www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



Silica-Based Nanocarriers for Controlled Drug Delivery: A Critical Review of Design Strategies and Biomedical Applications

Ankur Patel ¹, Farhad F Mehta², Pavini Suri³, Shivani Vashist⁴, Sunita Ankit Chaudhary⁵, Ramandeep Kaur ⁶, Swati B. Udugade⁷, Piyali Dey ⁸*

Corresponding Author: Dr. Piyali Dey

Designation & Affiliation: Assistant Professor, Assam Down Town University, Shankar Madhab Path, Panikhaiti,

Guwahati, Assam

(Received: 07 January 2024 Revised: 12 February 2024 Accepted: 06 March 2024)

KEYWORDS

silica-based
nanocarriers,
controlled drug
delivery,
biomedical
applications,
synthesis, surface
modification,
stimuliresponsive
systems.

ABSTRACT:

Silica-based nanocarriers have garnered significant attention in biomedical research as promising platforms for controlled drug delivery, imaging, and theranostics. This review provides a comprehensive overview of the design strategies, biomedical applications, recent advances, and future perspectives of silica-based nanocarriers. Fundamentals of silica nanoparticles, including their structure, synthesis methods, surface modification techniques, and characterization methods, are discussed in detail. Design strategies for controlled drug delivery, such as encapsulation methods, triggered release mechanisms, and targeting strategies, are elucidated, highlighting their potential for enhancing therapeutic efficacy and minimizing off-target effects. Biomedical applications of silicabased nanocarriers, including cancer therapy, imaging, treatment of infectious diseases, and gene delivery, are explored, showcasing their versatility and clinical relevance. Recent advances in the field, including emerging trends in nanocarrier research and innovative strategies for multifunctional and stimuli-responsive systems, are presented. Challenges and limitations, such as biocompatibility, scalability, and clinical translation, are discussed, underscoring the need for continued research and innovation. Future directions for research and development, including personalized medicine approaches and clinical translation strategies, are proposed, emphasizing the transformative potential of silicabased nanocarriers in biomedicine. Overall, this review provides valuable insights into the current state-of-the-art research and identifies opportunities for advancing the field of controlled drug delivery using silica-based nanocarriers.

¹Assistant Professor, Sardar Patel College of Pharmacy, Vidyanagar-Vadtal Road, Bakrol

²Assistant Professor, School of Pharmaceutical Sciences, U.T.D- Rajiv Gandhi Prouyogiki Vishwavidyalaya, University of Technology Of Madhya Pradesh, Bhopal, M.P

³Research Scholar, Manav Rachna International Institute of Research and Studies,

⁴Hod, Manav Rachna International Institute of Research and Studies

⁵Professor, Arihant School of Pharmacy and Bio Research Institute, Adalaj, Gandhinagar, Gujarat, India-382421

⁶Assistant Professor, Guru Kashi University, Talwandi Sabo, Bathinda

⁷Associate Professor, Department of Pharmaceutics, KVV'S, Krishna Institute Of Pharmacy, Karad

⁸Assistant Professor, Assam Down Town University, Shankar Madhab Path, Panikhaiti, Guwahati, Assam

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



Introduction

Controlled drug delivery systems have revolutionized the field of medicine by offering precise and targeted administration of therapeutic agents, minimizing side effects. and improving patient compliance[1]. Traditional drug delivery methods often lack specificity and may lead to systemic toxicity or degradation of the drug before it reaches its target site[2]. In contrast, controlled drug delivery systems allow for the sustained release of drugs at predetermined rates and locations within the body, enhancing therapeutic efficacy while reducing adverse effects. Silica-based nanocarriers represent a promising class of drug delivery systems due to their unique properties, including high surface area, tunable pore size, biocompatibility, and ease of functionalization[3]. These nanoparticles encapsulate a wide range of drugs, protect them from degradation, and facilitate controlled release kinetics, making them suitable candidates for various biomedical applications[4]. Silica-based nanocarriers have gained significant attention in recent years due to their unique properties and potential as controlled drug delivery systems. These nanoparticles, composed of silica particles with various coatings or modifications, offer several advantages for applications, including improved delivery solubility, enhanced targeting, and controlled release[5]. This review aims to explore the design strategies and biomedical applications of silica-based nanocarriers, highlighting their advantages and challenges. Silica, an essential component of glass, has been widely used in various fields, including nanotechnology. Its unique properties, such as high surface area, stability, and biocompatibility, make it an attractive choice for nanocarrier applications[6]. Silica-based nanocarriers can be engineered to possess specific characteristics, such as surface modifications, loading of drugs, and targeting ligands, to tailor their drug delivery capabilities. One of the key design strategies employed in silica-based nanocarriers is surface modification. By altering the surface chemistry, nanocarriers can selectively interact with target cells or tissues, enhancing drug delivery and targeting[7]. Surface modifications can include coating with polymers, surfactants, or targeting ligands, allowing for specific recognition and uptake by cells or tissues of interest. Another critical aspect of silica-based nanocarriers is their ability to encapsulate and deliver drugs. Nanocarriers can be developed using various methods, such as encapsulation within mesoporous silica particles or adsorption onto the surface[8]. The choice of encapsulation method depends on the drug properties, such as solubility and stability, as well as the desired release profile. Biomedical applications of silica-based nanocarriers are diverse and encompass various therapeutic areas. These applications include delivery of small molecules, proteins, nucleic acids, nanoparticles for imaging and diagnostics[9]. The use of nanocarriers can improve the therapeutic index of drugs, minimize side effects, and enhance drug delivery to specific target sites. This review article aims to provide a comprehensive overview of the design strategies and biomedical applications of silica-based nanocarriers for controlled drug delivery[10]. The scope of this review encompasses the synthesis, functionalization, and characterization of silica nanoparticles, as well as the mechanisms of controlled drug release and their applications in treating various diseases. By critically analyzing the current state-of-the-art research, this review aims to identify key challenges, emerging trends, and future directions in the field[11].

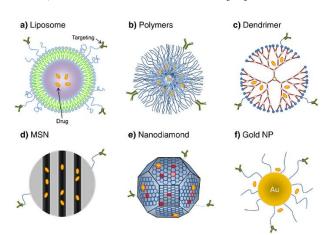


Figure 1: Various nanoparticles used to develop drug delivery systems.

Fundamentals of Silica-Based Nanocarriers

Silica-based nanocarriers represent a versatile class of drug delivery systems with unique properties that make them highly attractive for biomedical applications. Understanding the fundamentals of silica nanoparticles, including their structure, synthesis methods, surface modification techniques, and characterization methods,

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



is essential for designing and optimizing their performance as drug delivery vehicles[12].

A. Structure and Properties of Silica Nanoparticles

Silica nanoparticles are composed of silicon dioxide (SiO2) and exhibit a range of structural and physicochemical properties that influence their behavior as drug carriers[13]. At the nanoscale, silica particles can exist in various forms, including spheres, rods, tubes, and mesoporous structures. The size and morphology of silica nanoparticles can be tailored through synthesis methods, affecting their surface area, pore size, and drug-loading capacity[14]. The unique properties of silica nanoparticles make them ideal candidates for drug delivery applications. Their high surface area-to-volume ratio provides ample space for drug loading, while their tunable pore size allows for controlled release kinetics. Additionally, nanoparticles are biocompatible, inert, and stable under physiological conditions, minimizing the risk of toxicity and degradation in biological systems[15].

B. Synthesis Methods of Silica Nanoparticles

Silica nanoparticles can be synthesized using various methods, each offering distinct advantages in terms of particle size, morphology, and surface chemistry. Common synthesis routes include sol-gel processes, microemulsion techniques, and template-assisted methods [16].

1. Sol-Gel Process: The sol-gel process is the most widely used method for synthesizing silica nanoparticles. It involves the hydrolysis and condensation of silica precursors, such as tetraethyl orthosilicate (TEOS) or sodium silicate, in the presence of a catalyst and solvent. The reaction can be controlled to produce nanoparticles with desired sizes and shapes by adjusting parameters such as temperature, pH, and reaction time[17].

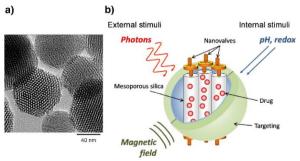


Figure 2: Mesoporous silica nanoparticles synthesized by the sol–gel method.

- 2. Microemulsion Technique: In the microemulsion method, surfactants are used to stabilize nanoscale droplets of water and oil in a continuous phase. Silica precursors are added to the water phase, where they undergo hydrolysis and condensation to form nanoparticles within the confined spaces of the droplets. This method allows for precise control over particle size and morphology and can produce monodisperse nanoparticles with narrow size distributions[18].
- 3. Template-Assisted Methods: Template-assisted synthesis involves using preformed templates, such as micelles or colloidal particles, as scaffolds for silica nanoparticle growth[19]. The silica precursor is introduced into the template structure, where it undergoes condensation to form nanoparticles with defined shapes and sizes dictated by the template geometry. Template-assisted methods enable the synthesis of silica nanoparticles with complex structures, such as hollow spheres or mesoporous materials[20].

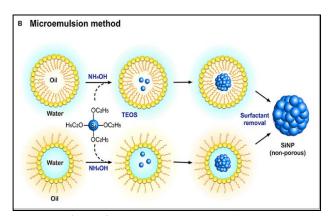


Figure 3: Microemulsion Technique.

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



C. Surface Modification Techniques for Functionalization

Surface modification of silica nanoparticles plays a crucial role in tailoring their properties for specific drug delivery applications. Functionalization strategies involve the attachment of functional groups or biomolecules to the nanoparticle surface to impart desired characteristics, such as targeting specificity, stealth behavior, or stimuli responsiveness[21].

- 1. Silane Coupling Agents: Silane coupling agents, such as (3-aminopropyl)triethoxysilane (APTES) or (3-mercaptopropyl)trimethoxysilane (MPTMS), are commonly used to modify the surface of silica nanoparticles[22]. These agents possess reactive functional groups, such as amino, thiol, or epoxy groups, that can chemically bind to the silica surface through siloxane linkages. The terminal functional groups of silane coupling agents can then be further modified or conjugated with ligands, polymers, or drugs to impart specific functionalities to the nanoparticles[23].
- 2. Polymer Coatings: Polymer coatings provide an effective way to functionalize silica nanoparticles while imparting stability and biocompatibility. Polymers, such as polyethylene glycol (PEG), polyethyleneimine (PEI), or poly(lactic-co-glycolic acid) (PLGA), can be adsorbed or covalently attached to the nanoparticle surface to form a protective layer[24]. Polymer coatings can improve the colloidal stability of silica nanoparticles, prolong circulation time in vivo, and prevent nonspecific interactions with biological components[25].
- 3. Biomolecule Conjugation: Biomolecules, such as peptides, antibodies, or nucleic acids, can be conjugated to the surface of silica nanoparticles to confer targeting specificity or enhance cellular uptake[26]. Bioconjugation techniques, such as covalent coupling or affinity binding, enable the attachment of biomolecules to the nanoparticle surface while preserving their biological activity. Functionalized silica nanoparticles can selectively target diseased cells or tissues, improving the efficacy and safety of drug delivery[27].

D. Characterization Techniques for Silica-Based Nanocarriers

Characterization of silica nanoparticles is essential for evaluating their physicochemical properties, stability, and performance as drug delivery vehicles. A variety of analytical techniques are available to characterize silicabased nanocarriers, including imaging techniques, spectroscopic methods, and surface analysis techniques[28].

- 1. Transmission Electron Microscopy (TEM): TEM is a powerful imaging technique used to visualize the morphology, size, and structure of silica nanoparticles at the nanoscale. By transmitting electrons through a thin specimen, TEM provides high-resolution images that reveal detailed information about particle shape, size distribution, and internal structure [29].
- 2. Dynamic Light Scattering (DLS): DLS is a non-invasive technique used to measure the hydrodynamic size and size distribution of nanoparticles in solution. By analyzing the fluctuations in light scattering intensity caused by Brownian motion, DLS provides information about the particle size distribution and polydispersity index of silica nanoparticles in suspension[30].
- 3. Fourier Transform Infrared Spectroscopy (FTIR): FTIR spectroscopy is used to characterize the chemical composition and surface functional groups of silica nanoparticles. By measuring the absorption of infrared radiation by molecular bonds, FTIR provides information about the presence of functional groups, such as silanol groups (Si-OH), siloxane bonds (Si-OSi), or organic moieties, on the nanoparticle surface[31].
- **4. Brunauer-Emmett-Teller** (**BET**) Surface Area Analysis: BET surface area analysis is employed to determine the specific surface area and pore structure of silica nanoparticles. By measuring the adsorption of gas molecules onto the nanoparticle surface at various pressures, BET analysis provides information about the surface area, pore volume, and pore size distribution of silica-based nanocarriers[32].
- 5. Zeta Potential Measurement: Zeta potential measurement is used to assess the surface charge and

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



colloidal stability of silica nanoparticles in solution. By measuring the electrophoretic mobility of particles in an electric field, zeta potential analysis provides information about the surface charge density and potential stability of nanoparticles against aggregation or flocculation[33].

Design Strategies for Controlled Drug Delivery

Controlled drug delivery systems offer precise and targeted release of therapeutic agents, minimizing side effects and improving patient outcomes. Silica-based nanocarriers provide a versatile platform for designing controlled drug delivery systems, allowing for the encapsulation of drugs, triggered release mechanisms, and targeting strategies. Additionally, stability and biocompatibility considerations are crucial for the development of safe and effective drug delivery systems[34].

A. Encapsulation Methods for Drug Loading

Encapsulation methods are employed to load drugs into silica nanoparticles while protecting them from degradation and facilitating controlled release. Various techniques, including physical encapsulation, adsorption, and covalent attachment, can be utilized depending on the physicochemical properties of the drug[35].

- 1. Physical Encapsulation: In physical encapsulation, drugs are physically entrapped within the pores or matrix of silica nanoparticles through passive diffusion or capillary action. This method is suitable for hydrophobic drugs that can partition into the hydrophobic domains of silica nanoparticles. Physical encapsulation offers high drug loading capacity and sustained release kinetics but may result in burst release depending on the drug-nanoparticle interactions [36].
- 2. Adsorption: Adsorption involves the adsorption of drug molecules onto the surface of silica nanoparticles through electrostatic or hydrophobic interactions. This method is simple, cost-effective, and applicable to a wide range of drugs with diverse physicochemical properties. However, adsorption may lead to drug desorption or leaching over time, affecting the stability

and release kinetics of the drug-loaded nanoparticles[37].

3. Covalent Attachment: Covalent attachment involves chemically conjugating drug molecules to functional groups on the surface of silica nanoparticles through covalent bonds. This method provides stable drugnanoparticle conjugates with controlled drug loading and release properties. Covalent attachment offers precise control over drug loading and release kinetics but requires functionalization of the nanoparticle surface with appropriate linker molecules [38].

B. Triggered Release Mechanisms

Triggered release mechanisms enable on-demand release of drugs from silica-based nanocarriers in response to specific stimuli or environmental cues. pH-responsive systems and stimuli-responsive systems, such as temperature, light, or magnetic fields, offer spatiotemporal control over drug release, enhancing therapeutic efficacy and minimizing off-target effects[39].

- 1. pH-Responsive Systems: pH-responsive systems exploit variations in pH between different physiological the acidic environments, such as microenvironment and neutral extracellular space, to trigger drug release[40]. Silica nanoparticles can be functionalized with pH-sensitive groups, such as acidlabile bonds or pH-responsive polymers, that undergo conformational changes or degradation in response to changes in pH. This results in the release of encapsulated drugs in acidic environments, such as tumors or inflamed tissues, while maintaining drug stability in neutral pH environments[41].
- 2. Stimuli-Responsive Systems: Stimuli-responsive systems utilize external stimuli, such as temperature, light, or magnetic fields, to trigger drug release from Temperature-responsive silica nanoparticles[42]. polymers, such as poly(N-isopropylacrylamide) (PNIPAM), undergo a phase transition from a swollen to a collapsed state in response to changes in temperature, leading to controlled drug release. Lightresponsive systems incorporate photoresponsive molecules, such as azobenzene derivatives or spiropyran, that undergo reversible photoisomerization

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



in the presence of light, enabling spatiotemporal control over drug release. Magnetic-responsive systems utilize magnetic nanoparticles embedded within silica matrices to generate heat under an alternating magnetic field, triggering drug release through thermal activation[43].

C. Targeting Strategies

Targeting strategies aim to enhance the accumulation of drug-loaded silica nanoparticles at specific sites within the body, improving therapeutic efficacy and minimizing off-target effects. Passive targeting exploits physiological phenomena, such as the enhanced permeability and retention (EPR) effect, while active targeting involves functionalizing nanoparticles with ligands that bind to specific receptors overexpressed on diseased cells or tissues[44].

- 1. Passive Targeting: Passive targeting relies on the passive accumulation of drug-loaded silica nanoparticles at sites of disease through the EPR effect[45]. In tumors and inflamed tissues, abnormal angiogenesis and leaky vasculature lead to enhanced permeability and retention of nanoparticles, allowing for their preferential accumulation in the diseased tissue. Silica nanoparticles with appropriate size, surface charge, and surface modifications can exploit the EPR effect to achieve selective accumulation and prolonged retention in tumors or inflamed tissues[46].
- 2. Active Targeting: Active targeting involves functionalizing silica nanoparticles with targeting ligands, such as antibodies, peptides, or small molecules, that bind to specific receptors overexpressed on the surface of diseased cells or tissues[47]. Ligand-functionalized nanoparticles can actively target tumor cells, inflammatory cells, or pathogens, enhancing cellular uptake and intracellular drug delivery. Targeting ligands can be conjugated to the surface of silica nanoparticles through covalent attachment or affinity binding, enabling specific recognition and binding to target cells or tissues[48].

D. Stability and Biocompatibility Considerations

Stability and biocompatibility are critical considerations in the design of silica-based nanocarriers to ensure their safety and efficacy in biomedical applications. Silica nanoparticles should exhibit high colloidal stability, minimal aggregation, and low toxicity to biological systems[49].

- 1. Colloidal Stability: Colloidal stability is essential to prevent aggregation or sedimentation of silica nanoparticles in physiological fluids and biological environments. Surface modification with hydrophilic polymers, such as polyethylene glycol (PEG), or zwitterionic molecules, such as zwitterionic polymers or phospholipids, can enhance the colloidal stability of silica nanoparticles by preventing protein adsorption and opsonization[50].
- 2. Biocompatibility: Biocompatibility is crucial to minimize adverse effects and ensure compatibility with biological systems. Silica nanoparticles should exhibit low cytotoxicity, minimal immunogenicity, and favorable interactions with cells and tissues. Surface modification with biocompatible polymers or coatings can improve the biocompatibility of silica nanoparticles and reduce the risk of adverse reactions in vivo[51].

Biomedical Applications of Silica-Based Nanocarriers

Silica-based nanocarriers have demonstrated significant potential for a wide range of biomedical applications, including cancer therapy, imaging, treatment of infectious diseases, and gene delivery. Their unique properties, such as tunable pore size, high surface area, and biocompatibility, make them attractive platforms for targeted drug delivery and imaging [52].

A. Cancer Therapy

Cancer remains a significant health challenge worldwide, and innovative therapeutic approaches are urgently needed to improve patient outcomes. Silicabased nanocarriers offer several strategies for cancer therapy, including chemotherapy, photodynamic therapy (PDT), and radiotherapy [53].

1. Chemotherapy: Silica nanoparticles can serve as effective carriers for chemotherapeutic drugs, such as paclitaxel, doxorubicin, or cisplatin, by encapsulating or conjugating them to the nanoparticle surface[54]. By improving drug solubility, stability, and circulation

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



time, silica-based nanocarriers enhance drug delivery to tumor sites while minimizing off-target effects and systemic toxicity. Moreover, targeted delivery of chemotherapeutic agents using ligand-functionalized silica nanoparticles enables selective accumulation in tumor cells, enhancing therapeutic efficacy and reducing side effects[55].

- 2. Photodynamic Therapy (PDT): Photodynamic therapy involves the administration of photosensitizing agents that accumulate in tumor tissue followed by irradiation with light of a specific wavelength, leading to the generation of reactive oxygen species (ROS) and tumor cell death[56]. Silica nanoparticles can encapsulate photosensitizing agents, such as porphyrins or phthalocyanines, and facilitate their delivery to tumor sites. Additionally, surface modification of silica nanoparticles with targeting ligands enables selective uptake by tumor cells, enhancing the specificity and efficacy of PDT while minimizing damage to healthy tissues[57].
- 3. Radiotherapy: Silica nanoparticles be functionalized with radioisotopes, gold such as nanoparticles or radionuclides, for use radiotherapy[58]. By encapsulating or conjugating radioisotopes to the nanoparticle surface, silica-based nanocarriers enable targeted delivery of radiation to tumor sites, enhancing tumor cell killing while sparing surrounding healthy tissues. Moreover, multifunctional silica nanoparticles with integrated imaging capabilities can facilitate real-time monitoring of radiotherapy response and treatment efficacy[59].

B. Imaging Applications

Imaging plays a crucial role in the diagnosis, staging, and monitoring of diseases, including cancer and infectious diseases. Silica-based nanocarriers offer versatile platforms for imaging applications, including magnetic resonance imaging (MRI) contrast agents and fluorescent imaging agents[60].

1. MRI Contrast Agents: Silica nanoparticles can be functionalized with paramagnetic or superparamagnetic agents, such as gadolinium chelates or iron oxide nanoparticles, for use as MRI contrast agents[61]. By encapsulating or conjugating contrast agents to the

nanoparticle surface, silica-based nanocarriers enable enhanced visualization of anatomical structures and pathological changes. Additionally, surface modification of silica nanoparticles with targeting ligands facilitates targeted delivery of MRI contrast agents to specific tissues or cells, improving imaging sensitivity and specificity[62].

2. Fluorescent Imaging Agents: Silica nanoparticles can incorporate fluorescent dyes or quantum dots for use as fluorescent imaging agents[63]. By encapsulating or conjugating fluorescent probes to the nanoparticle surface, silica-based nanocarriers enable sensitive detection and visualization of biological processes in vitro and in vivo. Moreover, multifunctional silica nanoparticles with integrated targeting ligands or therapeutic agents enable simultaneous imaging and therapy, facilitating personalized medicine approaches for disease diagnosis and treatment[64].

C. Treatment of Infectious Diseases

Infectious diseases, including bacterial infections, viral infections, and fungal infections, pose significant public health threats worldwide. Silica-based nanocarriers offer novel strategies for the treatment of infectious diseases, including targeted delivery of antibiotics, antiviral drugs, and vaccines [65].

D. Gene Delivery Applications

Gene therapy holds promise for the treatment of genetic disorders, cancer, and other diseases by delivering therapeutic nucleic acids, such as DNA or RNA, to target cells or tissues[66]. Silica-based nanocarriers provide efficient and safe platforms for gene delivery, protecting nucleic acids from degradation and facilitating their intracellular delivery. By encapsulating or conjugating nucleic acids to the nanoparticle surface, silica-based nanocarriers enable targeted gene delivery to specific cells or tissues, enhancing therapeutic efficacy while minimizing off-target effects[67].

Recent Advances and Future Perspectives

Silica-based nanocarriers have emerged as promising platforms for controlled drug delivery, imaging, and theranostics due to their unique properties and versatile

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



applications[68]. Recent advances in silica-based nanocarrier research have led to novel strategies for enhanced drug delivery, imaging sensitivity, and therapeutic efficacy. However, several challenges and limitations remain, necessitating continued research and innovation to address current gaps and unlock the full potential of silica-based nanocarriers in biomedical applications[69].

A. Emerging Trends in Silica-Based Nanocarrier Research

- 1. Multifunctional Nanocarriers: Recent research has focused on developing multifunctional silica-based nanocarriers with integrated imaging and therapeutic capabilities. By incorporating contrast agents, therapeutic drugs, and targeting ligands into a single nanoparticle platform, multifunctional nanocarriers enable simultaneous imaging and therapy, facilitating personalized medicine approaches and enhancing treatment efficacy[70].
- 2. Stimuli-Responsive Nanocarriers: Stimuli-responsive silica nanoparticles capable of responding to external triggers, such as pH, temperature, light, or magnetic fields, have garnered significant interest for controlled drug release and targeted therapy[71]. By incorporating stimuli-responsive moieties into the nanoparticle structure, researchers can achieve spatiotemporal control over drug release, improving therapeutic outcomes while minimizing off-target effects[72].
- 3. Theranostic Nanoparticles: Theranostic silica nanoparticles combine diagnostic and therapeutic functionalities within a single platform, enabling real-time monitoring of treatment response and disease progression. By integrating imaging agents, therapeutic drugs, and targeting ligands into a single nanoparticle system, theranostic nanoparticles offer a synergistic approach to personalized medicine, enabling tailored treatment strategies and improved patient outcomes [73].

B. Challenges and Limitations in the Field

1. Biocompatibility and Toxicity: Despite their biocompatible nature, silica nanoparticles may still induce cytotoxicity or immunogenicity depending on

their size, surface charge, and surface functionalization. Addressing concerns related to biocompatibility and toxicity is essential to ensure the safety and efficacy of silica-based nanocarriers in clinical applications[74].

- 2. Scalability and Manufacturing: The scalability and reproducibility of silica nanoparticle synthesis remain significant challenges for translation to large-scale manufacturing. Developing scalable and cost-effective synthesis methods while maintaining control over particle size, morphology, and surface properties is crucial for the widespread adoption of silica-based nanocarriers in clinical practice[75].
- 3. In Vivo Behavior and Biodistribution: Understanding the in vivo behavior and biodistribution of silica-based nanocarriers is essential for predicting their pharmacokinetics, bioavailability, and therapeutic efficacy. Further research is needed to elucidate the mechanisms of nanoparticle clearance, metabolism, and tissue distribution to optimize nanoparticle design and improve therapeutic outcomes[76].

C. Future Directions for Research and Development

- 1. Targeted Drug Delivery: Future research should focus on developing targeted drug delivery strategies using silica-based nanocarriers for specific diseases and pathological conditions. By engineering nanocarriers with targeting ligands that selectively bind to diseased cells or tissues, researchers can enhance drug accumulation and therapeutic efficacy while minimizing off-target effects[77,77].
- 2. Personalized Medicine: Personalized medicine approaches, including patient-specific drug formulations and treatment regimens, hold promise for improving treatment outcomes and minimizing adverse effects[78]. By leveraging the versatility of silica-based nanocarriers, researchers can develop personalized drug delivery systems tailored to individual patient needs, optimizing treatment efficacy and patient satisfaction[79,80].
- 3. Clinical Translation: Accelerating the clinical translation of silica-based nanocarriers from bench to bedside requires interdisciplinary collaboration between researchers, clinicians, regulatory agencies, and industry

www.jchr.org

JCHR (2024) 14(2), 3624-3636 | ISSN:2251-6727



partners[81]. Addressing regulatory requirements, safety concerns, and manufacturing challenges is essential for advancing silica-based nanocarriers from preclinical studies to clinical trials and eventual commercialization[82,83].

Conclusion

Silica-based nanocarriers represent a versatile and promising platform for controlled drug delivery, imaging, and theranostics in biomedical applications. With their tunable properties, including size, surface and stimuli responsiveness, chemistry, nanoparticles offer tailored solutions for targeted therapy, enhanced imaging sensitivity, and personalized medicine approaches. Recent advances in silica-based nanocarrier research have led to the development of multifunctional platforms capable of integrating imaging agents, therapeutic drugs, and targeting ligands, enabling simultaneous diagnosis and treatment diseases. However, challenges biocompatibility, scalability, and clinical translation remain to be addressed to realize the full potential of silica-based nanocarriers in clinical practice. By fostering interdisciplinary collaboration, addressing safety concerns, and advancing manufacturing techniques, silica-based nanocarriers hold promise for revolutionizing drug delivery and imaging technologies, ultimately improving patient outcomes and advancing the field of precision medicine. Continued research and innovation in this area are essential for overcoming current limitations and unlocking the transformative potential of silica-based nanocarriers in biomedicine.

Conflict of interest

None

References

- H. Ow, D. R. Larson, M. Srivastava, B. A. Baird, W. W. Webb, and U. Wiesner, "Bright and stable core-shell fluorescent silica nanoparticles," Nano Lett., vol. 5, pp. 113–117, 2005.
- Q. He, J. Shi, M. Zhu, Y. Chen, and F. Chen, "The three-stage in vitro degradation behavior of mesoporous silica in simulated body fluid," Microporous Mesoporous Mater., vol. 131, pp. 314– 320, 2010.

- 3. T. Liu, L. Li, X. Teng, X. Huang, H. Liu, and D. Chen, "Single and repeated dose toxicity of mesoporous hollow silica nanoparticles in intravenously exposed mice," Biomaterials, vol. 32, pp. 1657–1668, 2011.
- 4. C. Fu, T. Liu, L. Li, H. Liu, D. Chen, and F. Tang, "The absorption, distribution, excretion and toxicity of mesoporous silica nanoparticles in mice following different exposure routes," Biomaterials, vol. 34, pp. 2565–2575, 2013.
- P. Zhao, H. Jiang, T. Jiang, Z. Zhi, C. Wu, and C. Sun, "Inclusion of celecoxib into fibrous ordered mesoporous carbon for enhanced oral bioavailability and reduced gastric irritancy," Eur. J. Pharm. Sci., vol. 45, pp. 639–647, 2012.
- Y. Zhang, T. Jiang, Q. Zhang, and S. Wang, "Inclusion of telmisartan in mesocellular foam nanoparticles: drug loading and release property," Eur. J. Pharm. Biopharm., vol. 76, pp. 17–23, 2010.
- E. J. Hong, D. G. Choi, and M. S. Shim, "Targeted and effective photodynamic therapy for cancer using functionalized nanomaterials," Acta Pharm. Sin. B, vol. 6, pp. 297–307, 2016.
- 8. Q. Zhao, T. Wang, J. Wang, L. Zheng, T. Jiang, and G. Cheng, "Fabrication of mesoporous hydroxycarbonate apatite for oral delivery of poorly water-soluble drug carvedilol," J. Non Cryst. Solids, vol. 358, pp. 229–235, 2012.
- 9. W. Xu, J. Riikonen, and V. P. Lehto, "Mesoporous systems for poorly soluble drugs," Int. J. Pharm., vol. 453, pp. 181–197, 2013.
- 10. L. Jia, J. Shen, Z. Li, D. Zhang, Q. Zhang, and C. Duan, "Successfully tailoring the pore size of mesoporous
- 11. silica nanoparticles: exploitation of delivery systems for poorly water-soluble drugs," Int. J. Pharm., vol. 439, pp. 81–91, 2012.
- 12. W. Zhu, L. Wan, C. Zhang, Y. Gao, X. Zheng, and T. Jiang, "Exploitation of 3D face-centered cubic mesoporous silica as a carrier for a poorly watersoluble drug: influence of pore size on release rate," Mater. Sci. Eng. C, vol. 34, pp. 78–85, 2014.
- 13. E. Ahmadi, N. Dehghannejad, S. Hashemikia, M. Ghasemnejad, and H. Tabebordbar, "Synthesis and surface modification of mesoporous silica nanoparticles and its application as carriers for sustained drug delivery," Drug Deliv., vol. 21, pp. 164–172, 2014.

www.jchr.org



- 14. H. Geng, Y. Zhao, J. Liu, Y. Cui, Y. Wang, and Q. Zhao, "Hollow mesoporous silica as a high drug loading carrier for regulation insoluble drug release," Int. J. Pharm., vol. 510, pp. 184–194, 2016.
- 15. B. Chen, Z. Wang, G. Quan, X. Peng, X. Pan, and R. Wang, "In vitro and in vivo evaluation of ordered mesoporous silica as a novel adsorbent in liquisolid formulation," Int. J. Nanomed., vol. 7, pp. 199–209, 2012.
- 16. L. Hu, H. Sun, Q. Zhao, N. Han, L. Bai, and Y. Wang, "Multilayer encapsulated mesoporous silica nanospheres as an oral sustained drug delivery system for the poorly water-soluble drug felodipine," Mater. Sci. Eng. C, vol. 47, pp. 313–324, 2015.
- 17. Z. Wang, B. Chen, G. Quan, F. Li, Q. Wu, and L. Dian, "Increasing the oral bioavailability of poorly water-soluble carbamazepine using immediate-release pellets supported on SBA-15 mesoporous silica," Int. J. Nanomed., vol. 7, pp. 5807–5818, 2012.
- 18. Y. Hu, X. Dong, L. Ke, S. Zhang, D. Zhao, and H. Chen, "Polysaccharides/mesoporous silica nanoparticles hybrid composite hydrogel beads for sustained drug delivery," J. Mater. Sci., vol. 52, pp. 3095–3109, 2017.
- 19. H. Maeda, J. Wu, T. Sawa, Y. Matsumura, and K. Hori, "Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review," J. Control. Release, vol. 65, pp. 271–284, 2000.
- K. Xiao, J. Luo, W. L. Fowler, Y. Li, J. S. Lee, and L. Xing, "A self-assembling nanoparticle for paclitaxel delivery in ovarian cancer," Biomaterials, vol. 30, pp. 6006–6016, 2009.
- 21. D. Ren, F. Kratz, and S. W. Wang, "Protein nanocapsules containing doxorubicin as a pHresponsive delivery system," Small, vol. 7, pp. 1051–1060, 2011.
- 22. B. M. Dicheva, T. L. ten Hagen, D. Schipper, A. L. Seynhaeve, G. C. Van Rhoon, and A. M. Eggermont, "Targeted and heat-triggered doxorubicin delivery to tumors by dual targeted cationic thermosensitive liposomes," J. Control. Release, vol. 195, pp. 37–48, 2014.
- 23. L. Qiu, M. Qiao, Q. Chen, C. Tian, M. Long, and M. Wang, "Enhanced effect of pH-sensitive mixed copolymer micelles for overcoming multidrug

- resistance of doxorubicin," Biomaterials, vol. 35, pp. 9877–9887, 2014.
- 24. S. Hak, E. Helgesen, H. H. Hektoen, E. M. Huuse, P. A. Jarzyna, and W. J. Mulder, "The effect of nanoparticle polyethylene glycol surface density on ligand-directed tumor targeting studied in vivo by dual modality imaging," ACS Nano, vol. 6, pp. 5648–5658, 2012.
- 25. P. Bhatt, V. Kumar, M. K. Malik, and T. Kumar, "Citrus Flavonoids: Recent Advances and Future Perspectives On Preventing Cardiovascular Diseases," in The Flavonoids, pp. 131-152, 2024.
- 26. P. Bhatt et al., "Functional and tableting properties of alkali-isolated and phosphorylated barnyard millet (Echinochloa esculenta) starch," ACS Omega, vol. 8, no. 33, pp. 30294–305, 2023.
- 27. T. Asefa and Z. Tao, "Biocompatibility of mesoporous silica nanoparticles," Chem. Res. Toxicol., vol. 25, pp. 2265–2284, 2012.
- 28. Y. Gao, Y. Chen, X. Ji, X. He, Q. Yin, and Z. Zhang, "Controlled intracellular release of doxorubicin in multidrug-resistant cancer cells by tuning the shell-pore sizes of mesoporous silica nanoparticles," ACS Nano, vol. 5, pp. 9788–9798, 2011.
- 29. M. Ekkapongpisit, A. Giovia, C. Follo, G. Caputo, and C. Isidoro, "Biocompatibility, endocytosis, and intracellular trafficking of mesoporous silica and polystyrene nanoparticles in ovarian cancer cells: effects of size and surface charge groups," Int. J. Nanomed., vol. 7, pp. 4147–4158, 2012.
- 30. J. L. Vivero-Escoto, I. I. Slowing, B. G. Trewyn, and V. S.-Y. Lin, "Mesoporous silica nanoparticles for intracellular controlled drug delivery," Small, vol. 6, pp. 1952–1967, 2010.
- 31. H. Hillaireau and P. Couvreur, "Nanocarriers' entry into the cell: relevance to drug delivery," Cell. Mol. Life Sci., vol. 66, pp. 2873–2896, 2009.
- 32. P. Bhatt et al., "Development and characterization of fast dissolving buccal strip of frovatriptan succinate monohydrate for buccal delivery," Int J Pharm Investig, vol. 11, no. 1, pp. 69–75, 2021.
- 33. P. Bhatt et al., "Artificial intelligence in pharmaceutical industry: Revolutionizing drug development and delivery," The Chinese Journal of Artificial Intelligence, 2023.
- 34. P. Bhatt, S. Singh, S. K. Sharma, and V. Kumar, "Blockchain technology applications for improving

www.jchr.org



- quality of electronic healthcare system," in Blockchain for Healthcare Systems, pp. 97–113. Boca Raton: CRC Press, 2021.
- 35. Z. X. Li, J. C. Barnes, A. Bosoy, J. F. Stoddart, and J. I. Zink, "Mesoporous silica nanoparticles in biomedical applications," Chem. Soc. Rev., vol. 41, pp. 2590–2605, 2012.
- 36. H. Yang, C. Lou, M. Xu, C. Wu, H. Miyoshi, and Y. Liu, "Investigation of folate-conjugated fluorescent silica nanoparticles for targeting delivery to folate receptor-positive tumors and their internalization mechanism," Int. J. Nanomed., vol. 6, pp. 2023–2032, 2011.
- 37. J. S. Kim, T. J. Yoon, K.N. Yu, M. S. Noh, M. Woo, and B. G. Kim, "Cellular uptake of magnetic nanoparticle is mediated through energy-dependent endocytosis in A549 cells," J. Vet. Sci., vol. 7, pp. 321–326, 2006.
- 38. Q. Liu, J. Zhang, W. Xia, and H. Gu, "Magnetic field enhanced cell uptake efficiency of magnetic silica mesoporous nanoparticles," Nanoscale, vol. 4, pp. 3415–3421, 2012.
- 39. J. Lu, M. Liong, S. Sherman, T. Xia, M. Kovochich, and A. E. Nel, "Mesoporous silica nanoparticles for cancer therapy: energy-dependent cellular uptake and delivery of paclitaxel to cancer cells," Nanobiotechnology, vol. 3, pp. 89–95, 2007.
- 40. T. H. Chung, S. H. Wu, M. Yao, C. W. Lu, Y. S. Lin, and Y. Hung, "The effect of surface charge on the uptake and biological function of mesoporous silica nanoparticles in 3T3-L1 cells and human mesenchymal stem cells," Biomaterials, vol. 28, pp. 2959–2966, 2007.
- 41. C. Morelli, P. Maris, D. Sisci, E. Perrotta, E. Brunelli, and I. Perrotta, "PEG-templated mesoporous silica nanoparticles exclusively target cancer cells," Nanoscale, vol. 3, pp. 3198–3207, 2011.
- 42. Slowing, B. G. Trewyn, and V. S. Lin, "Effect of surface functionalization of MCM-41-type mesoporous silica nanoparticles on the endocytosis by human cancer cells," J. Am. Chem. Soc., vol. 128, pp. 14792–14793, 2006.
- 43. Sarkar, S. Ghosh, S. Chowdhury, B. Pandey, and P. Sil, "Targeted delivery of quercetin loaded mesoporous silica nanoparticles to the breast cancer cells," Biochim. Biophys. Acta, vol. 1860, pp. 2065–2075, 2016.

- 44. Lu, Z. Li, J. I. Zink, and F. Tamanoi, "In vivo tumor suppression efficacy of mesoporous silica nanoparticles-based drug-delivery system: enhanced efficacy by folate modification," Nanomedicine, vol. 8, pp. 212–220, 2012.
- 45. N. Ž. Knežević, J. Mrđanović, I. Borišev, S. Milenković, D. Janaćković, and F. Cunin, "Hydroxylated fullerene-capped, vinblastine-loaded folic acid-functionalized mesoporous silica nanoparticles for targeted anticancer therapy," RSC Adv., vol. 6, pp. 7061–7065, 2016.
- 46. S. Ahamed, P. Bhatt, S. J. Sultanuddin, R. Walia, M. A. Haque, and S. B. InayathAhamed, "An Intelligent IoT enabled Health Care Surveillance using Machine Learning," in 2022 International Conference on Advances in Computing, Communication and Applied Informatics (ACCAI). IEEE, 2022.
- 47. V. Ahmed, S. Sharma, and P. Bhatt, "Formulation and evaluation of sustained release tablet of diltiazem hydrochloride," International Journal of Pharmaceutical Sciences and Research, vol. 11, no. 5, pp. 2193–2198, 2020.
- 48. E. Al-Snafi, S. Singh, P. Bhatt, and V. Kumar, "A review on prescription and non-prescription appetite suppressants and evidence-based method to treat overweight and obesity," GSC biol pharm sci, vol. 19, no. 3, pp. 148–155, 2022.
- 49. Baskar, S. Ramakrishna, and A. Daniela La Rosa, Eds., Encyclopedia of green materials. Singapore: Springer Nature Singapore, 2022.
- 50. P. Bhatt, A. Kumar, and R. Shukla, "Nanorobots recent and future advances in cancer or dentistry therapy- A review," Am J PharmTech Res, vol. 9, no. 3, pp. 321–331, 2019.
- 51. P. Bhatt et al., "Plasma modification techniques for natural polymer-based drug delivery systems," Pharmaceutics, vol. 15, no. 8, p. 2066, 2023.
- 52. P. Bhatt, R. Shukla, and R. Shankar, "Comparative study and in vitro evaluation of sustained release marketed formulation of aceclofenac sustained release tablets," Pharma Science Monitor, vol. 9, no. 2, 2018.
- 53. P. Bhatt, "Mouth Dissolving Tablets Challenges, Preparation Strategies with a Special Emphasis on Losartan Potassium—A Review," World J. Pharm. Pharm. Sci, vol. 7, no. 9, pp. 271-287, 2018.

www.jchr.org



- 54. C. Goyal et al., "Estimation of shelf-life of Balachaturbhadrika syrup containing different sweetening agents," Res J Pharm Technol, pp. 5078–5083, 2022.
- 55. T. Kaur and S. Singh, "Controlled release of bilayered malvidin tablets using 3D printing techniques," J Pharm Res Int, pp. 70–78, 2021.
- 56. M. Kaurav et al., "In-depth analysis of the chemical composition, pharmacological effects, pharmacokinetics, and patent history of mangiferin," Phytomed Plus, vol. 3, no. 2, p. 100445, 2023.
- 57. Kumar, P. Bhatt, and N. Mishra, "Irritable bowel Syndrome with reference of Alosetron Hydrochloride and Excipient profile used in the manufacturing of Alosetron tablet-A review," J Chem Pharm Sci, vol. 12, no. 03, pp. 71–78, 2019.
- 58. M. K. Malik, P. Bhatt, and T. Kumar, "Significance of chemically derivatized starch as drug carrier in developing novel drug delivery devices," Nat Prod J, vol. 12, 2022.
- 59. M. K. Malik et al., "Preclinical safety assessment of chemically cross-linked modified mandua starch: Acute and sub-acute oral toxicity studies in Swiss albino mice," ACS Omega, vol. 7, no. 40, pp. 35506–35514, 2022.
- 60. M. K. Malik et al., "Phosphorylation of alkali extracted mandua starch by STPP/STMP for improving digestion resistibility," ACS Omega, vol. 8, no. 13, pp. 11750–11767, 2023.
- 61. Pankaj, "Anti-cancer cyclodextrin nanocapsules based formulation development for lung chemotherapy," J Pharm Res Int, pp. 54–63, 2021.
- 62. Pankaj, "Cyclodextrin modified block polymer for oral chemotherapy," J Pharm Res Int, pp. 21–29, 2021.
- 63. V. Raghuwanshi et al., "Recent Advances In Nanotechnology For Combating Against Corona Virus Infection," Journal of Pharmaceutical Negative Results, pp. 1811-1820, 2022.
- 64. K. Sahu et al., "Utility of nanomaterials in wound management," in Nanotechnological Aspects for Next-Generation Wound Management, pp. 101–130. Elsevier, 2024.
- 65. S. K. Sharma et al., "Combined therapy with ivermectin and doxycycline can effectively alleviate the cytokine storm of COVID-19 infection amid vaccination drive: A narrative review," J Infect Public Health, vol. 15, no. 5, pp. 566–572, 2022.

- 66. S. K. Sharma and P. Bhatt, "Controlled release of bilayered EGCG tablets using 3D printing techniques," J Pharm Res Int, pp. 5–13, 2021.
- 67. S. K. Sharma and S. Singh, "Antimicrobial Herbal Soap Formulation," Journal of Pharmaceutical Research International, vol. 32, no. 36, pp. 82-88, 2020.
- 68. S. Singh et al., "Cardiovascular comorbidity of COVID-19 disease: A review," WJPMR, vol. 8, no. 4, pp. 216–225, 2022.
- 69. S. Singh et al., "Phytonanotechnology: Enhancing delivery of plant based therapeutics," J Nanomed Nanotechnol, vol. 10, no. 2, pp. 1000685–1000691, 2019.
- 70. S. Singh, P. Bhatt, A. Singh, and T. Kumar, "Nanotechnology Applications in Combating Viral Infections," in Applications of Nanotechnology in Human Health. Boca Raton: CRC Press, 2023.
- 71. S. Singh, P. Bhatt, A. Singh, and T. Kumar, "Polymeric nanoparticles for targeted drug delivery system for cancer therapy: A review," Int J Drug Dev Res, vol. 11, no. 3, pp. 36–48, 2019.
- 72. R. K. Singh et al., "Emerging role of nanotechnology for safe and effective drug delivery," J Pharm Chem Biol Sci, vol. 7, no. 1, pp. 1–11, 2019.
- 73. S. Singh et al., "Polymeric nanoparticles for targeted drug delivery system for cancer therapy: A review," Int J Drug Dev Res, vol. 11, no. 3, pp. 36–48, 2019.
- 74. S. Singh et al., "Phytonanotechnology: Enhancing delivery of plant based therapeutics," J Nanomed Nanotechnol, vol. 10, no. 2, pp. 1000685–1000691, 2019.
- 75. S. Singh et al., "Role of nanotechnology in enhancing the biodegradation of natural and synthetic polymers," in Advances in Polymer Sciences and Technology. Singapore: Springer, 2023.
- 76. R. Walia et al., "Antimicrobial and wound healing potential of hesperidin-chitosan nanoparticles loaded hydrogel system," International Journal of Biological Macromolecules, vol. 149, pp. 291-299, 2020.
- 77. Y. Chen, H. Chen, S. Zhang, F. Chen, L. Zhang, and J. Zhang, "Core/shell structured hollow mesoporous nanocapsules: a potential platform for simultaneous cell imaging and anticancer drug delivery," ACS Nano, vol. 4, pp. 6001–6013, 2010.

www.jchr.org



- 78. M. Ma, H. Chen, Y. Chen, X. Wang, F. Chen, and X. Cui, "Au capped magnetic core/mesoporous silica shell nanoparticles for combined photothermo-/chemo-therapy and multimodal imaging," Biomaterials, vol. 33, pp. 989–998, 2012
- 79. Y. Chen, H. Chen, S. Zhang, F. Chen, L. Zhang, and J. Zhang, "Multifunctional mesoporous nanoellipsoids for biological bimodal imaging and magnetically targeted delivery of anticancer drugs," Adv. Funct. Mater., vol. 21, pp. 270–278, 2011.
- 80. Lu, Z. Li, J. I. Zink, and F. Tamanoi, "Mesoporous silica nanoparticles as a delivery system for hydrophobic anticancer drugs," Small, vol. 3, pp. 1341–1346, 2007.
- 81. Slowing, B. G. Trewyn, and V. S. Lin, "Mesoporous silica nanoparticles for intracellular delivery of membrane-impermeable proteins," J. Am. Chem. Soc., vol. 129, pp. 8845–8849, 2007.
- 82. N. Hao, L. Li, Q. Zhang, X. Huang, X. Meng, and Y. Zhang, "The shape effect of PEGylated mesoporous silica nanoparticles on cellular uptake pathway in Hela cells," Microporous Mesoporous Mater., vol. 162, pp. 14–23, 2012.
- 83. Z. Tao, B. Toms, J. Goodisman, and T. Asefa, "Mesoporous silica microparticles enhance the cytotoxicity of anticancer platinum drugs," ACS Nano, vol. 4, pp. 789–794, 2010.