

Biomedical Applications of Silica (SiO₂) Nanoparticles

Fiorentis E¹, Gatou MA^{1*}, Lagopati N² and Pavlatou EA¹

¹General Chemistry Laboratory, School of Chemical Engineering, National Technical University of Athens, Greece

²Medical School National & Kapodistrian University of Athens, Greece

*Corresponding author: Gatou MA, General Chemistry Laboratory, School of Chemical Engineering, National Technical University of Athens, Zografou, Athens 15780, Greece

ARTICLE INFO

Received: 📅 June 04, 2023

Published: 📅 June 20, 2023

Citation: Fiorentis E, Gatou MA, Lagopati N and Pavlatou EA. Biomedical Applications of Silica (SiO₂) Nanoparticles. Biomed J Sci & Tech Res 51(1)-2023. BJSTR. MS.ID.008057.

ABSTRACT

Silica nanoparticles (SiNPs) are widely utilized in various industries, such as food, synthetic processes, medical diagnosis and drug delivery, owing to their adjustable particle size, extensive surface area and excellent biocompatibility. Numerous studies have explored the biomedical applications of SiNPs, including the customization of their surfaces and structures to target different types of cancers and facilitate disease diagnosis. This mini review encompasses recent research on the biomedical applications of SiNPs, incorporating fundamental discoveries and ongoing exploratory advancements of their research, and particularly their implementation in drug delivery systems for the diagnosis and treatment of various diseases within the human body, holding potential for practical developments in the future.

Keywords: Silica Nanoparticles; Mesoporous Silica; Porous Nanomaterials; Biomedical Applications; Drug Delivery; Therapy; Diagnosis

Abbreviations: NSCLC : Non-Small Cell Lung Cancer; COPD: Chronic Pulmonary Obstructive Disease; MSNs: Mesoporous Silica Nanoparticles; PEG: Polyethylene Glycol; IBD: Inflammatory Bowel Disease; ROS: Reactive Oxygen Species; MSN: Mesoporous Silica Nanoparticles; MI: Myocardial Infarction; MCM41-COOH: Mesoporous Silica Nanoparticles; CNTs: Magnetic Carbon Nanotubes; US: Ultrasound; ICG: Indocyanine Green; PTT: Photothermal Therapy; PL: Photoluminescence; ALI: Acute Lung Injury; SPOI: Superparamagnetic Iron Oxide; IGF: Insulin-Like Growth Factor; SNP: Sodium Nitroprusside; PA: Photoacoustic

Introduction

Silica, also known as silicon dioxide (SiO₂), is the most abundant compound found on the Earth's crust as silicate minerals [1]. The manufacturing of silica nanoparticles (SiNPs) has experienced significant growth, establishing them as the second largest nanomaterial produced globally [2]. SiNPs, as an inorganic material, possess uniform pore size, controllable particle size, large surface area and surface that can be easily modified, due to the presence of Si-OH bonds. Additionally, they exhibit excellent biocompatibility [3]. These characteristics make the inorganic silica skeleton more stable in the face of temperature fluctuations, organic solvents and acidic conditions compared to traditional drug delivery systems [4]. This mini-review article provides an overview of recent research advancements in the biomedical utilization of SiNPs, specifically focusing on their role as

carriers for drugs and auxiliary reagents in diagnostics. The applications of SiNPs as drug carriers are examined within various systems of the human body. Furthermore, the present mini review explores the utilization of SiNPs in medical diagnostics, highlighting their distinct functions.

Biomedical Applications of Silica Nanoparticles

Drug Delivery and Therapy

Respiratory ailments such as lung cancer, acute lung injury (ALI), pneumonia and viral infections are among the primary respiratory diseases [5]. SiNPs have been explored as potential drug carriers for respiratory treatment. Mesoporous silica nanoparticles (M-SiNPs) have been utilized in the creation of an aerosol possessing a water basis, in order to facilitate the delivery of medication through inha-

lation [6]. In a mouse model of airway inflammation [7], M-SiNPs loaded with dexamethasone with PEG-PEI groups demonstrated the potential for drug transfer via inhalation. Researchers [8] have developed versatile and biocompatible drug carriers by incorporating avidin-functionalized M-SiNPs for lung-specific drug delivery. Mesoporous SiNPs loaded siRNA has been also developed [9] to facilitate targeted transportation to alveolar macrophages. In the case of ALI resulting from failure of mitochondria to function normally, (Wang, et al. [10]) synthesized Se@SiNPs with enhanced porosity, possessing antioxidant properties that effectively targeted mitochondria. Among various types of lung cancers, non-small cell lung cancer (NSCLC) stands out as the most prevalent, characterized by a significantly low 5-year survival rate of only 15% [11]. To address this, M-SiNPs loaded with myricetin and conjugated with siRNA and folic acid were employed to target lung cancer cells, effectively inhibiting tumor growth both *in vivo* and *in vitro* (Zhou, et al. [11,12]) reported on the formation of hollow mesoporous silica nanoparticles loaded with erlotinib that presented the ability to form a gel at body's temperature, enabling a sustained drug release for topical therapy of NSCLC.

For damaging lung cancer cell DNA, drugs against cancer, such as doxorubicin and cyclosporin, were encapsulated within photoluminescent QDs@M-SiNPs [13]. Additionally, core-shell SiNPs (< 8 nm), were conjugated with gefitinib-dipeptide drug linkers by (Madajewski, et al. [14]) as carriers for drugs characterized by small molecules, leading to improved drug dosage and effectiveness during the reduction of dose-limiting toxicity. García-Fernández and co-researchers [15] showcased the potential of gated-mesoporous silica nanoparticles (MSNs) as a promising method for delivering glucocorticoids directly to inflamed lungs in ALI conditions. By utilizing the combined passive and active targeting capabilities offered by engineered MSNs, this approach enables precise and targeted drug release while minimizing unwanted side effects. These findings hold promise for the treatment of various severe respiratory conditions such as Chronic Pulmonary Obstructive Disease (COPD), asthma, pulmonary fibrosis, respiratory infectious diseases, and COVID-19, where lung injury plays a crucial role. SiNPs with a size >7 nm predominantly accumulate in the liver, as liver cells have mechanisms to eliminate foreign substances through enzymatic breakdown or excretion into the bile. Engineered SiNPs of sizes equal to 10 nm, as well as 100 nm, have been proved to act as safe carriers for drug and gene delivery [16].

Liver diseases encompass conditions, such as liver cancer, fatty liver, liver cirrhosis and liver fibrosis. M-SiNPs loaded with miR-33 antagonists have been synthesized for specifically targeting liver tissue and addressing lipid metabolic disorders [17], thus resulting in approximately fivefold increased uptake of miR-33 antagonists by hepatocytes. Hollow M-SiNPs encapsulating ammonia borane exhibited sustained release in an acidic environment such as the stomach, leading to indirect reduction of liver fat content and direct modulation of hepatic lipid metabolism for the treatment of fatty liver dis-

ease [18]. Extensive research has been conducted on SiNPs-based delivery systems for liver cancer, which is considered the riskiest and most life-threatening among liver diseases. Novel approaches include the development of Janus gold M-SiNPs functionalized with folic acid for targeted chemo-radiotherapy using prodrugs like tirapazamine or berberine (Lv, et al. [19,20]) employed covalent attachment of co-glycyrrhetic acid to M-SiNPs as a drug loading platform specifically targeting cancer cells (Zhang, et al. [21]). designed SiNPs coated with polyamidoamine-aptamer for dual-controlled release of CRISPR/Cas9 gene therapy and sorafenib drug, enabling accurate gene editing and tumor growth suppression. SiNPs responsive to high glutathione levels in tumor tissue have also been developed. In their study, (Wong, et al. [22]) developed a versatile nanopatform by combining a thiol-activatable photosensitizer based on ZnPc and a doxorubicin (Dox) release system triggered by singlet oxygen within mesoporous silica nanoparticles (MSNs).

This nano-delivery system, which responds to multiple stimuli, offers valuable insights for the advancement of MSN-based drug delivery systems with enhanced control over drug release. Additionally, a novel drug delivery system was developed to enhance the effectiveness of paclitaxel (PTX) in liver cancer therapy. This system involved synthesizing a thiol-terminated polyethylene glycol (PEG)-PTX conjugate and utilizing it to develop a promising drug delivery system with thiol-functionalized SiNPs with high potential for clinical use towards cancer treatment [23]. When it comes to the gastrointestinal tract, SiNPs offer potential solutions to overcome various barriers such as the diverse pH environment and the mucosal layer [24], enabling targeted drug discharge at specific locations. Gastrointestinal disorders primarily affect the intestines and encompass conditions like colitis, microbial imbalances, and colon cancer. By incorporating multiple gating mechanisms, M-SiNPs were designed to respond to different stimuli, and the use of hydrolyzed starch-capped M-SiNPs triggered by pancreatin proved to be a suitable drug delivery system with minimal side effects [25].

To mitigate drug release in the gastric environment which is acidic, Juere and co-researchers [26] combined M-SiNPs with a pH-responsive protein called succinylated β -lactoglobulin (Gao, et al. [27]). modified SiNPs using deoxycholic acid and coated their surfaces with sulfobetaine 12, for effectively preventing lysosomal entry and enhancing drug absorption throughout the intestinal segments. In their study, (Nguyen, et al. [28]) demonstrated that by applying SPL polymer to cargo-loaded-mesoporous silica nanoparticles, the release of drugs could be controlled in response to the pH conditions mimicking the colon. Moreover, the coated MSNs exhibited superior delivery of drugs into RAW 264.7 macrophages and LS 174T cells, compared to mesoporous silica nanoparticles without the coating. These findings present promising prospects for utilizing SPL-coated nanoparticles in the targeted delivery of drugs, especially those with limited ability to permeate cell membranes, to macrophages and colorectal cancer

cells, leading potentially to enhanced treatment approaches for inflammatory bowel disease (IBD) and colorectal cancer. Furthermore, Cheng and co-researchers [29], proposed an innovative approach for delivering drugs, involving the self-assembly of Trp-CS, previously complexed with CB[8] and Azo-HA on the surface of M-SiNPs. This system offered a combined strategy for targeting the gut microbiota in the treatment of IBD. Moreover, a novel silica-based redox nanocarrier loaded with a hydrophobic anti-inflammatory drug (silymarin) exhibited anti-inflammatory effects through reactive oxygen species (ROS) scavenging [30].

Cardiovascular diseases, being the leading factor of global mortality, encompass conditions, such as myocardial ischemia-reperfusion injury, myocardial infarction and heart failure [31]. Mesenchymal stem cells have emerged as a promising therapeutic approach for heart diseases because of their ability to engage endogenous stem cells and release paracrine factors that enhance cell proliferation [32]. Leveraging this characteristic, Chen et al. synthesized a superparamagnetic mesocellular foam SiO₂@Fe₃O₄ nanoparticle using an in-situ growth approach. The incorporation of superparamagnetic iron oxide (SPIO) improved the colloidal stability, zeta-potential, magnetization and sustained release behavior for insulin-like growth factor (IGF) of the nanoparticles [32]. The therapeutic effects of stem cells are predominantly mediated by the secretion of exosomes, which play a crucial role in angiogenesis and have potential for myocardial infarction treatment. However, the practical application of exosomes is limited by their reduced yield and complex purification procedure [33]. To overcome these challenges, Yao et al. developed a novel delivery system for miRNA, utilizing a self-assembled nanocomplex that mimics exosomes and is camouflaged with a stem cell membrane. This nanocomplex, based on mesoporous silica, exhibited an increased capacity for miRNA and provided effective protection for miRNA in biological fluids [34].

M-SiNPs have been utilized to enhance the therapeutic efficacy as a therapeutic approach for myocardial ischemia and inflammation by improving the availability of curcumin, leading to a cardio-protective effect [35]. In the case of chronic heart failure, which is characterized by elevated levels of reactive oxygen species in the heart, a diagnostic molecule (FL2) capable of sensing hydrogen peroxide (H₂O₂) was incorporated onto captopril-loaded M-SiNPs to enable targeted drug delivery [36]. Endothelial cell dysfunction is closely associated with cardiovascular diseases (Farooq, et al. [37]). investigated the application of titania coating on a vascular function model to enhance the compatibility and controlled release of sodium nitroprusside (SNP) loaded into mesoporous silica nanoparticles (MSN). They proposed that the utilization of titania-coated MSNs for delivering drugs to the blood vessels could be a promising approach for effective clinical treatment of cardiovascular disorders. Additionally, also in 2018, Tsao and co-researchers indicated that the internalization of PLGA [poly(DL-lactide-co-glycolide)]-pSi (porous silica nanoparticles)

within neonatal cardiac cells can trigger apoptotic signaling effects and facilitate the development of new blood vessels in cardiomyocytes [38]. Additionally, (Pikwong, et al. [39]) presented a novel approach by developing GSNPs (Graphene Oxide-Based Silica Nanoparticles) to encapsulate rhSLPI (recombinant human Secretory Leukocyte Protease Inhibitor), which demonstrated no cardiac cell toxicity and effectively reduced cardiac cell death and injury in an in vitro simulated ischemia/reperfusion (sI/R) model. These findings offer valuable insights for future investigations in pre-clinical animal models, with potential implications for the treatment of ischemic heart disease. (Li, et al. [40]) successfully prepared mesoporous silica nanoparticles (MSNs) conjugated with CD11b antibody and loaded with NGR1.

These MSN-NGR1-CD11b antibody nanoparticles exhibited enhanced targeting of NGR1 to the site of myocardial infarction (MI) upon administration. NGR1 effectively protected H9C2 cells and primary cardiomyocytes from oxidative stress injury induced by H₂O₂ and OGD. Moreover, the MSN-NGR1-CD11b antibody nanoparticles mitigated localized inflammation and stimulated angiogenesis in the damaged myocardium, resulting in enhanced cardiac function after MI. These effects were achieved by enhancing the activation of AKT and MAPK signaling pathways, as well as the nuclear translocation of YAP. The aforementioned study introduced a novel approach for myocardial-targeted drug delivery using MSNs, and offers new research avenues for exploring other biomaterials with myocardium-targeting capabilities. According to (Wang, et al. [41]). Quercetin's therapeutic effectiveness through oral administration appears to be limited in achieving the desired therapeutic concentration in cardiac tissues. This highlights the need for improved formulations that can provide sustained release, offering advantages such as extended quercetin release to the cardiac region and reducing the frequency of injections required. In this study, we have developed PLGA-coated superparamagnetic nano-silica as a means to control drug release behavior from the nanobiocarriers. The SiN@QC-PLGA nanobiocomposite demonstrates enhanced properties that closely resemble those of native myocardium, allowing for cell activation, attachment, proliferation, and expression of heart proteins. Consequently, this type of antioxidant quercetin delivery system holds potential for use in the prevention of atherosclerosis and other similar cardiovascular diseases.

Medical Diagnosis

Silica nanoparticles have emerged as potent carriers for drug delivery and imaging contrast agents [42], offering valuable insights into disease state and progression. Extensive research has focused on functionalized fluorescent SiNPs for imaging applications. For instance, fluorescently-labeled mesoporous silica nanoparticles that specifically target polyps in the colon could function as contrast agents for endoscopic imaging, aiming to facilitate the early detection of colorectal polyps and cancer [43]. Fluorescent M-SiNPs with embedded PEGylated MoS₂ have been also effectively synthesized using

a simple method, resulting in stable nanoparticles. The nanoparticles exhibited remarkable targeted fluorescent bioimaging capabilities and demonstrated an effective photothermal effect against MDA-MB-231 cancer cells [44]. Also, fluorescent silica nanoparticles with specific functionalization were developed and prepared to exclusively target cancer cells for bioimaging assessment. The surface of the nanoparticles was additionally modified with a 2000 Da PEG layer and folic acid to ensure excellent water stability and improve the selectivity towards cancer cells, respectively [45]. During cancer cell metastasis, tumor cells interact with bone components, including inorganic minerals, which may lead to bone mineralization (Chiou et al. [46]). presented the advancement of a cell labeling method utilizing fluorescent SiNPs. This technique enabled the simultaneous imaging of cells, bone marrow and mineralized matrix for both *in vitro* and *in vivo* investigations. (Estevão, et al. [47]) successfully prepared and utilized hybrid nanoparticles consisting of Ir complexes incorporated into mesoporous silica nanoparticles (MCM41-COOH) for the purpose of photodynamic therapy in liver cancer cells.

Our findings demonstrated effective encapsulation of the Ir complexes within the MCM41@COOH nanoparticles, with encapsulation efficiencies exceeding 30%. The functionalized nanoparticles exhibited significant production of singlet oxygen upon light irradiation. In cellular assays, these nanoparticles demonstrated low toxicity towards both healthy and cancerous cell strains in the absence of light, while exhibiting potent photodynamic effects when exposed to light, with short illumination times and low nanoparticle concentrations. Magnetic nanoparticles have applications in both *in vivo* and *in vitro* imaging. The creation of an innovative hybrid nanomaterial, magnetic carbon nanotubes (CNTs) coated with M-SiNPs and presenting enhanced loading capacity of therapeutic molecules has been reported by (Singh, et al. [48]). This nanomaterial served dual purposes of drug delivery and imaging. Through the use of magnetism, the hybrid nanocarriers demonstrated a significant uptake by cells and exhibited positive biological effects. The potential applications of this unique multifunctional nanocarrier lie in drug delivery and imaging systems [48]. Within their study, (Rao, et al. [49]). created a type of mesoporous silica nanoparticles called reactive oxygen species (ROS)-responsive MSNs (RMSNs). These RMSNs were designed with a gadolinium (Gd)-DOTA complex acting as the ROS-responsive gatekeeper and polyethylene glycol (PEG)-conjugated chlorin e6 serving as the ROS generator.

The purpose of these nanoparticles was to combine magnetic resonance (MR) imaging with photodynamic chemotherapy, allowing for guided treatment. In order to address concerns regarding the toxicity of gadolinium-based contrast agents, Fe@FeO_x nanoparticles have been explored as a viable alternative [50]. For highly sensitive MRI, (Yuan, et al. [51]) designed mesoporous silica nanoparticles coated with liquid Perflubron as hosts for ¹²⁹Xe, enabling precise targeting of lung cancer cells and allowing imaging after surface alteration with

the peptide sequence RGD. Ultrasound constitutes a low-cost and safe real-time imaging technique widely used in operating rooms given its excellent spatial and temporal resolution [52]. In a study by (Lieberman, et al. [53]), iron-coated SiNPs filled with perfluoropentane gas were functionalized with diethylenetriaminepentaacetic acid to enable tumor identification and biodistribution analysis. To enhance hydrophobicity, the researchers covalently attached perfluorodecyltriethoxysilane, known for its low surface energy and superhydrophobic properties, to the surface of SiNPs that were coated with β -cyclodextrin. These modified particles were utilized for combined antivasular and chemo-sonodynamic therapy [54]. Montoya et al. in 2020, devised a new approach for producing innovative GSNs (F127-hMSNs) that combine small particle size with high responsiveness to ultrasound (US). The F127-hMSNs were created by modifying hydrophobic ~50 nm MSNs with a biocompatible amphiphilic copolymer called Pluronic F127. They achieved continuous ultrasound imaging for up to 20 minutes, thus anticipating that the GSNs developed within their study could find various applications in clinical settings, such as molecular US imaging of solid tumors, drug delivery and cancer treatment [52].

SiNPs have the potential to serve as radiosensitizers during radiolabeled imaging applications. Innovative radioactive labels can be employed to monitor the spread, degradation and eradication of silica nanoparticles *in vivo*. In a study by (Bindini, et al. [55]), zirconium-89 (⁸⁹Zr) was used to label both the dense core and mesoporous shell of core-shell silica nanoparticles, demonstrating stable biodistribution over a period of 6 hours. In another approach, (Chen, et al. [56]) utilized ⁸⁹Zr to label the oxygen donors of deprotonated silanol groups on the surface of silica nanoparticles (Portilho, et al. [57]). reported that doped with dacarbazine and labeled with technetium 99 metastable, magnetic core M-SiNPs, demonstrated their effectiveness and dependability as a nano-imaging agent for melanoma. Furthermore, (Detappe, et al. [58]) have introduced a new SiBiGdNP, which served as a contrast agent for dual-modality imaging (MR and CT), as well as clinical radiation dose amplification. The incorporation of Gd atoms provided positive contrast enhancement for MR imaging, while the inclusion of both Gd and Bi atoms enabled CT imaging contrast. The SiBiGdNP synthesis involved a top-down approach using a silica structure carrying DOTA-Gd, which has been proved to be safe for routine intravenous administration, enabling on-site radiosensitization and enhancing image contrast for the detection of lung cancer.

Photoacoustic (PA) imaging comprises a hybrid imaging technique that utilizes both light and sound to generate images. It involves the use of short NIR laser pulses to stimulate thermoacoustic waves within a tissue containing chromophores based on nanoparticles [59]. In a study by (Chaudhary, et al. [59]), two contrast agents were developed using indocyanine green (ICG) loaded into magnetic silica nanoparticles (M-SiNPs). One agent utilized amine-modified M-SiNPs, while the other employed layer-by-layer polyelectrolyte

coatings on ICG-M-SiNPs. Both agents exhibited enhanced PA signals compared to pure ICG. (Shao, et al. [60]) developed rattle-structured polydopamine@mesoporous silica nanoparticles for *in vivo* applications in photoacoustic (PA) imaging and enhanced low-temperature Photothermal Therapy (PTT). These nanoparticles were designed to achieve complementary effects by inhibiting autophagy and altering glucose metabolism, thereby improving the effectiveness of the therapy. For the diagnosis of liver diseases [61], Lee et al. developed a PA contrast agent known as HA-SiNP conjugates to enhance the PA imaging contrast specifically in the liver. The feasibility of these HA-SiNP conjugates as a liver-targeted and biocompatible PA contrast agent was successfully demonstrated.

In future investigations, HA-SiNP conjugates could be utilized for liver-targeted drug delivery, cirrhosis targeting, and liver cancer targeting and therapy, utilizing the numerous HA receptors such as CD44 and HA receptor for endocytosis. Therefore, they demonstrated that the light-absorbing HA-SiNP conjugates hold significant promise as a liver-targeted PA imaging contrast agent and liver-targeted drug transfer agent. To achieve personalized medicine, researchers have developed multifunctional nanoprobes that combine fluorescent and magnetic imaging capabilities (Cheng et al. [62]). successfully synthesized a dual-modal bioimaging nanoprobe for targeted photoluminescence (PL) and magnetic resonance (MR) imaging. This nanoprobe was created by conjugating iridium(III) complexes, gadolinium(III), and RGD peptide onto SiNPs. In comparison to the Ir@SiO₂-Gd NPs, the Ir@SiO₂-Gd-RGD NPs demonstrated significantly improved brightness in photoluminescence and enhanced MR signal specifically at the tumor site. Their findings highlighted the considerable potential of the Ir@SiO₂-Gd-RGD NPs for future applications in cancer diagnosis and treatment. (He, et al. [63]) presented a new approach for synthesizing Gd³⁺-loaded red fluorescent mesoporous silica nanoparticles (MSNs).

This involved directly encapsulating an AIEgen (TPATBT) and subsequently loading Gd³⁺ using APTES. In comparison to commonly reported blue-green fluorescent nanoparticles, the red fluorescence exhibited by these nanoparticles enabled better tissue penetration while minimizing phototoxicity and interference from autofluorescence. Their study offered an alternative strategy for designing and fabricating highly efficient fluorescent nanoparticles that can serve as MR imaging probes. Similarly, according to (Tsou, et al. [64]), an eco-friendly drug delivery system utilizing rMSNEuGd@Fucoidan has been effectively synthesized. This material incorporated two imaging metals, Eu³⁺ and Gd³⁺ into SiNPs to confer dual-imaging capabilities to the system. (Wu, et al. [65]) attached nucleus-penetrating peptide and hyaluronic acid to SiNPs to enable dual imaging and targeting functions for prostate cancer depiction. In another study by (Du, et al. [66]), the antibody specific to prostate-specific membrane antigen and Cy7, a fluorescent substance, were conjugated with Mn2O@M-SiNPs for tumor detection (Ovejero-Paredes, et al. [67]). underscored

the significant potential of our fibrous SiO₂-based nanoplatform as a theranostic agent for breast cancer in mouse models. Through the inclusion of the targeting moiety folic acid, the produced nanomaterials exhibit selective accumulation inside the tumor's region following systemic administration, demonstrating their drug targeting ability. Additionally, the incorporation of the NIRF dye enables facile visualization and *in vivo* fluorescence imaging, facilitating diagnostic activities. Furthermore, the synergistic effect of chlorambucil and tin-based metallodrug contributes to an enhanced therapeutic efficacy against human breast adenocarcinoma, thereby showcasing the multitiered capabilities of the nanoplatform. In addition, according to (Esmaeili, et al. [68]) based on the obtained results, the MCM@CS@Au-Apt(CUR) nanosystem demonstrates potential as a cancer nanotheranostics platform for pH-dependent fluorescence imaging and targeted delivery of curcumin to specific cells. Specifically, when MUC-1 positive tumor cells are present, the aptamer conjugated to the nanosystem exhibits high-affinity binding to its target, resulting in the formation of an aptamer-target complex. Consequently, the double strands of DNA aptamer are separated, resulting in a slight fluorescence signal because of the limited affinity of mononucleotides to MCM@CS@Au. Through alterations monitoring in the fluorescence intensity, the progress of targeted drug transfer can be tracked.

Conclusion

Silica nanoparticles (SiNPs), given their favorable physical and chemical properties, have gained significant attention as drug delivery systems, as well as both reagents and carriers in medical diagnostics. Their ability to target specific organs and release drugs or therapeutic agents has been explored extensively in various human systems with physical barriers. While the majority of SiNP research in drug delivery has focused on cancer targeting, this review also highlights their potential in addressing other diseases across different human body systems. In the realm of medical diagnosis, SiNPs exhibit five distinct types of physical imaging reactions, and recent advancements in SiNP research have been summarized. SiNPs have arisen as a promising biomedical platform, revolutionizing disease treatment and diagnosis. However, there is still a considerable journey ahead for clinical translation and commercialization of SiNPs, which will rely on the evolution of standardized and unified methods for the biological evaluation of nanoplatforms.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Diab R, Canilho N, Pavel IA, Haffner FB, Girardon M, et al. (2017) Silica-based systems for oral delivery of drugs, macromolecules and cells. *Advances in Colloid and Interface Science* 249: 346-362.
2. Hsu SY, Morris R, Cheng F (2021) Signaling pathways regulated by silica nanoparticles. *Molecules* 26(5): 1398.

3. Mallick T, Karmakar A, Bag I, Sahu, Mishra M, et al. (2020) Carbazole analog anchored fluorescent silica nanoparticle showing enhanced biocompatibility and selective sensing ability towards biomacromolecule. *Dyes and Pigments* 173: 107994.
4. Florek J, Caillard R, Kleitz F (2017) Evaluation of mesoporous silica nanoparticles for oral drug delivery - current status and perspective of MSNs drug carriers. *Nanoscale* 9(40): 15252-15277.
5. García-Fernández A, Sancenon F, Martinez Manez R (2021) Mesoporous silica nanoparticles for pulmonary drug delivery. *Advanced Drug Delivery Reviews* 177: 113953.
6. Li X, Xue M, Raabe OG, Aaron HL, Eisen EA, et al. (2015) Aerosol drop-let delivery of mesoporous silica nanoparticles: a strategy for respiratory-based therapeutics. *Nanomedicine* 11(6): 1377-1385.
7. Gulin-Sarfraz T, Jonasson S, Wigenstam E, von Haartman E, Bucht A, et al. (2019) Feasibility study of mesoporous silica particles for pulmonary drug delivery: therapeutic treatment with dexamethasone in a mouse model of airway inflammation. *Pharmaceutics* 11(4): 149.
8. van Rijt SH, Bolukbas DA, Argyo C, Wipplinger K, Naureen M, et al. (2016) Applicability of avidin protein coated mesoporous silica nanoparticles as drug carriers in the lung. *Nanoscale* 8(15): 8058-8069.
9. Fischer T, Winter I, Drumm R, Schneider M (2021) Cylindrical microparticles composed of mesoporous silica nanoparticles for the targeted delivery of a small molecule and a macromolecular drug to the lungs: exemplified with curcumin and siRNA. *Pharmaceutics* 13(6): 844.
10. Wang M, Wang K, Deng G, Liu X, Wu X, et al. (2020) Mitochondria-modulating porous Se@SiO₂ nanoparticles provide resistance to oxidative injury in airway epithelial cells: implications for acute lung injury. *International Journal of Nanomedicine* 15: 2287-2302.
11. Song Y, Zhou B, Du X, Wang Y, Zhang J, et al. (2020) Folic acid (FA)-conjugated mesoporous silica nanoparticles combined with MRP-1 siRNA improves the suppressive effects of myricetin on non-small cell lung cancer (NSCLC). *Biomedicine & Pharmacotherapy* 125: 109561.
12. Zhou X, He X, Shi K, Yuan L, Yang Y, et al. (2020) Injectable thermosensitive hydrogel containing erlotinib-loaded hollow mesoporous silica nanoparticles as a localized drug delivery system for NSCLC therapy. *Advanced Science* 7(23): 2001442.
13. Chen F, Zhang H, Jiang L, Wei W, Liu C, et al. (2019) Enhancing the cytotoxic efficacy of combined effect of doxorubicin and Cyclosporin encapsulated photoluminescent graphene dotted mesoporous nanoparticles against lung cancer cell-specific drug targeting for the nursing care of cancer patients. *Journal of Photochemistry and Photobiology B: Biology* 198: 111578.
14. He J, Gong C, Qin J, Li M, Huang S (2019) Cancer cell membrane decorated silica nanoparticle loaded with miR495 and doxorubicin to overcome drug resistance for effective lung cancer therapy. *Nanoscale Research Letters* 14(1): 339.
15. García Fernández A, Sancho M, Bisbal V, Amorós P, Marcos MD, et al. (2021) Targeted-lung delivery of dexamethasone using gated mesoporous silica nanoparticles. A new therapeutic approach for acute lung injury treatment. *Journal of Controlled Release* 10(337): 14-26.
16. Tuncel O, Kahraman E, Bagci G, Atabey N, Ozelik S (2021) Engineered silica nanoparticles are biologically safe vehicles to deliver drugs or genes to liver cells. *Materials Science and Engineering: C* 119: 111585.
17. Tao Y, Xu S, Wang J, Xu L, Zhang C, et al. (2020) Delivery of microRNA-33 antagomirs by mesoporous silica nanoparticles to ameliorate lipid metabolic disorders. *Frontiers in Pharmacology* 11: 921.
18. Jin Z, Sun Y, Yang T, Tan L, Lv P, et al. (2021) Nanocapsule-mediated sustained H2 release in the gut ameliorates metabolic dysfunction-associated fatty liver disease. *Biomaterials* 276: 121030.
19. Wang Z, Chang ZM, Shao D, Zhang F, Chen F, et al. (2019) Janus gold triangle-mesoporous silica nanoplatforams for hypoxia-activated radio-chemo-photothermal therapy of liver cancer. *ACS Applied Materials & Interfaces* 11(38): 34755-34765.
20. Lv Y, Li J, Chen H, Bai Y, Zhang L (2017) Glycyrrhetic acid-functionalized mesoporous silica nanoparticles as hepatocellular carcinoma-targeted drug carrier. *International Journal of Nanomedicine* 12: 4361-4370.
21. Zhang BC, Luo BY, Zou JJ, Wu PY, Jiang LJ, et al. (2020) Co-delivery of sorafenib and CRISPR/Cas9 based on targeted core-shell hollow mesoporous organosilica nanoparticles for synergistic HCC therapy. *ACS Applied Materials & Interfaces* 12(51): 57362-57372.
22. Wong RCH, Ng DKP, Fong WP, Lo PC (2020) Glutathione- and light-controlled generation of singlet oxygen for triggering drug release in mesoporous silica nanoparticles. *Journal of Materials Chemistry B* 8: 4460-4468.
23. Xia Q, Li L, Zhao L (2017) Silica nanoparticle-based dual-responsive nanoprodug system for liver cancer therapy. *Experimental and Therapeutic Medicine* 14(3): 2071-2077.
24. Wang Y, Zhao Y, Cui Y, Zhao Q, Zhang Q, et al. (2018) Overcoming multiple gastrointestinal barriers by bilayer modified hollow mesoporous silica nanocarriers. *Acta Biomaterialia* 65: 405-416.
25. Gonzalez Alvarez M, Coll C, Gonzalez-Alvarez I, Gimenez C, Aznar E, et al. (2017) Gated mesoporous silica nanocarriers for a "two-step" targeted system to colonic tissue. *Molecular Pharmaceutics* 14(12): 4442-4453.
26. Juere E, Del Favero G, Masse F, Marko D, Popat A, et al. (2020) Gastro-protective protein-silica nanoparticles formulation for oral drug delivery: *In vitro* release, cytotoxicity and mitochondrial activity. *European Journal of Pharmaceutics and Biopharmaceutics* 151: 171-180.
27. Gao Y, He Y, Zhang H, Zhang Y, Gao T, et al. (2021) Zwitterion-functionalized mesoporous silica nanoparticles for enhancing oral delivery of protein drugs by overcoming multiple gastrointestinal barriers. *Journal of Colloid and Interface Science* 582(A): 364-375.
28. Nguyen CTH, Webb RI, Lambert LK, Strounina E, Lee EC, et al. (2017) Bi-functional succinylated ε-polylysine-coated mesoporous silica nanoparticles for pH-responsive and intracellular drug delivery targeting the colon. *ACS Applied Materials & Interfaces* 9(11): 9470-9483.
29. Cheng S, Shen H, Zhao S, Zhang Y, Xu H, et al. (2020) Orally administered mesoporous silica capped with the cucurbit[8]uril complex to combat colitis and improve intestinal homeostasis by targeting the gut microbiota. *Nanoscale* 12: 15348-15363.
30. Nguyen TT, Trinh NT, Tran HN, Tran HT, Le PQ, et al. (2021) Improving silymarin oral bioavailability using silica-installed redox nanoparticle to suppress inflammatory bowel disease. *Journal of Controlled Release* 331: 515-524.
31. Liu CJ, Yao L, Hu YM, Zhao BT (2021) Effect of quercetin-loaded mesoporous silica nanoparticles on myocardial ischemia-reperfusion injury in rats and its mechanism. *International Journal of Nanomedicine* 16: 741-752.
32. Chen F, Ruike Zhao E, Hableel G, Hu T, Kim T, et al. (2019) Increasing the efficacy of stem cell therapy via triple-function inorganic nanoparticles. *ACS Nano* 13(6): 6605-6617.
33. Liu B, Lee BW, Nakanishi K, Villasante A, Williamson R, et al. (2018) Cardi-

- ac recovery via extended cell-free delivery of extracellular vesicles secreted by cardiomyocytes derived from induced pluripotent stem cells. *Nature Biomedical Engineering* 2(5): 293-303.
34. Yao C, Wu W, Tang H, Jia X, Tang J, et al. (2020) Self-assembly of stem cell membrane-camouflaged nanocomplex for microRNA-mediated repair of myocardial infarction injury. *Biomaterials* 257: 120256.
35. Yadav YC, Pattnaik S, Swain K (2019) Curcumin loaded mesoporous silica nanoparticles: assessment of bioavailability and cardioprotective effect. *Drug Development and Industrial Pharmacy* 45(12): 1889-1895.
36. Tan SY, The C, Ang CY, Li M, Li P, et al. (2017) Responsive mesoporous silica nanoparticles for sensing of hydrogen peroxide and simultaneous treatment toward heart failure. *Nanoscale* 9(6): 2253-2261.
37. Farooq A, Shukur A, Astley C, Tosheva L, Kelly P, et al. (2018) Titania coating of mesoporous silica nanoparticles for improved biocompatibility and drug release within blood vessels. *Acta Biomaterialia* 76: 208-216.
38. Tsao CJ, Pandolfi L, Wang X, Minardi S, Lupo C, et al. (2018) Electrospun patch functionalized with nanoparticles allows for spatiotemporal release of VEGF and PDGF-BB promoting *in vivo* neovascularization. *ACS Applied Materials & Interfaces* 10(51): 44344-44353.
39. Pikwong F, Chouyratchakarn W, Phutiyothin C, Chanabodeehalermrung B, Baipaywad P, et al. (2023) Development of gelatin-silicon dioxide nanoparticles (GSNPs) encapsulating recombinant human secretory leukocyte protease inhibitor (rhSLPI) for reducing *in vitro* myocardial ischemia/reperfusion injury. *Materials Today: Proceedings*.
40. Li H, Zhu J, Xu YW, Mou F, Shan X, et al. (2022) Notoginsenoside R1-loaded mesoporous silica nanoparticles targeting the site of injury through inflammatory cells improves heart repair after myocardial infarction. *Redox Biology* 54: 102384.
41. Wang L, Feng M, Li Y, Du Y, Wang H, et al. (2019) Fabrication of superparamagnetic nano-silica@ quercetin-encapsulated PLGA nanocomposite: Potential application for cardiovascular diseases. *Journal of Photochemistry and Photobiology B: Biology* 196: 111508.
42. Baeza A, Vallet Regi M (2020) Mesoporous silica nanoparticles as therapeutic antitumoral nanomedicines. *Pharmaceutics* 12(10): 957.
43. Chen NT, Souris JS, Cheng SH, Chu CH, Wang YC, et al. (2017) Lectin-functionalized mesoporous silica nanoparticles for endoscopic detection of premalignant colonic lesions. *Nanomedicine: Nanotechnology, Biology and Medicine* 13(6): 1941-1952.
44. Wang J, Xu M, Wang K, Chen Z (2019) Stable mesoporous silica nanoparticles incorporated with MoS₂ and AIE for targeted fluorescence imaging and photothermal therapy of cancer cells. *Colloids and Surfaces B: Biointerfaces* 174: 324-332.
45. Prieto Montero R, Katsumi A, Cajaraville MP, López Arbeloa I, Martínez-Martínez V (2020) Functionalized fluorescent silica nanoparticles for bioimaging of cancer cells. *Sensors* 20(19): 5590.
46. Chiou AE, Hinckley JA, Khaitan R, Varsano N, Wang J, et al. (2021) Fluorescent silica nanoparticles to label metastatic tumor cells in mineralized bone microenvironments. *Small* 17(15): e2001432.
47. Estevão BM, Vilela RRC, Geremias IP, Zanoni KPS, de Camargo ASS, et al. (2022) Mesoporous silica nanoparticles incorporated with Ir(III) complexes: From photophysics to photodynamic therapy. *Photodiagnosis and Photodynamic Therapy* 40: 103052.
48. Singh RK, Patel KD, Kim JJ, Kim TH, Kim JH, et al. (2014) Multifunctional hybrid nanocarrier: magnetic CNTs ensheathed with mesoporous silica for drug delivery and imaging system. *ACS Applied Materials & Interfaces* 6(4): 2201-2208.
49. Rao VN, Han SH, Lee H, Nguyen VQ, Jeon S, et al. (2018) ROS-responsive mesoporous silica nanoparticles for MR imaging-guided photodynamically maneuvered chemotherapy. *Nanoscale* 10(20): 9616-9627.
50. Mathieu P, Coppel Y, Respaud M, Nguyen QT, Boutry S, et al. (2019) Silica coated iron/iron oxide nanoparticles as a nano-platform for T2 weighted magnetic resonance imaging. *Molecules* 24(24): 4629.
51. Yuan Y, Guo Q, Zhang X, Jiang W, Ye C, et al. (2020) Silica nanoparticle coated perfluorooctyl bromide for ultrasensitive MRI. *Journal of Materials Chemistry B* 8(23): 5014-5018.
52. Montoya Mira J, Wu L, Sabuncu S, Sapre A, Civitci F, et al. (2020) Gas-stabilizing sub-100 nm mesoporous silica nanoparticles for ultrasound theranostics. *ACS Omega* 5(38): 24762-24772.
53. Liberman A, Wu Z, Barback CV, Viveros R, Blair SL, et al. (2013) Color Doppler ultrasound and gamma imaging of intratumorally injected 500 nm iron-silica nanoshells. *ACS Nano* 7(7): 6367-6377.
54. Ho YJ, Wu CH, Jin QF, Lin CY, Chiang PH, et al. (2020) Superhydrophobic drug-loaded mesoporous silica nanoparticles capped with beta-cyclodextrin for ultrasound image-guided combined antivasculature and chemo-sonodynamic therapy. *Biomaterials* 232: 119723.
55. Bindini E, Ramirez MLA, Rios X, Cossio U, Simo C, et al. (2021) *In Vivo* tracking of the degradation of mesoporous silica through (89) Zr radio-labeled core-shell nanoparticles. *Small* 17(30): 2101519.
56. Chen F, Goel S, Valdovinos HF, Luo H, Hernandez R, et al. (2015) *In vivo* integrity and biological fate of chelator-free zirconium-89-labeled mesoporous silica nanoparticles. *ACS Nano* 9(8): 7950-7959.
57. Portilho FL, Helal-Neto E, Sánchez Cabezas S, Rocha Pinto S, Nascimento dos Santos S, et al. (2018) Magnetic core mesoporous silica nanoparticles doped with dacarbazine and labeled with ^{99m}Tc for early and differential detection of metastatic melanoma by single photon emission computed tomography. *Artificial Cells, Nanomedicine, and Biotechnology* 46(1): 1080-1087.
58. Detappe A, Thomas E, Tibbitt MW, Kunjachan S, Zavidij O, et al. (2017) Ultrasmall silica-based bismuth gadolinium nanoparticles for dual magnetic resonance-computed tomography image guided radiation therapy. *Nano Letters* 17(3): 1733-1740.
59. Chaudhary Z, Khan GM, Abeer MM, Pujara N, Wan-Chi Tse B, et al. (2019) Efficient photoacoustic imaging using indocyanine green (ICG) loaded functionalized mesoporous silica nanoparticles. *Biomaterials Science* 7(12): 5002-5015.
60. Shao L, Li Y, Huang F, Wang X, Lu J, et al. (2020) Complementary autophagy inhibition and glucose metabolism with rattle-structured polydopamine@ mesoporous silica nanoparticles for augmented low-temperature photothermal therapy and *in vivo* photoacoustic imaging. *Theranostics* 10(16): 7273-7286.
61. Lee D, Beack S, Yoo J, Kim SK, Lee C, et al. (2018) *In vivo* photoacoustic imaging of livers using biodegradable hyaluronic acid-conjugated silica nanoparticles. *Advanced Functional Materials* 28(22): 1800941.
62. Cheng M, Zhou L, Ma J, Mu J, Yi C, et al. (2019) Iridium(III) and gadolinium(III) loaded and peptide-modified silica nanoparticles for photoluminescence and magnetic resonance (dual) imaging. *Materials Science and Engineering: C* 104: 109972.
63. He Z, Jiang R, Long W, Huang H, Liu M, et al. (2020) 64Red aggregation-induced emission luminogen and Gd³⁺ codoped mesoporous silica nanoparticles as dual-mode probes for fluorescent and magnetic resonance imaging. *Journal of Colloid and Interface Science* 567: 136-144.
64. Tsou MH, Lee CC, Wu ZY, Lee ZH, Lin HM (2021) Mesoporous silica

- nanoparticles with fluorescent and magnetic dual-imaging properties to deliver fucoidan. *International Journal of Biological Macromolecules* 188: 870-878.
65. Wu ZY, Lee CC, Lin HM (2019) Hyaluronidase-responsive mesoporous silica nanoparticles with dual-imaging and dual-target function. *Cancers* 11(5): 697.
66. Du D, Fu HJ, Ren WW, Li XL, Guo LH (2020) PSA targeted dual-modality manganese oxide-mesoporous silica nanoparticles for prostate cancer imaging. *Biomedicine & Pharmacotherapy* 121: 109614.
67. Ovejero Paredes K, Díaz-García D, Mena-Palomo I, Marciello M Lozano-Chamizo L, et al. (2022) Synthesis of a theranostic platform based on fibrous silica nanoparticles for the enhanced treatment of triple-negative breast cancer promoted by a combination of chemotherapeutic agents. *Biomaterials Advances* 137: 212823.
68. Esmaeili Y, Khavani M, Bigham A, Sanati A, Bidram E, et al. (2022) Mesoporous silica@chitosan@gold nanoparticles as "on/off" optical biosensor and pH-sensitive theranostic platform against cancer. *International Journal of Biological Macromolecules* 202: 241-255.

ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.51.008057

Gatou MA. Biomed J Sci & Tech Res



This work is licensed under Creative Commons Attribution 4.0 License

Submission Link: <https://biomedres.us/submit-manuscript.php>



Assets of Publishing with us

- Global archiving of articles
- Immediate, unrestricted online access
- Rigorous Peer Review Process
- Authors Retain Copyrights
- Unique DOI for all articles

<https://biomedres.us/>