patents and experimental demonstrations (14,16). MSN research has expanded exponentially since 2013, reflecting their growing relevance in cancer therapy, targeted delivery, and stimuli-responsive drug release, with publications rising from fewer than 50 annually before 2012 to more than 450 in 2021 (1). Their ability to deliver hydrophilic, hydrophobic, and sensitive therapeutic agents—combined with immediate, sustained, and responsive release properties—makes MSNs versatile platforms in biomedical applications. Despite advantages such as high drug-loading capacity, biodegradability, and ease of functionalization, challenges including complex synthesis, potential aggregation, long-term toxicity concerns, and high production costs remain barriers to clinical translation (9,10). Overall, MSNs represent a transformative approach in nanomedicine, offering significant potential to enhance therapeutic outcomes, reduce systemic toxicity, and support the development of precision drug delivery technologies.

Keywords: Mesoporous silica nanoparticles (MSNs); Drug delivery systems; Controlled release; Targeted therapy; Nanomedicine; Surface functionalization; Stimuli-responsive delivery; Biocompatible nanocarriers.

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Introduction:

Nanoparticle technology has emerged as one of the most influential domains in modern scientific research due to its ability to manipulate materials at the molecular and atomic scale, enabling advanced functionalities in medicine, energy, and materials science (1). Among the various nanomaterials explored, mesoporous silica nanoparticles (MSNs) have gained exceptional importance because of their highly ordered pore structure, uniform particle size distribution, and exceptionally large surface area, which provide superior physicochemical properties compared to other nanocarriers (6). The mesoporous architecture of MSNs enables high drug-loading efficiency, improved dispersion of hydrophobic molecules, and controlled release behavior, making them ideal candidates for pharmaceutical and biomedical applications (4). Furthermore, their abundant surface silanol groups allow easy chemical functionalization with polymers, targeting ligands, peptides, or antibodies, thus enhancing their biocompatibility, targeting precision, and interaction with cellular environments (5). Due to these properties, MSNs have demonstrated remarkable versatility in drug delivery, imaging, biosensing, gene transport, and tissue engineering applications, establishing them as a multifunctional nanoplatform in contemporary nanomedicine (1,3). Their ability to interface effectively with biological systems—through controlled size, surface charge, and surface modification—has further solidified the role of MSNs as a leading material in therapeutic and diagnostic nanotechnology (2).

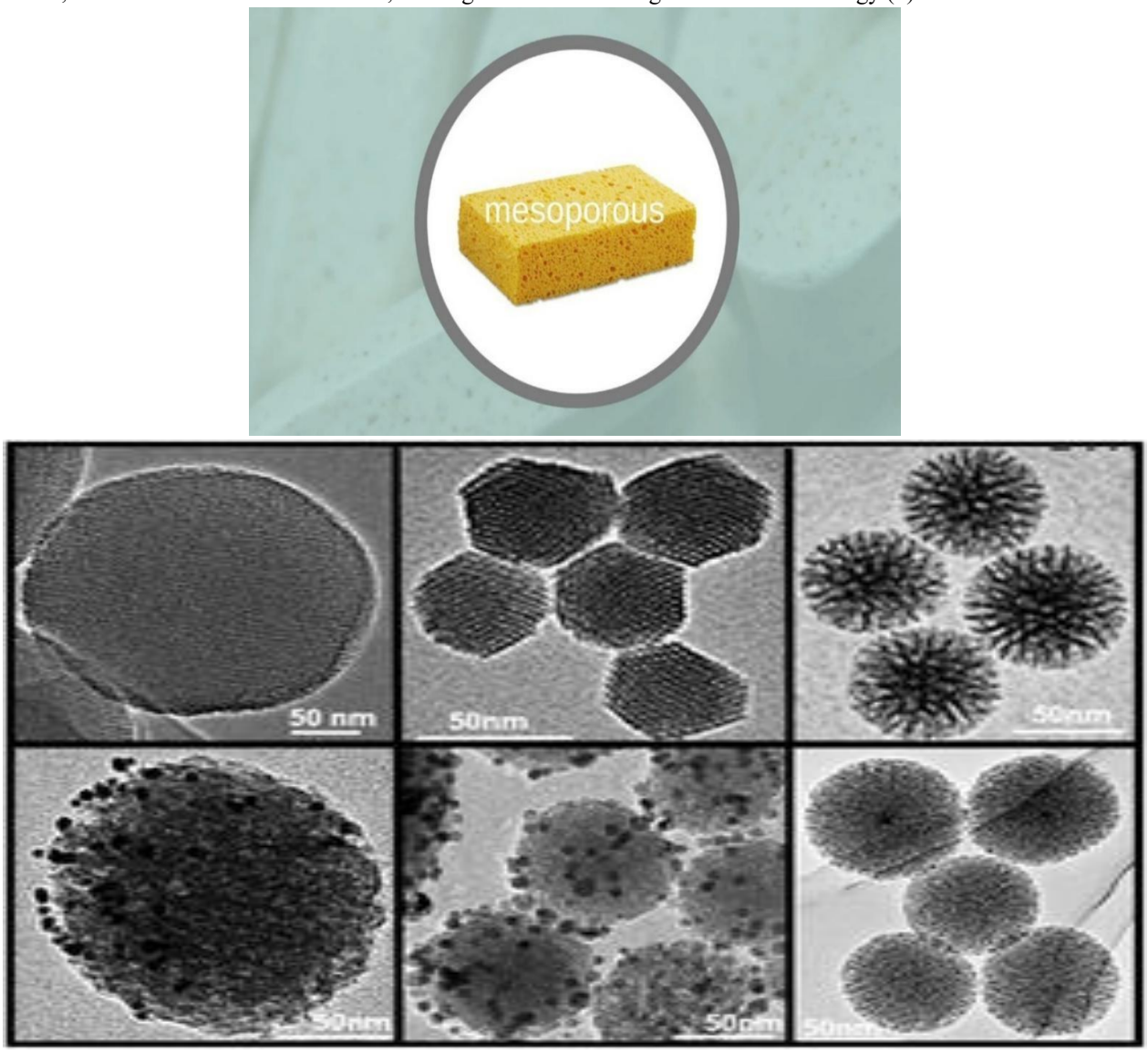

Figure 1: Schematic Representation of a Mesoporous Structure Using a Sponge Analog

History of Mesoporous Silica Nanoparticles (MSNs)

Mesoporous silica materials have been widely studied for more than four decades, initially described as zeolite–silica gel hybrids with uniform and well-defined pores (15). A major scientific breakthrough occurred in 1992 when the Mobil Research Group discovered the M41S family using a surfactant-templated synthesis, which introduced highly ordered mesoporous silica with tunable pore sizes (12). This innovation laid the foundation for the development of mesoporous silica nanoparticles (MSNs) as modern nanocarriers.

The concept of utilizing MSNs for drug delivery was formally proposed in 1998 when Müller, Recker, and Röser filed a patent demonstrating that mesoporous silicates could encapsulate pharmacologically active agents (14). This was followed by additional advances in 1999 by Schüth and co-workers, who further established the utility of mesoporous silica in controlled drug delivery (16). By 2001, Balkus and colleagues provided experimental validation of MSN-based drug loading and release, documenting one of the first systematic studies in this domain (8). Since then, MSNs have undergone rapid evolution, becoming one of the most versatile nanomaterials in biomedical nanotechnology.

Trends in MSN-Based Drug Delivery

A review of ISI Web of Science data shows that publications on MSNs remained below 50 per year between 2005 and 2012. A noticeable increase began in 2013, with annual publications reaching approximately 50, then accelerating steadily to over 450 publications by 2021. This rapid growth highlights the expanding global interest in the biomedical and pharmaceutical applications of MSNs (1).

Chemistry of Mesoporous Silica Nanoparticles

MSNs are synthesized using inorganic precursors such as tetraalkoxysilanes (e.g., tetraethyl orthosilicate, TEOS) or sodium silicate through a sol–gel process directed by surfactants (19). Adjusting pH during synthesis allows precise control over hydrolysis and condensation rates, which determines the structural ordering of the silica network (9). The resulting framework is amorphous and rich in surface silanol (Si–OH) groups, providing reactive sites for chemical functionalization. These functional groups support the attachment of polymers, targeting ligands, and stimuli-responsive moieties, making MSNs highly tunable nanocarriers (22).

Synthesis of MSNs

The synthesis of MSNs typically involves a surfactant-templated sol–gel approach:

Step 1: Surfactant Micelle Formation

Water, sodium hydroxide (NaOH), and cetyltrimethylammonium bromide (CTAB) are mixed and heated at 80 °C to form micelles that act as soft templates (15).

Step 2: Addition of Silica Precursor

TEOS is added, followed by hydrolysis and condensation reactions at 80 °C for an additional 2 hours, leading to the formation of the silica framework around the micelles.

Step 3: Purification

The reaction mixture is washed, filtered, and dried to remove unreacted precursors and impurities.

Step 4: Surfactant Removal

CTAB is removed via calcination or solvent extraction to obtain pure mesoporous silica nanoparticles with open pores available for drug loading (11).

Advantages of MSNs

MSNs possess several characteristics that make them superior drug delivery carriers:

1. High Drug Loading Capacity

The large surface area and tunable pore size allow encapsulation of significant quantities of both hydrophilic and hydrophobic drugs (17).

2. Controlled and Sustained Release

The porous network enables predictable drug release kinetics, enhancing therapeutic outcomes (18).

3. Biocompatibility and Biodegradability

Silica safely degrades into non-toxic silicic acid, ensuring good biocompatibility (10).

4. Easy Surface Functionalization

MSNs can be modified with targeting ligands such as peptides, folate, hyaluronic acid, and antibodies to improve tissue-specific delivery (13).

5. Protection of Sensitive Drugs

Encapsulation shields unstable molecules from pH, enzymatic, and oxidative degradation (23).

6. Enhanced Cellular Uptake

Nanoscale size and modifiable surface charge support efficient internalization into cells (15).

7. Stimuli-Responsive Release

MSNs can be engineered to respond to pH, temperature, enzymes, redox conditions, or light (20).

Disadvantages of MSNs

1. Complex Synthesis and Functionalization

Precise control of reaction parameters is required to maintain structural uniformity (9).

2. Potential Aggregation

Nanoparticles may aggregate in biological fluids, affecting performance (1).

3. Limited Long-Term Toxicity Data

Chronic exposure effects in humans are still under evaluation.

4. Possible Burst Release

Unmodified MSNs may release a large proportion of drug too quickly.

5. High Production Cost

Functionalization and purification steps are cost-intensive.

6. Potential Immunogenicity

Improper surface chemistry may trigger immune responses (10).

Applications of MSNs in Drug Delivery

1. Immediate Drug Delivery

Hydrophobic drugs often suffer from poor solubility and limited bioavailability. MSNs keep drugs in an amorphous state, enhancing dissolution and absorption (11).

2. Sustained Drug Release

MSNs provide prolonged therapeutic activity with reduced dosing frequency. Modified MSNs allow fine-tuning of the release rate (20).

3. Targeted Drug Delivery

Due to the Enhanced Permeation and Retention (EPR) effect, MSNs accumulate in tumor tissues. Ligand-conjugated MSNs such as folate-MSNs significantly improve cancer-targeting efficiency (13).

4. Stimuli-Responsive Delivery

MSNs can release drugs in response to:

- **pH changes** (19)
- **Redox gradients** (20)
- **Enzymes** (21)
- **Temperature/light** (18)

These smart systems minimize side effects and improve therapeutic precision.

History of MSNs:-

For more than four decades, Scientists have been familiar with Mesoporous Silica materials, a term originally used to describe zeolite–silica gel blends Characterized by uniform and well define pores. A significant break through Came in 1992 when two independent research terms almost Simultaneously reported the creation of organic-templated mesoporous Silica. The possibility of employing mesoporous silica nanoparticles (MSNs) as drug-delivery system surface only in 1998, when Muller, Reck drug-delivery system and Roser filed a patent proposing that mesoporous silicates Could incorporate pharmacologically active agents. A year later, schuth and Collaborators expanded on this concept By 2001, Balkus and co- workers documented" this for first time.

Conclusion

Mesoporous silica nanoparticles (MSNs) have emerged as one of the most versatile and powerful nanocarriers in modern drug delivery due to their tunable pore architecture, high surface area, and modifiable surface chemistry. Over the past two decades, extensive research has demonstrated their ability to efficiently encapsulate both hydrophilic and hydrophobic drugs, enhance cellular uptake, and enable controlled, sustained, and stimuli-responsive drug release (20, 23). The significant increase in global publications after 2013 further reflects the rapid expansion of MSN-based biomedical research, especially in cancer therapy, targeted delivery, and nanotheranostics (1).

Despite their advantages, challenges such as complex synthesis, potential aggregation, incomplete long-term toxicity data, and high production costs highlight the need for further optimization (9). Continued advancements in surface functionalization, biocompatibility engineering, and stimuli-responsive gatekeeping mechanisms are expected to enhance their clinical translation. Overall, MSNs represent a highly promising platform for next-generation drug delivery systems, with strong potential to improve therapeutic outcomes, reduce adverse effects, and contribute significantly to the field of precision nanomedicine.

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