MAAEN JOURNAL FOR MEDICAL SCIENCES

Volume 2 | Issue 2 Article 1

Advanced Mesoporous Silica Nanoparticles: Synthesis, Characteristics and Applications

Asmaa Abdelaziz Mohamed
College of Pharmacy, Al-Zahraa University for women, Karbala, Iraq, asmaa.abdelaziz@alzahraa.edu.iq

Marwa Malik Kamil
College of Pharmacy, Al-Mustansiriyah University, Baghdad, Iraq

Firas Aziz Rahi
Department of Pharmacy, Al-Nisour University college, Baghdad, Iraq, firas.aziz@nuc.edu.iq

Noor Zuhair Kbah
College of Pharmacy, Al-Zahraa University for women, Karbala, Iraq

REVIEW

Advanced Mesoporous Silica Nanoparticles: Synthesis, Characteristics, and Applications

Asmaa A. Mohamed Bayoumi [a,*], Marwa M. Kamil [b], Firas A. Rahi [c], Noor Z. Kbah [a]

[a] College of Pharmacy, Al-Zahraa University for Women, Karbala, Iraq
[b] College of Pharmacy, Al-Mustansiriyah University, Baghdad, Iraq
[c] Department of Pharmacy, Al-Nisour University College, Baghdad, Iraq

Abstract

Recent breakthroughs in pharmaceutical delivery methods employing a range of carriers have radically transformed modern diagnostic and therapeutic practices. Mesoporous silica nanoparticles (MSNs) were created due to the demand for substances with superior thermal and chemical capabilities. These ordered porous substances have generated a lot of interest as carriers due to their distinct advantages over the competition. They may be made economically using a simple process. Moreover, the shape, pore size, and particle size may all be changed by modifying the synthesis's conditions. Investigations on MSNs as drug carriers have reportedly accelerated in recent years, highlighting the potential benefits of such a drug delivery approach. MSNs have proven to be effective transporters for anticancer, anti-inflammatory, and neurological medications. This review discusses the origin, synthesis, and most recent applications of MSN.

Keywords: Applications, Mesoporous, Nanoparticles, Nasal delivery, Synthesis

1. Introduction

The cornerstone of science in the twenty-first century is modern nanotechnology. The detection and treatment of diseases have steadily improved over time as a result of the use of nanotechnology in biomedicine. Due to the properties of nanocarriers, such as their extended surface area and the presence of numerous sizes, shapes, and chemical properties, the development of nanomedicine and the use of green technology for its manufacturing have been beneficial for therapy. Additionally, to their advantages, these have shown to be non-toxic, biocompatible, and biodegradable [1]. Polymeric nanoparticles and lipid-based nanocarriers have transformed the treatment of many diseases, particularly cancer. Many of these nanomedicine products have been authorized and are on the market such as Vyxeos (daunorubicin/cytarabine) solid lipid based which is used for Acute myeloid leukaemia and Adynovate (Antihemophilic Factor (Recombinant)) polymer-based for Haemophilia [2,3].

Mesoporous silica nanoparticles (MSNs), also known as mesoporous silica nanoparticles, have become increasingly popular recently. Due to its uniform and controllable pore size and gating, it is a novel and potentially effective drug carrier. Researchers have effectively used these carriers to carry a range of payloads, including medicines and macromolecules including proteins, DNA, and RNA [4]. A vast body of literature is accessible, and studies are continually being conducted to assess potential novel applications for MSNs in drug delivery. There have been numerous evaluations of MSNs' role in enhancing drug solubility, as a controlled/sustained drug delivery method, and in applications in biomedicine [5]. Specific Mobil Crystalline Materials (MCM-41) and Santa Barbara Amorphous Kind (SBA-15) are the subject of patent applications for MSNs. To explain the elements that influencing the form and size of MSNs, an outline of

Received 27 February 2023; revised 21 May 2023; accepted 27 May 2023.
Available online 16 August 2023

* Corresponding author.
E-mail address: asmaa.abdelaziz@alzahraa.edu.iq (A.A. Mohamed Bayoumi).

https://doi.org/10.55810/2789-9136.1019

the synthesis and theory underlying their development is given. The main studies on the subject of MSNs concerning small-molecule-based biomedical applications and relevant patents for therapy are included [6].

The channel structure of Michigan State University (MSU-1), which was created utilizing polyethylene oxide (PEO) as a structure changer where the pores between the comparatively small particles give this material its substantial wall thickness and significant textural mesoporosity [7]. If functionalized, silica displays increased drug loading and offers a regulated drug release. Numerous key features of various mesoporous materials, including Mobil Crystalline Matter-41(MCM-41), Santa Barbara Amorphous-15 SBA-15, Technische Universiteit Delft (TUD), MCM-50 and Hollow Mesoporous Silica (HMS) are useful for drug delivery applications [8].

2. MSNs synthesis

MSNs could be produced in alkaline, acidic, and neutral environments. The reaction settings were changed, producing particles of various sizes and shapes. The first modification to Stober's invention by introducing a cationic surfactant was made to produce a spherical MCM-41 [9,10]. There are several variations in procedures that produce stable, monodisperse MSNs as a result of ongoing research. The particle size must be homogenous for MSNs to be an optimal drug vehicle, and the pore volume must be high to maximize loading efficiency.

The parameters of synthesis can be adjusted by varying the temperature, pH, and concentration of the surfactant. Using a liquid crystal template method, silica is hydrolyzed and condensed onto the surface of surfactant micelles to produce MSNs. Tetraethyl orthosilicate, a liquid form of silica, becomes solid silica [11].

3. Formation mechanism of MSNs

To create particles with the correct drug delivery capabilities, a full understanding of the MSN production mechanism is necessary. According to the first studies on the mechanism, silica networks are produced by using diluted non-ionic surfactants, as no signs of typical mesostructured materials were found [12]. The literature has demonstrated that the hydrolyzed silica is adsorbed surrounding the micelles, or the silica and surfactant first interact, forming a core-like structure in SBA-15 [13]. There have been attempts to identify the precise mechanism underlying the formation to foresee the alterations that would occur during progress. It was discovered that the silicate ions have a tendency to adsorb to the micelles in the development phase of the early hydrolysis of tetramethyl orthosilicate (TMOS), a silica source. The early hydrolysis of the silica precursor reduces the charges surrounding the surfactant, which lowers the intermicellar repulsion and promotes the continued development of tiny aggregates of silica. Transmission analysis indicated that after 400 s, the reaction mixture contained enough distinct hexagonally organized silica mesopores [14].

Employing the method of synchrotron small-angle X-ray scattering, a different theory for the production of MSNs known as the "swelling-shrinking process" (SAXS) was put forth. This method works when tetraethyl orthosilicate (TEOS) is employed as the precursor and no solvent is added. Initially Cetyltrimethylammonium bromide (CTAB) produces ellipsoidal micelles with a hydrophobic tail serving as their inner core. After the addition of TEOS, it dissolved in the lipophilic core, leading to the expansion and transformation of the ellipsoidal micelles into spherical micelles. Due to the electrostatic attraction, the negatively charged hydrolyzed TEOS adsorbs onto the positively charged CTAB micelles, TEOS is then entirely consumed, leading to the shrinking of the micelle. Micelles continue to constrict as hydrolysis and condensation occur simultaneously until all TEOS is hydrolyzed and the silica shell forms. The surrounding micelles combine, producing particles and a mesoporous structure [15,16].

Vazquez et al. (2017) synthesized silica carriers by sol–gel, using TEOS as the silica precursor and (CTAB) as the pore creator, and the porosity was significantly altered by the addition of CTAB. According to the results of a characterization study, the formulation of the synthesized carriers was influenced as the morphology shifted from spheres to rods with increasing porosity [17].

4. Characteristics of MSNs

Mesoporous synthesis requires using of surfactant. Then, Surfactant should be removed which is followed by further steps to modify functional groups. Successful tailoring of MSN surface-oriented functional groups achieves improved controlling of interfacial interactions and providing further functionality including drug loading and targeting [18,19].

4.1. Size

Synthesize particles of the right size for optimal retention period and clinical efficacy to avoid body

clearance and excessive renal filtration. 20–80 nm NPs are best for avoiding physiological "traps" and accumulating target sites [20]. MSNs in this size range can reach target areas better than larger MSNs [21]. Depending on the synthesis process, TEOS-synthesized MSNs may be less effective in vivo due to size limits. TMOS-based MSNs tend to congregate after synthesis, although their lower size of ~30 nm before modification makes this issue negligible [22]. Alcohols, amines, inorganic bases, and salts can affect particle size. They modify silica precursor hydrolysis and condensation. Accelerating reaction kinetics shrinks particles. Triethanolamine was employed instead of NaOH and NH4OH by Moller et al. (TEA). It gives a basic pH and complexes nanoparticles. TEOS: TEA molar ratios of 1:1 to 1:4 produced the highest particle size [23]. Qiao [24] argued that the system's initial pH considerably affects MSN particle size. For instance, using sodium phosphate increases particle size of MSNs. PEG-silane capping on silica particles also sterically stabilizes particle development. When PEG-silane was applied immediately after TMOS, the particle size was 5 nm, but after 50 min, it was >13 nm [25].

4.2. Shape and porosity

In vivo MSN behavior and physiological destiny depend on MSN core structure. MSNs are usually spheres or rods. Sol–gel reaction cosolvent identity and volume ratio relative to water determine the final shape [26]. Temperature and magnetic stir speed affect synthesized rod MSN aspect ratio (AR). MSN form and aspect ratio considerably affect in vivo circulation time and penetration. Rod-shaped MSNs of suitable AR (about 2.1–2.5) have higher blood circulation times and tumor penetration depths than spherical or other rods [27]. Pore form, diameter, and number define MSN porosity. Synthesis cosolvents determine pore shape. When strong bases like NaOH are employed as cosolvents, honeycomb pores form [28,29]. Other cosolvents like triethylanolamine (TEA) create wormhole apertures in the synthesis step. Honeycomb MSNs have larger pore spaces and more stable colloidal suspensions than wormhole MSNs [23]. Vacuum-assisted vapor deposition of TEOS or TMOS after MSN synthesis reduced pore size by ~0.5 nm [30,31]. Adjusting pore size lets you fine-tune loaded molecule release rates and MSN core functional surface area. This increase in surface area may boost MSN–cell connections, but it also increases MSN contacts with healthy cells, raising the likelihood of harmful effects [32].

5. Latest applications

5.1. Chemotherapy

MSNs have emerged in recent years as promising drug delivery systems (DDS) thanks to their distinct characteristics and ability to enhance chemotherapy. When combined with other cancer medicines, MSN-based chemotherapy has a synergistic effect that makes treatment much more effective.

Electrostatic adsorption, hydrophobic interactions, and covalent binding are methods that can be used to load the drug into the MSN's core or surface. If left unaltered, these silica surfaces have a negative charge due to the hydroxyl group of the tetraethyl orthosilicate (TEOS). Therefore, the negatively charged pores and surfaces of MSNs are more likely to absorb the water-soluble hydrophilic medicines, while the majority of hydrophobic anticancer medications bind to MSNs through a hydrophobic contact. The organic solvent can be used to dissolve the hydrophobic medication, which is then combined with the MSN solution before being vacuum dried to remove the solvent. In addition, it is simple to functionalize the silica surface's functional group in order to make it exist for chemical conjugation. PEGylation is necessary to increase the MSNs' circulating half-life, which is constrained for traditional MSNs. It is possible to graft polymers onto the MSN's porous structure. As gatekeepers, these polymers regulate the drug's release from the porous structure. MSNs are capable of both passive and active targeting through size regulation and conjugation [33–35].

Zhang Y. et al. (2022) formulated a pH-responsive formulation of MSNs. Through an amide link, the MSNs were loaded with an anticancer agent (cisplatin (CP), chloroquine (CQ), and histidine (His)-tagged targeting a specific peptide. The pores of the MSNs were then sealed with Cu2+ by chelating the His-tag. Utilizing the targeting effect of the peptide, the nanoparticles exhibited pH-responsive release and efficiently targeted tumor cells, increasing the chemotherapeutic impact of CP. Both in vitro and in vivo assessment revealed its capability of killing tumor cells [36]. Gu Y et al. (2022) also created and characterized resveratrol MSNs for breast cancer management. MSNs were characterized in vitro [37].

5.2. Ant-inflammatory

MSNs are effective carriers for rapid delivery of local therapeutics such as osteostatin, which has anti-osteoporotic properties when injected into the

bone marrow. Alendronate MSNs, for instance, can administer biomolecules intravenously to bones [38].

Kim SJ et al. (2022) proposed MSNs as a dexamethasone carrier that may have a persistent anti-inflammatory impact. MSNs have been confirmed to have an optimal loading efficiency of around 76%, which is roughly twice that of the mesopore silica, SBA-15. Moreover, dexamethasone MSNs permit sustained-release behavior with approximately 92% within 100 h, revealing prolonging of dexamethasone effect than pure substance during the same period [39].

5.3. Drug delivery for neurological drugs

A lot of drugs can treat neurological disorders but cannot protect against neural loss. Furthermore, poor solubility and bioavailability were attributed to an inability to cross the blood–brain barrier (BBB). Therefore, nanoparticle formulations were able to optimize therapeutic bioavailability. For this reason, mesoporous silica, gold, and silver nanoparticles are used for Alzheimer's disease (AD) and Parkinson disease management [40].

Effective immobilization of MSNs on the surface of Bifidobacterium was developed by Liu N. et al. Imaging of MSNs with fluorescence in the gastrointestinal system (GIT) after intranasal delivery demonstrated that MSNs-Bi may be transferred from the brain to the periphery of the gut. Intranasal injection of Bifidobacterium MSNs (MSNs-Bi) suppressed intestinal inflammation. These results suggested that their intranasal administration may be a useful treatment method for retarding the incidence of AD [41].

Díaz-García D (2022) formulated MSNs as Amyotrophic Lateral Sclerosis (ALS) therapeutic with a mix of neuroprotective (leptin) and anti-inflammatory (pioglitazone), having promising therapeutic abilities in neurological disorders. The MSNs materials were characterized using various techniques, that emphasize the incorporation of both drugs and were then evaluated in vivo. Neurodegenerative disorders, such as amyotrophic lateral sclerosis (ALS), have slowed progression and improved significantly [42].

6. Limitations

Although multiple efforts have been made to explore the creation and applicability of these unique MSNs, fabrication and performance issues still hinder their commercialization. Biosafety, colloidal stability, and degradability affect performance qualities and processing scale-up, causing a huge gap between lab-scale progress and commercialization [43]. Advanced MSN safety is yet to be solved. Toxicity analyses with detailed investigation on nephrotoxicity, immunogenicity, and others have yet to be determined. Silica-based systems, including typical MSNs, have been examined in these research [44–46]. However, changes in manufacturing processes and nanoplatform morphologies, such as impregnating various conjugates to modify surfaces and siliceous frameworks, may affect their safety profile. Colloidal stability of nanoformulations affects dose distribution, systemic circulation, delivery patterns, and clearance [47–48]. MSNs are stable in physiological fluids and negative in charge, which makes them repel biological membranes and limit their transport. Polymers and transition metal-modified siliceous frameworks improve colloidal stability, overcoming this constraint. In addition to such alterations, it is necessary to address aggregation problems by stringently limiting the size of particles of these sorts and optimizing the charge on their surfaces for proper application to avoid repeated functionalization. Third, advanced MSN prototypes must be degraded safely. In biological applications, these two properties are critical since non-degradable materials can cause accumulation-induced toxicity [49].

7. Conclusion

In this review, we have investigated the production and use of MSNs as a good drug delivery system. Because of their peculiar characteristics of variable pore size and elevated loading capacity, they are extensively used as nanocarriers. It is possible to produce MSNs with variable particle sizes, shapes, and pores by varying the molar content of the reactants. Customizing MSNs' pore size and surface characteristics improves loading and alters the release. We discussed in details the synthesis, formation and applications in successful drug delivery and the main points were investigated deeply. We concluded that MSNs are powerful delivery systems for enhancement of many drugs characteristics.

References

[1] Kankala RK, Zhang YS, Wang SB, Lee CH, Chen AZ. Supercritical fluid technology: an emphasis on drug delivery and related biomedical applications. Adv. Healthc. Mater 2017;6:1700433. https://doi.org/10.1002/adhm.201700433.

[2] Mitchell MJ, Billingsley MM, Haley RM, Wechsler M, Peppas N, Langer R. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov 2021;20:101–24. https://doi.org/10.1038/s41573-020-0090-8.

[3] Han YH, Kankala R, Wang SB, Chen AZ. Leveraging engineering of indocyanine green-encapsulated polymeric nanocomposites for biomedical applications. Nanomaterials 2018;8:360. https://doi.org/10.3390/nano8060360.
[4] Jafari S, Derakhshankhah H, Alaei L, Fattahi A, Varnamkhasti BS, Saboury AA. Mesoporous silica nanoparticles for therapeutic/diagnostic applications. Biomed Pharmacother 2019;109:1100–11. https://doi.org/10.1016/j.biopha.2018.10.167.
[5] Bharti C, Nagaich U, Pal AK, Gulati N. Mesoporous silica nanoparticles in target drug delivery system: a review. Int J Pharm Investig 2015;5(3):124. https://doi.org/10.4103/2230-973X.160844.
[6] Castillo RR, Lozano D, Vallet-Regí M. Mesoporous silica nanoparticles as carriers for therapeutic biomolecules. Pharmaceutics 2020;12(5):432. https://doi.org/10.3390/pharmaceutics12050432.
[7] Fotoohi B, Mercier L. Modification of pore structure and functionalization in MSU-X silica and application in adsorption of gold thiosulfate. Microporous Mesoporous Mater 2014;190:255–66. https://doi.org/10.1016/j.micromeso.2014.02.020.
[8] Pagar NS, Karandikar PR, Chandwadkar AJ, Deshpande RM. Synthesis, characterization and catalytic study of mesoporous carbon materials prepared via mesoporous silica using non-surfactant templating agents. J Porous Mater 2020;28(2):423–33. https://doi.org/10.1007/s10934-020-01003-x.
[9] Stober W, Fink A, Bohn E. Controlled growth of monodisperse silica spheres in the micron size range. J Colloid Interface Sci 1968;26:62–9. https://doi.org/10.1016/0021-9797(68)90272-5.
[10] Ge L, Feng Y, Dai Y, Wang R, Ge T. Imidazolium-based ionic liquid confined into ordered mesoporous MCM-41 for efficient dehumidification. Chem Eng J 2023;452:139116. https://doi.org/10.1016/j.cej.2022.139116.
[11] Blin JL, Impéror-Clerc M. Mechanism of self-assembly in the synthesis of silica mesoporous materials: in situ studies by X-ray and neutron scattering. Chem Soc Rev 2013;42:4071–82. https://doi.org/10.1039/c2cs35362h.
[12] Liu Z, Fontana F, Python A, Hirvonen JT, Santos HA. Microfluidics for production of particles. Mechanism, Methodology, and Applications 2020;16(9):e1904673. https://doi.org/10.1002/smll.201904673.
[13] Czajka A, Liao G, Mykhaylyk OO, Armes SP. In situ small-angle X-ray scattering studies during the formation of polymer/silica nanocomposite particles in aqueous solution. Chem Sci 2021;12(42):14288–300. https://doi.org/10.1039/d1sc03353k.
[14] Hollamby MJ, Borisova D, Brown P, Eastoe J, Grillo I, Shchukin D. Growth of mesoporous silica nanoparticles monitored by time-resolved small-angle neutron scattering. Langmuir 2012;28:4425–33. https://doi.org/10.1021/la203097x.
[15] Skou S, Gillilan R, Ando N. Synchrotron-based small-angle X-ray scattering of proteins in solution. Nat Protoc 2014;9:1727–39. https://doi.org/10.1038/nprot.2014.
[16] Li Z, Zhang Y, Feng N. Mesoporous silica nanoparticles: synthesis, classification, drug loading, pharmacokinetics, biocompatibility, and application in drug delivery. Expet Opin Drug Deliv 2019;16(3):219–37. https://doi.org/10.1080/17425247.2019.1575806.
[17] Vazquez IN, Gonzalez Z, Ferrari B, Castro Y. Synthesis of mesoporous silica nanoparticles by sol–gel as nanocontainer for future drug delivery applications. Bol Soc Espanola Ceram Vidr 2017;56(3):139–45. https://doi.org/10.1016/j.bsecv.2017.03.002.
[18] Kango S, Kalia S, Celli A, Njuguna J, Habibi Y, Kumar R. Surface modification of inorganic nanoparticles for development of organic–inorganic nanocomposites—a review. Prog Polym Sci 2013;38:1232–61. https://doi.org/10.1016/j.progpolymsci.2013.02.003.
[19] Yegorov AS, Ivanov VS, Antipov AV, Wozniak AI, Tcarkova KV. Chemical modification methods of nanoparticles of silicon carbide surface. Orient J Chem 2015;31:1269–75. https://doi.org/10.13005/ojc/310303.
[20] Tao Z. Mesoporous silica-based nanodevices for biological applications. RSC Adv 2014;4:18961–80. https://doi.org/10.1039/c3ra47166g.
[21] Mamaeva V, Sahlgren C, Lindén M. Mesoporous silica nanoparticles in medicine—recent advances. Adv Drug Deliv Rev 2013;65:689–702. https://doi.org/10.1016/j.addr.2012.07.018.
[22] Cheng CJ, Tietjen GT, Saucier-Sawyer JK, Saltzman WM. A holistic approach to targeting disease with polymeric nanoparticles. Nat Rev Drug Discov 2015;14:239–47. https://doi.org/10.1038/nrd4503.
[23] Möller K, Kobler J, Bein T. Colloidal suspensions of nanometer-sized mesoporous silica. Adv Funct Mater 2007;17:605–12. https://doi.org/10.1002/adfm.200600578.
[24] Qiao ZA, Zhang L, Guo M, Liu Y, Huo Q. Synthesis of mesoporous silica nanoparticles via controlled hydrolysis and condensation of silicon alkoxide. Chem Mater 2009;21:3823–9. https://doi.org/10.1021/cm901335k.
[25] Ma K, Werner-Zwanziger U, Zwanziger J, Wiesner U. Controlling growth of ultrasmall sub-10 nm fluorescent mesoporous silica nanoparticles. Chem Mater 2013;25:677–91. https://doi.org/10.1021/cm303242h.
[26] Rahmani S, Durand JO, Charnay C, Lichon L, Férid M, Garcia M, et al. Synthesis of mesoporous silica nanoparticles and nanorods: application to doxorubicin delivery. Solid State Sci 2017;68:25–31. https://doi.org/10.1016/j.solidstatesciences.2017.04.003.
[27] Frickenstein AN, Hagood JM, Britten CN, Abbott BS, McNally MW, Vopat CA, et al. Mesoporous silica nanoparticles: properties and strategies for enhancing clinical effect. Pharmaceutics 2021;13(4):570. https://doi.org/10.3390/pharmaceutics13040570.
[28] Gurka MK, Pender D, Chuong P, Fouts BL, Sobelov A, McNally MW, et al. Identification of pancreatic tumors in vivo with ligand-targeted, pH responsive mesoporous silica nanoparticles by multispectral optoacoustic tomography. J Contr Release 2016;231:60–7. https://doi.org/10.1016/j.jconrel.2015.12.055.
[29] Zeiderman MR, Morgan DE, Christein JD, Grizzle WE, McMasters KM, McNally LR. Acidic pH-targeted chitosan-capped mesoporous silica coated gold nanorods facilitate detection of pancreatic tumors via multispectral optoacoustic tomography. ACS Biomater Sci Eng 2016;2:1108–20. https://doi.org/10.1021/acsbiomaterials.6b00111.
[30] Jambhrunkar S, Yu M, Yang J, Zhang J, Shrotri A, Endo-Munoz L, et al. Stepwise pore size reduction of ordered nanoporous silica materials at angstrom precision. J Am Chem Soc 2013;135:8444–7. https://doi.org/10.1021/ja402463h.
[31] Liberman A, Mendez N, Trogler WC, Kummel AC. Synthesis and surface functionalization of silica nanoparticles for nanomedicine. Surf Sci Rep 2014;69:132–58. https://doi.org/10.1016/j.surfrep.2014.07.001.
[32] Lin YS, Haynes CL. Impacts of mesoporous silica nanoparticle size, pore ordering, and pore integrity on hemolytic activity. J Am Chem Soc 2010;132:4834–42. https://doi.org/10.1021/ja910846q.
[33] Ying G, Dongruo G, Jie S, Qiwen W. A review of mesoporous silica nanoparticle delivery systems in chemo-based combination cancer therapies. Front Chem 2020;8:598722. https://doi.org/10.3389/fchem.2020.598722.
[34] Rajani C, Borisa P, Karanwad T, Borade Y, Patel V, Rajpoot K, et al. Cancer-targeted chemotherapy: emerging role of the folate anchored dendrimer as drug delivery nanocarrier. Pharmaceutical Applications of Dendrimers 2020;vols. 151–98. https://doi.org/10.1016/b978-0-12-814527-2.00007-x.
[35] Alyassin Y, Sayed GS, Mehta P, Ruparelia K, Arshad SM, Rasekh M, et al. Application of mesoporous silica nanoparticles as drug delivery carriers for chemotherapeutic agents. Drug Discov Today 2020;25(8):1513–20. https://doi.org/10.1016/j.drudis.2020.06.006.
[36] Zhang Y, Lou J, Williams GR, Ye Y, Ren D, Shi A, et al. Cu^{2+}-Chelating mesoporous silica nanoparticles for synergistic chemotherapy/chemodynamic therapy. Pharmaceutics 2022;14(6):1200. https://doi.org/10.3390/pharmaceutics14061200.

[37] Gu Y, Fei Z. Mesoporous silica nanoparticles loaded with resveratrol are used for targeted breast cancer therapy. Journal of Oncology 2022;2022:8471331. https://doi.org/10.1155/2022/8471331.
[38] Mora-Raimundo P, Lozano D, Manzano M, Vallet-Regí M. Nanoparticles to knockdown osteoporosis-related gene and promote osteogenic marker expression for osteoporosis treatment. ACS Nano 2019;13(5):5451–64. https://doi.org/10.1021/acsnano.9b00241.
[39] Kim SJ, Choi Y, Min KT, Hong S. Dexamethasone-loaded radially mesoporous silica nanoparticles for sustained anti-inflammatory effects in rheumatoid arthritis. Pharmaceutics 2022;14(5):985. https://doi.org/10.3390/pharmaceutics14050985.
[40] Ribeiro TC, Sábio RM, Carvalho GC, Fonseca-Santos B, Chorilli M. Exploiting mesoporous silica, silver and gold nanoparticles for neurodegenerative diseases treatment. Int J Pharm 2022;624:121978. https://doi.org/10.1016/j.ijpharm.2022.121978.
[41] Liu N, Yang C, Liang X, Cao K, Xie J, Luo Q, et al. Mesoporous silica nanoparticle-encapsulated Bifidobacterium attenuates brain Aβ burden and improves olfactory dysfunction of APP/PS1 mice by nasal delivery. J Nanobiotechnol 2022;20(1):439. https://doi.org/10.1186/s12951-022-01642-z.
[42] Díaz-García D, Ferrer-Donato Á, Méndez-Arriaga JM, Cabrera-Pinto M, Díaz-Sánchez M, Prashar S, et al. Design of mesoporous silica nanoparticles for the treatment of amyotrophic lateral sclerosis (ALS) with a therapeutic cocktail based on leptin and pioglitazone. ACS Biomater Sci Eng 2022;8(11):4838–49. https://doi.org/10.1021/acsbiomaterials.2c00865.
[43] Liu X, Jiang J, Chan R, Ji Y, Lu J, Liao Y-P, et al. Improved efficacy and reduced toxicity using a custom-designed irinotecan-delivering silicasome for orthotopic colon cancer. ACS Nano 2019;13:38–53. https://doi.org/10.1021/acsnano.8b06164.
[44] Zhao Y, Wang Y, Ran F, Cui Y, Liu C, Zhao Q, et al. A comparison between sphere and rod nanoparticles regarding their in vivo biological behavior and pharmacokinetics. Sci Rep 2017;7:4131. https://doi.org/10.1038/s41598-017-03834-2.
[45] Zhang Q, Xu H, Zheng S, Su M, Wang J. Genotoxicity of mesoporous silica nanoparticles in human embryonic kidney 293 cells. Drug Test Anal 2015;7:787–96. https://doi.org/10.1002/dta.1773.
[46] Li L, Liu T, Fu C, Tan L, Meng X, Liu H. Biodistribution, excretion, and toxicity of mesoporous silica nanoparticles after oral administration depend on their shape. Nanomedicine 2015;11:1915–24. https://doi.org/10.1016/j.nano.2015.07.004.
[47] Schneid AC, Silveira CP, Galdino FE, Ferreira LF, Bouchmella K, Cardoso MB. Colloidal stability and redispersibility of mesoporous silica nanoparticles in biological media. Langmuir 2020;36:11442–9. https://doi.org/10.1021/acs.langmuir.0c01571.
[48] Meng H, Xue M, Xia T, Ji Z, Tarn DY, Zink JI, et al. Use of size and a copolymer design feature to improve the biodistribution and the enhanced permeability and retention effect of doxorubicin-loaded mesoporous silica nanoparticles in a murine xenograft tumor model. ACS Nano 2011;5:4131–44. https://doi.org/10.1021/nn200809t.
[49] Chen W, Cheng C-A, Zink JI. Spatial, temporal, and dose control of drug delivery using noninvasive magnetic stimulation. ACS Nano 2019;13:1292–308. https://doi.org/10.1021/acsnano.8b06655.