Indonesian Journal of Pharmaceutics
IdJP
ISSN : 2597-8748

Vol. 5, Issue 3, 2023 (508-521)
http://journal.unpad.ac.id/IdJP

Review Article: Advancing Cancer Treatment With Mesoporous Silica Nanoparticle-Based Theranostics

Delphine Wirawan, Alfa Fildzah Hulwana*, Yedi Herdiana

Department Pharmaceutics and Technology of Pharmacy. Faculty of Pharmacy, Padjadjaran University, Sumedang, West Java, Indonesia 45363

Submitted: 02/08/2024, Revised: 06/09/2024, Accepted: 20/12/2024, Published: 24/01/2025

ABSTRACT

Cancer is a major cause of death globally. It is often detected at a late stage, while conventional treatments are more effective during the early and middle stages. These traditional treatments also cause many side effects due to the lack of targeted delivery. Nanotechnology, particularly mesoporous silica nanoparticles (MSNs), has been investigated for cancer treatment and diagnosis. Theranostics, which combine therapy and diagnostics, can provide simultaneous treatment and detection, potentially lowering mortality rates. A literature review was conducted using keywords such as mesoporous silica nanoparticles, cancer, diagnosis, and therapy in online databases like PubMed. The results of this review were analyzed and compared with existing literature, aiming to provide a comprehensive overview of mesoporous silica nanoparticles as current cancer treatment and diagnosis.

Keywords: MSNs, cancer, theranostic, therapy, literature.

*Corresponding author,
e-mail: alfa21001@mail.unpad.ac.id A. F. Hulwana)

https://doi.org/10.24198/idjp.v5i3.56808

1. Introduction

One of the leading causes of death in the world is cancer. In 2022, there were 408.661 new cases of cancer and 242.988 deaths caused by cancer in Indonesia(1). Cancer is a disease when abnormal cell growth occurs in the human body. Abnormalities can start at almost anywhere in the body. Mutation in certain genes cause abnormalities in cell, leads to cancer(2). Cancer is a genetic disease. Gene mutations in cancer can be result of exposure to carcinogens or happens spontaneously during DNA replication(3).

There are different types of cancer. Different types of cancer require different types of treatment. In 2022, top three cancers that caused death in Indonesia are lung, liver, and breast(1). Traditional cancer treatment such as chemotherapy, radiotherapy, or surgery have few limitations. Traditional cancer treatment can cause damage to non-cancerous tissues, as they are not targeted therapy(4).

Diagnosis of cancer is pretty challenging. Most cancers are detected in the middle or late stages. Meanwhile, conventional cancer treatments are effective only for early and middle stages. Hence, it is hard to treat advanced stage cancer patients(5).

Several therapeutic treatments for cancer have been developed. Application of nanotechnology for cancer treatment has been largely used these days. Nanoparticles as drug delivery system for cancer treatment shows several advantages over traditional cancer treatment. Nanoparticle delivery systems, such as albumin, liposomes, and polymeric have been approved for cancer treatment(6).

Nanoparticles in cancer treatment have several distinctive features, such as increasing efficacy, reducing toxicity, targeted drug delivery, increasing drug pharmaceutical properties, visualization of site drug delivery by combining therapeutic agents and imaging modalities, and improved methods for detecting cancer and capturing images(6).

One of the most thoroughly researched inorganic nanoparticles are mesoporous silica nanoparticles(7). Mesoporous silica nanoparticles (MSNs) are silica nanoparticles with a porous structure, typically ranging in size from 30 to 300 nm. They facilitate endocytosis by target cells while exhibiting low toxicity(8).

These mesoporous silica nanoparticles or MSNs were first discovered in 1992 by Mobil Co. researchers which were developed again for drug delivery in 2001. Nanoparticles have honeycomb-like pore diameters with hundreds of cylindrical pores between 2 and 50 nm independent reservoirs that can encapsulate a large number of desired drug molecules that are considered most suitable for drug delivery and controlled release purposes(9).

Due to their porosity, they have high pore volume (>0.9 cm^3/g) and high surface area (>700 m^2/g) resulting in high loading capacity within the pores. Mesoporous silica nanoparticles have customizable size, good biocompatibility, and regular and uniform pores. Their surface contains silanol groups that make them easily functionalized. Due to their loading capacity, biocompatibility, and easy functionalization, they have attracted much attention as a possible tool for drug delivery (10).

Mesoporous silica nanoparticles have been used for theranostics. Theranostics is a developing area that utilizes a single formulation for both diagnostic and therapeutic purposes. Drug or imaging agents are loaded into the pores of mesoporous silica nanoparticles.

MSNs are considered promising for mesoporous silica nanoparticles. MSNs are considered promising for cancer treatment due to their versatility in size and ability to transport substantial payloads. MSNs can improve solubility of anticancer moieties, as most of them are hydrophobic(11). Besides that, mesoporous nano shells can be modified with selected agents as required for specific targeting purposes.

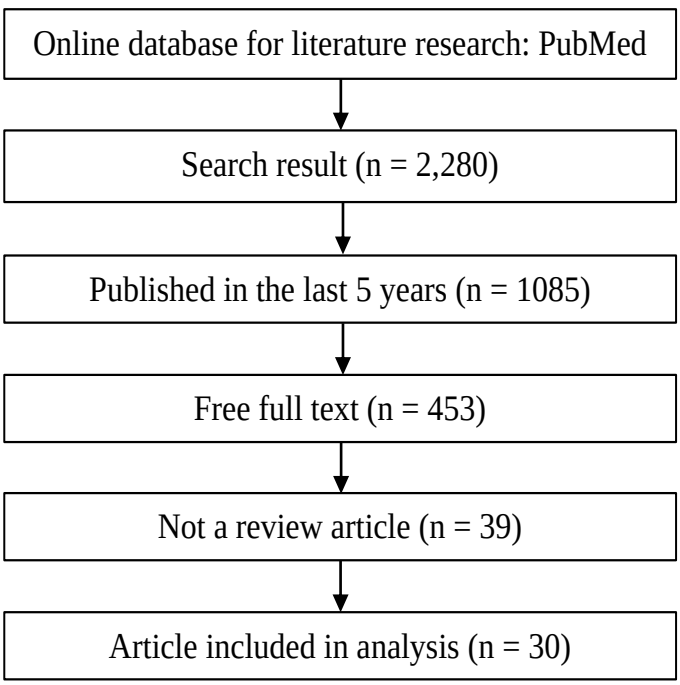
Conventional cancer treatment lacks target specificity, therefore it can damage other healthy tissues(5). MSNs able to prevent early release of the cargoes before reaching the targeted site. Hence, MSNs can be used for cancer targeted therapy(12). MSNPs provide excellent target specificity by allowing the attachment of different ligands tailored to the desired targeting site(13).

This review focuses on the potential of mesoporous silica nanoparticles (MSNs) for fighting cancer. MSNs' large surface area and tunable pores make them ideal for delivering drugs and improving cancer treatment. The review will explore how MSNs can deliver drugs directly to cancer cells, release drugs slowly and steadily, and help overcome cancer's resistance to drugs. Additionally, MSNs show promise in early cancer detection through imaging techniques. The review will compare MSNs to traditional treatments like chemotherapy, highlighting the potential benefits.

2. Method

A literature review was conducted using keywords mesoporous silica nanoparticles, cancer, diagnosis, and therapy on online database, PubMed. Reference journals used span the last five years (2019 - 2024). Inclusion criteria are research on mesoporous silica nanoparticles for cancer treatment and free full text. Exclusion criteria are articles categorized as reviews or systematic reviews and published more than five years ago.

Table 1. Methods performed for review.



3. Result

Data were gathered from a review of several journals. A total of 30 journals were utilized for this literature review, and their summaries are presented in Table 2.

Table 2. Overviews of MSNs as a solution for drug limitations.

Cargos	Limitation	Resolution	Reference
Thiabendazole	Poor water solubility hence limits its biological activity.	TBZ-loaded MCM-41 nanoparticles exhibit enhanced efficacy in destroying cancer cells, requiring a lower dosage while achieving greater stability. Amplify cytotoxicity against PC-3 cells by 2.8 times compared to TBZ alone.	(14)
5-fluorouracil and curcumin	Toxic, side effect, lack of tumor targeting	Enhances their effectiveness against tumors, with no discernible signs of toxicity.	(15)
Curcumin and naphthoquinone	CurNQ have pH specific solubility at the pH of tumor microenvironment, pH 6.8.	Display strong inherent fluorescence, facilitating their use in detection and potential imaging applications. Demonstrating selective toxicity towards cancer cells.	(16)
Sunitinib	Side effects restrained SUN effectiveness.	MSNP-PEG/SUN exhibited increased release at pH levels of 5.4. The targeted delivery of SUN using engineered MSNPs with the MUC16 aptamer proved effective at the cellular level	(17)
Umbelliprenin	Insoluble and has poor bioavailability.	Enhances therapeutic effectiveness and minimizes side effects by regulating drug release. Improves colloidal stability, hence facilitating better accumulation at the tumor site.	(18)
Selenium	Slow cellular uptake of Se result in extracellular Se accumulation and lead to adverse effects on bone healthy cells.	Exhibited greater selectivity for cancer cells over healthy osteoblasts. Exposure to Se-MSN resulted in ROS production and the induction of apoptosis.	(19)
Colchicine	Toxicity which causes severe side effects on normal cells.	Inhibition of HCT116 colon cancer cells was observed. Additionally, MSNsPCOL/CG-FA exhibited low inhibition in normal BJ1 cells (4%) compared to free COL (~60%).	(20)
Exemestane	Poor bioavailability and undergoes significant hepatic metabolism.	Exemestane-loaded nanoparticles are non-toxic and suitable for intravenous use. Enhancing exemestane release while minimizing side effects in the human body. Can act as MRI contrast agents for cancer diagnosis.	(21)

Doxorubicin	Non-selective action on cells, causing severe side effects	Enhanced cell death in MCF-7 and HeLa cells while maintaining the pharmaceutical effectiveness of DOX. Reduce cytotoxicity in non-tumoral cells.	(22)
Manganese oxide	Current imaging techniques have limitations in detecting small and early-stage tumors.	Enable more precise imaging approach, potentially reducing false positives. Detect prostate cancer with high sensitivity and enhancing diagnostic accuracy. Able to detect cancer at earlier stages than current standard imaging techniques allow. Mn-SMSN@DOX-IR-780 also induced more cytotoxic ROS than DOX alone.	(23)
miR-200c-3p	Rapid degradation by cellular and serum nucleases leads to instability, and their small size and negative charge result in low ability to cross cell membranes.	Target the CD44 receptor and escape from endosomes/lysosomes, which is essential for delivering miRNA into the cytosol. This system effectively delivers miR-200c-3p to tumors without significant toxicity.	(24)
Curcumin	Low solubility in water, limited bioavailability, and rapid metabolism	Enhance bioavailability and anticancer effectiveness of Curcumin against breast cancer cells. Demonstrated selective targeting specifically to MCF-7 breast cancer cells.	(25)
Resveratrol	Low water solubility, low bioavailability, easy oxidation and decomposition, and fast metabolism in body.	The use of Res-loaded MSNs showed better anticancer effects compared to treatment with Res alone in gastric cancer therapy.	(26)
Epirubicin	Resistance and recurrence in colorectal cancer can reduce the survival rates.	Allow traceability using three imaging modalities, enhancing both diagnosis and theranostic applications. Enables accurate imaging throughout various stages of treatment and facilitates targeted delivery of anti-cancer drugs towards HT-29 cells.	(27)
Quercetin	Limited water solubility, low bioavailability, poor oxidative stability, and extensive biotransformation restrict its applicability.	Greater targeting precision, enhanced ability to act as a contrast agent for MRI cancer detection, reduced toxicity, and protecting quercetin from degradation under acidic conditions to gastric pH.	

LINC00589	Viral vectors can cause potential virulence and other side effects, and possible changes caused by gene insertion also increase the risk of tumorigenesis in clinical applications.	LINC00589 delivered by PMSN can suppress GC metastasis in vitro and in vivo. The expression levels of hnRNPA1 and PKM2 in mouse tumor tissues treated with PMSN-LINC00589 were significantly lower than the expression levels in mouse tumor tissues treated with PMSN control.	(28)
Organotin(IV) Fragment	There is a lack of specificity in organotin(IV) compounds that needs to be improved for potential dual applications against cancer and bacterial infections, but there is also a need to improve the therapeutic activity, bioavailability and even solubility of cytotoxic agents.	Organotin(IV) fragments namely 2-MSN-Sn and 2-SBA-Sn showed selectivity against cancer cells. 2-MSN-Sn was significantly more active than 1-MSN-Sn, and the activity against MDA-MB-231 cancer cells was higher than that of healthy HEK-293T cells.	(29)
Morin Hydrate Encapsulation	Morin have low aqueous solubility and limited bioavailability.	Encapsulation of MH facilitates its release in vitro, as MH crystals transition to an amorphous state when loaded onto MSNs this increases solubility and dissolution rate. Enhanced release of MH at acidic pH, shows that morin-containing MSNs may be a promising nano-delivery system for treatment of melanoma skin cancer.	(30)
Glucosamine	Glucosamine reacts with a chloro-modified structure, and methotrexate is conjugated to the hydroxyl group of glucose.	The modified Glucosamine structure exhibits a controlled release of methotrexate in simulated tumor fluid may act as a glucose transporter targeting agent and exhibit enhanced cancer cell uptake.	(31)
Sonodynamic therapy	Lack of sonosensitizers capable of generating sufficient amounts of reactive oxygen species (ROS) in response to ultrasound (US) exposure.	AS exposure enhanced cavitation-mediated ROS production, PFH@P-MSTN demonstrated considerably greater antitumor effectiveness than P-MSTN.	(32)

Lipid coated MSN	Premature drug release and lower biocompatibility	The lipid coating prevents drug release along with reducing premature leakage. Moreover, better biocompatibility and interaction of cationic liposomes with cell membranes enhance cellular uptake.	(33)
Manganese-doped	The production of cytotoxic ROS (-OH) is limited by the restricted supply of endogenous H2O2, which reduces the efficiency of CDT.	SMSN is equipped with Fenton-like activity that can catalyze endogenous H2O2 into lethal ROS by structurally in situ doping with the transition metal Mn, thereby enhancing CDT.	(34)
Triantennary GalNAc-Fungsional Multi-Responsif	Created new formulations of tailored mesoporous silica nanoparticles that can effectively and precisely deliver anticancer medications to hepatocellular carcinoma (HCC) cells.	Mesoporous silica nanoparticles that are redox-responsive were functionalized by loading the anthracycline medication epirubicin onto triantennary N-acetylgalactosamine (GalNAc) ligand groups, which have a strong affinity for asialoglycoprotein receptors that are overexpressed in HCC cells.	(35)
MCF-7 KCR cancer cell	Multidrug resistance	Delivery of Rho123 and MMC via MSNs to multidrug-resistant cells increases and possibly prolongs intracellular drug concentrations, resulting in greater cytotoxic effects, indicating potential of MSNs to overcome multidrug-resistant cancers.	(9)
5-Fluorouracil	Need to improve effectiveness and reduce drug toxicity.	In the treatment of gynecological cancer, 5-FU encapsulation and functionalization of MSN-NH2 with folic acid may serve as potential carriers of 5-FU. The amine surface of MSN-NH2 nanoparticles may lower the risk of toxicity to cervical and ovarian cancer cells.	(36)
Eu3+/Gd3+ co-doped hydroxyapatite	Materials with low mechanism resistance.	Conducted pH-sensitive hybrid systems based on silica and hydroxyapatite with photoluminescent and magnetic properties to evaluate the potential use of these systems in targeted drug delivery	(37)

Fe2+ and glutathione (GSH)	The pre synthesis of each component and the additional conjugation via chemical bonds are part of a complex construction process. This can lead to inefficient integration and limit production and applications.	Mesoporous silicon nanocarriers (MSNs) enable facile tumor targeting and tumor responsiveness by leveraging effective and non-destructive physical interactions for synergistic chemo-catalytic-photothermal guided wavelength fluorescence imaging for tumor therapy.	(38)
Anti-GPC1	Resistant PANC1 cells with Gem	Simultaneous targeting and delivery of gemcitabine and ferulic acid to PANC-1 cells was made possible by silica nanoparticles with anti-GPC1 antibodies.	(39)
Carboxylated chitosan	pH-sensitive release, endosomal or lysosomal release, and modified release (partial carboxylation) should be studied. This is done to control drug release kinetics to increase drug dosage and reduce cancer cell death.	The conjugation of aptamers, or targeting agents, endo/lysosomal escape, and customizable drug release kinetics were made by coating of carboxylate chitosan over MSNs. These features increased the effectiveness of the drug delivery system.	(40)

4. Discussion

Mesoporous silica nanoparticles can be synthesized using various techniques. One such method is green synthesis method. Green synthesis method involves the use of environmentally friendly and non-toxic materials. In their study published in 2024, Ghobadi et al. utilized the green synthesis method to create silver nanoparticles (AgNPs) and functionalize mesoporous silica nanoparticles (MSNs) with amine groups(22).

Another method for synthesizing MSNs is the sol-gel method. In their research from 2023, Torabi et al. employed the sol-gel technique to fabricate MSNs designed for targeted delivery of sunitinib to ovarian cancer cells (17).

After the synthesis of MSNs, next steps typically involve characterization to assess their physical and chemical properties. Techniques such as Fourier-transform infrared spectroscopy (FT-IR), transmission electron microscopy (TEM), scanning electron microscopy (SEM), etc. Analysis are used to determine size, shape, surface area, pore size, and drug loading efficiency(17).

The surface of MSNs can be altered to create a targeted drug delivery system. Aptamers, such as MUC16 aptamers, are utilized for this purpose. In the case of ovarian cancer cells that express high levels of MUC16, these aptamers are employed to guide mesoporous silica nanoparticles (MSNPs) loaded with sunitinib directly to these cells. This strategy aims to increase drug accumulation within cancer cells while minimizing unintended effects on non-cancerous tissues(17).

Apart from MUC16 aptamers, another compound for targeted delivery is chitosan-glycine complex conjugated to folic acid. This complex acts as a targeting ligand for cancers. Colchicine, loaded into MSNs coated with the chitosan-glycine complex conjugated to folic acid, enhances antimitotic effects by binding to tubulin in cells, leading to cell death. This nano-delivery system specifically targets the interaction of folic acid with folate receptors, which are over-expressed on cancer cells. Once delivered, it releases colchicine into the cancer cells, resulting in tubulin inhibition. This approach achieved maximum tubulin inhibition (~90%) in HCT116 cancer cells(20).

MSNs can be surface-modified to enable controlled ion release in response to specific stimuli, such as pH changes. This modification helps prevent unwanted cargo release and minimizes harmful side reactions(19). Some pH-responsive polymeric materials have low mechanical resistance can be weakened by combining these polymers with mechanically resistant inorganic materials such as mesoporous silica nanoparticles (MSN) and hydroxyapatite (HA). Mesoporous silica has interesting properties such as high surface area and hydroxyapatite has been widely studied to aid bone regeneration, providing special properties adding multifunctionality to the system. (37).

The surface of MSNs can also be coated by lipids or Lip-Dox-MSNPs which provide a barrier to sustain drug release along with reducing premature leakage. The biocompatibility and enhanced interaction of cationic liposomes to the cell membrane will result in better cell uptake. From such forms it makes an effective approach for cancer treatment and maintains effective drug concentration to the cell site without systemic side effects(33) .

MSNs are not only used for drug delivery, but can also be an enhancer in other cancer therapies such as sonodynamic therapy. Sonodynamic therapy is limited by the lack of sonosensitizers capable of generating sufficient amounts of reactive oxygen species (ROS) in response to ultrasound (US) exposure. Therefore, MSNs with sol-gel method of mesoporous silica-titania NPs (MSTNs) were prepared by incorporating TiO2 NPs into colloidal MSNs, which were used as reservoirs for gas precursors(32). These modifications made in MSNs adjust the target, the materials used, and the reaction mechanisms that can occur so that the drug can reach its target correctly.

Some cancer drugs have limitations such as poor solubility, susceptibility to degradation, poor bioavailability, and lack of selectivity, which can lead to severe side effects. MSNs are well-known for enhancing the aqueous solubility of drugs by preventing their crystallization. Additionally, MSNs have a stable structure, making them resistant to degradation by pH and heat. Their mesoporous structure allows for a high drug loading rate(14).

Umbelliprenin, Exemestane, Curcumin, Resveratrol, and Thiabendazole has the same problem of lack of solubility, which affects its bioavailability after oral administration. To address this, for example with Thiabendazole, MCM-41 is used as a carrier to enhance TBZ delivery and bioavailability. Thiabendazole loaded into MCM-41 nanoparticles, which have a high drug loading capacity (19.1%), was synthesized to improve its solubility and bioavailability. The release of TBZ from these MCM-41 nanoparticles is pH-dependent. MCM-41 nanoparticles were able to preserve over 97% of TBZ after

12 hours of exposure to acidic gastric pH and 74% in natural intestinal pH at physiological temperature. This nano formulation of TBZ inhibited the proliferation and migration of PC-3 cells more effectively than TBZ alone(14).

miR-200c could be a potential therapeutic agent for breast cancer, but the use of miRNAs in vivo faces challenges, such as instability due to rapid degradation by cellular and serum nucleases, and low ability to cross cell membranes because of their small size and negative charge. To address these issues, miR-200c is loaded into MSNs attached with polyethyleneimine (PEI) and hyaluronic acid (HA)(24).

One limitation of MSNs as miRNA carriers is endosomal entrapment, where the miRNAs' biological function is impaired due to degradation. To overcome this, PEI is included in the nanoparticles. PEI becomes protonated in acidic pH, creating a "proton sponge" effect that allows the nanoparticles to escape from endosomes/lysosomes into the cytoplasm. Additionally, the nanoparticles are coated with HA, a biocompatible molecule that reduces protein adsorption to the nanodevices' surface and their immunogenicity. HA also targets the CD44 receptor, which is involved in tumor progression and overexpressed in breast cancer stem cells (BCSCs)(24).

Carboxylated chitosan has pH-sensitive release, endosomal or lysosomal release, and modified release (partial carboxylation) should be studied. This is done to control drug release kinetics to increase drug dosage and reduce cancer cell death(40).

Gemcitabine is a powerful anticancer drug, but some studies have shown that Gemcitabine is resistant to mutated p53 tumors. Ferulic acid inhibits proliferation and induces apoptosis via PI3K/Akt inhibition in osteosarcoma cells Structural study and morphological X-ray diffraction examination demonstrated an ordered hexagonal lattice with mesopores typical of MCM41 material, confirming the well-organized mesoporous silica nanoparticles.

Gemcitabine and ferulic acid might be delivered to PANC-1 cells more effectively and simultaneously thanks to the functionalization of silica nanoparticles with anti-GPC1 antibodies. The combination therapy is more effective than using individual conventional medications, according to the results. This enhances the efficiency of MSNs on cancerous cells and provides a platform for further in vivo research(39).

Nanotechnology allows concurrent diagnostic and therapy; hence earlier detection and treatment can be done and lower mortality rates(16). In their 2021 research, Freidus et al investigated MSNs loaded with Curcumin-Naphthoquinone (CurNQ) for cancer theranostics. CurNQ induced cytotoxicity in two ovarian cancer cell lines and exhibited intense fluorescence when soluble. This indicates CurNQ's potential for theranostic applications. However, CurNQ has pH-specific solubility, being soluble at the tumor microenvironment pH of 6.8. Therefore, MSNs are needed to deliver CurNQ to the tumor microenvironment for fluorescence detection. MSN_CurNQ displayed distinctive fluorescence sufficient to identify small clusters of nanoparticles and did not induce cytotoxicity in the healthy fibroblast cell line 3T3, demonstrating cancer-selective toxicity(16).

Quercetin loaded into MSNs also exhibits theranostic effects. Surface modification with Fe_3O_4 enhances its function as a contrasting agent.

Conjugation with folic acid improves the targeting of QN delivery. Additionally, mesoporous silica SBA-15 enhances the activity of QN in vitro and protects it from degradation due to gastric pH(41).

Manganese oxide loaded onto MSNs enables a more precise imaging approach and induces greater cytotoxicity compared to DOX alone. The surface of MSNs is attached with PSA, facilitating a more targeted drug delivery system. PSA-targeted MSNs offer improved imaging accuracy, reducing false positives. This method may allow for earlier detection of prostate cancer and enhance diagnostic accuracy.(23).

In research conducted in 2020, MSNs with two different nano silica structures were used to transform Cisplatin. Mesoporous silica nanoparticles were prepared using the template agent 1-hexadecyl trimethyl-ammonium bromide, which was then incorporated into Cisplatin. Meanwhile, sol-gel silica was prepared very quickly by using more acetic acid in the hydrolysis-condensation reaction of tetraethyl orthosilicate. Cisplatin was also added at the same time.

The silica nanostructure was described by spectroscopy, electronic microscopy, X-ray diffraction, and N2 adsorption-desorption. Using artificial cerebrospinal fluid, cisplatin release tests were performed in vitro. Finally, the toxicity of each silica nanostructure was tested with the C6 cancer cell line(42).

5. Conclusion

Cancer therapy typically exhibits side effects on healthy cells in the human body due to its lack of selectivity. Besides that, it is also susceptible to degradation. Therefore, a drug delivery system using mesoporous silica nanoparticles (MSNs) is needed to reach to targeted sites. MSNs surface can be modified to enhance drug delivery and therapeutic effects. Additionally, the combination of diagnosis and therapy is crucial to improving the prognosis of cancer treatment and reducing mortality rates.

6. References

[1] International Agency for Research on Cancer. Statistics at a glance, 2022 Top 5 most frequent cancers Number of new cases 408 661 Number of deaths 242 988 Number of prevalent cases (5-year) [Internet]. 2024 [cited 2024 Jul 4]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/360-indonesia-fact-sheet.pdf

[2] Brown JS, Amend SR, Austin RH, Gatenby RA, Hammarlund EU, Pienta KJ. Updating the Definition of Cancer. Molecular Cancer Research. 2023;21(11):1142–7.

[3] Nazarian R, Jazirehi AR. Epigenomics and Targeted Therapy in Cancer. Epigenomics. 2014 Dec;6(6):571–5.

[4] Shah J V., Gonda A, Pemmaraju R, Subash A, Bobadilla Mendez C, Berger M, et al. Shortwave Infrared-Emitting Theranostics for Breast Cancer Therapy Response Monitoring. Front Mol Biosci. 2020 Oct 6;7.

[5] Qu Z. Investigating Conventional and Novel Methods for Treatment of Cancer. In: ACM International Conference Proceeding Series. Association for Computing Machinery; 2023. p. 103–11.

[6] Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: Progress, challenges and opportunities. Vol. 17, Nature Reviews Cancer. Nature Publishing Group; 2017. p. 20–37.

[7] Wang Y, Huang L. Composite Nanoparticles for Gene Delivery. Adv Genet. 2014 Jan 1;88:111–37.

[8] Paul S, Hmar EBL, Pathak H, Sharma HK. An overview on nanocarriers. Nanocarriers for Drug-Targeting Brain Tumors. 2022 Jan 1;145–204.

[9] Igaz N, Bélteky P, Kovács D, Papp C, Rónavári A, Szabó D, et al. Functionalized Mesoporous Silica Nanoparticles for Drug-Delivery to Multidrug-Resistant Cancer Cells. Int J Nanomedicine. 2022;17:3079–96.

[10] Vaz-Ramos J, Cordeiro R, Castro MMCA, Geraldes CFGC, Costa BFO, Faneca H, et al. Supercritically dried superparamagnetic mesoporous silica nanoparticles for cancer theranostics. Materials Science and Engineering C. 2020 Oct 1;115.

[11] Saroj S, Rajput SJ. Composite smart mesoporous silica nanoparticles as promising therapeutic and diagnostic candidates: Recent trends and applications. Vol. 44, Journal of Drug Delivery Science and Technology. Editions de Sante; 2018. p. 349–65.

[12] Attia MS, Abdel-Mottaleb MSA, Mohamed EH. Smart nanovesicles for drug delivery. Systems of Nanovesicular Drug Delivery. 2022 Jan 1;367–85.

[13] Saroj S, Rajput SJ. Etoposide encapsulated functionalized mesoporous silica nanoparticles: Synthesis, characterization and effect of functionalization on dissolution kinetics in simulated and biorelevant media. J Drug Deliv Sci Technol. 2018 Apr 1;44:27–40.

[14] Esfahani MKM, Islam N, Cabot PJ, Izake EL. Development of Thiabendazole-Loaded Mesoporous Silica Nanoparticles for Cancer Therapy. ACS Biomater Sci Eng. 2022 Oct 10;8(10):4153–62.

[15] Wang D, Yu D, Liu X, Wang Q, Chen X, Hu X, et al. Targeting laryngeal cancer cells with 5-fluorouracil and curcumin using mesoporous silica nanoparticles. Technol Cancer Res Treat. 2020;19.

[16] Freidus LG, Kumar P, Marimuthu T, Pradeep P, Choonara YE. Theranostic Mesoporous Silica Nanoparticles Loaded With a Curcumin-Naphthoquinone Conjugate for Potential Cancer Intervention. Front Mol Biosci. 2021 May 20;8.

[17] Torabi M, Aghanejad A, Savadi P, Barzegari A, Omidi Y, Barar J. Fabrication of mesoporous silica nanoparticles for targeted delivery of sunitinib to ovarian cancer cells. BioImpacts. 2023 May 1;13(3):255–67.

[18] Edalatian Tavakoli S, Motavalizadehkakhky A, Homayouni Tabrizi M, Mehrzad J, Zhiani R. Study of the anti-cancer activity of a mesoporous silica nanoparticle surface coated with polydopamine loaded with umbelliprenin. Sci Rep. 2024 Dec 1;14(1).

[19] He L, Habibovic P, van Rijt S. Selenium-incorporated mesoporous silica nanoparticles for osteosarcoma therapy. Biomater Sci. 2023 Apr 19;11(11):3828–39.

[20] Abouaitah K, Hassan HA, Swiderska-Sroda A, Gohar L, Shaker OG, Wojnarowicz J, et al. Targeted nano-drug delivery of colchicine against colon cancer cells by means of mesoporous silica nanoparticles. Cancers (Basel). 2020 Jan 1;12(1).

[21] Laranjeira MS, Ribeiro TP, Magalhães AI, Silva PC, Santos JAM, Monteiro FJ. Magnetic mesoporous silica nanoparticles as a theranostic approach for breast cancer: Loading and release of the poorly soluble drug exemestane. Int J Pharm. 2022 May 10;619.

[22] Ghobadi M, Salehi S, Ardestani MTS, Mousavi-Khattat M, Shakeran Z, Khosravi A, et al. Amine-functionalized mesoporous silica nanoparticles decorated by silver nanoparticles for delivery of doxorubicin in breast and cervical cancer cells. European Journal of Pharmaceutics and Biopharmaceutics. 2024 Jun;114349.

[23] Du D, Fu HJ, Ren W wei, Li XL, Guo LH. PSA targeted dual-modality manganese oxide–mesoporous silica nanoparticles for prostate cancer imaging. Biomedicine and Pharmacotherapy. 2020 Jan 1;121.

[24] Garrido-Cano I, Adam-Artigues A, Lameirinhas A, Blandez JF, Candela-Noguera V, Lluch A, et al. Delivery of miR-200c-3p Using Tumor-Targeted Mesoporous Silica Nanoparticles for Breast Cancer Therapy. ACS Appl Mater Interfaces. 2023 Aug 16;15(32):38323–34.

[25] Mohebian Z, Babazadeh M, Zarghami N. In Vitro Efficacy of Curcumin-Loaded Amine-Functionalized Mesoporous Silica Nanoparticles against MCF-7 Breast Cancer Cells. Adv Pharm Bull. 2023;13(2):317–27.

[26] Lin M, Yao W, Xiao Y, Dong Z, Huang W, Zhang F, et al. Resveratrol-modified mesoporous silica nanoparticle for tumor-targeted therapy of gastric cancer. Bioengineered. 2021;12(1):6343–53.

[27] Abrishami A, Bahrami AR, Nekooei S, Sh. Saljooghi A, Matin MM. Hybridized quantum dot, silica, and gold nanoparticles for targeted chemo-radiotherapy in colorectal cancer theranostics. Commun Biol. 2024 Dec 1;7(1).

[28] Wang S, Wo L, Zhang Z, Zhu C, Wang C, Wang Y, et al. Delivery of LINC00589 via mesoporous silica nanoparticles inhibits peritoneal metastasis in gastric cancer. Cancer Lett. 2022 Nov 28;549.

[29] Ugalde-Arbizu M, Aguilera-Correa JJ, García-Almodóvar V, Ovejero-Paredes K, Díaz-García D, Esteban J, et al. Dual Anticancer and Antibacterial Properties of Silica-Based Theranostic Nanomaterials Functionalized with Coumarin343, Folic Acid and a Cytotoxic Organotin(IV) Metallodrug. Pharmaceutics. 2023 Feb 1;15(2).

[30] Cunha C, Marinheiro D, Ferreira BJML, Oliveira H, Daniel-da-Silva AL. Morin Hydrate Encapsulation and Release from Mesoporous Silica Nanoparticles for Melanoma Therapy. Molecules. 2023 Jun 1;28(12).

[31] Farjadian F, Faghih Z, Fakhimi M, Iranpour P, Mohammadi-Samani S, Doroudian M. Glucosamine-Modified Mesoporous Silica-Coated Magnetic Nanoparticles: A “Raisin-Cake”-like Structure as an Efficient Theranostic Platform for Targeted Methotrexate Delivery. Pharmaceutics. 2023 Oct 1;15(10).

[32] Lee J, Kim JH, You DG, Kim S, Um W, Jeon J, et al. Cavitation-Inducible Mesoporous Silica–Titania Nanoparticles for Cancer Sonotheranostics. Adv Healthc Mater. 2020 Oct 1;9(19).

[33] Amin MU, Ali S, Ali MY, Tariq I, Nasrullah U, Pinnapreddy SR, et al. Enhanced efficacy and drug delivery with lipid coated mesoporous silica nanoparticles in cancer therapy. European Journal of Pharmaceutics and Biopharmaceutics. 2021 Aug 1;165:31–40.

[34] Qin G, Xie W, Luo X, Zou G, Mo Q, Zhong W. Manganese-doped stellate mesoporous silica nanoparticles: A bifunctional nanoplatform for enhanced chemodynamic therapy and tumor imaging. Microporous and Mesoporous Materials. 2024 Apr 15;370.

[35] Cordeiro R, Carvalho A, Durães L, Faneca H. Triantennary GalNAc-Functionalized Multi-Responsive Mesoporous Silica Nanoparticles for Drug Delivery Targeted at Asialoglycoprotein Receptor. Int J Mol Sci. 2022 Jun 1;23(11).

[36] Almomen A, Alhowyan A. A Comprehensive Study on Folate-Targeted Mesoporous Silica Nanoparticles Loaded with 5-Fluorouracil for the Enhanced Treatment of Gynecological Cancers. J Funct Biomater. 2024 Mar 1;15(3).

[37] dos Apostolos RCR, Andrada A de S, Oliveira AF, Neto ESF, de Sousa EMB. pH-Sensitive Hybrid System Based on Eu3+/Gd3+ Co-Doped Hydroxyapatite and Mesoporous Silica Designed for Theranostic Applications. Polymers (Basel). 2023 Jun 1;15(12).

[38] Guo X, Zhu M, Yuan P, Liu T, Tian R, Bai Y, et al. Supporting Information for Facile formation of hierarchical mesoporous silica nanocarriers for tumor selective multi-model theranostics. 2021.

[39] Estevão BM, Comparetti EJ, Rissi NC, Zucolotto V. Anti-GPC1-modified mesoporous silica nanoparticles as nanocarriers for combination therapy and targeting of PANC-1 cells. Mater Adv. 2021 Aug 7;2(15):5224–35.

[40] Lohiya G, Katti DS. Carboxylated chitosan-mediated improved efficacy of mesoporous silica nanoparticle-based targeted drug delivery system for breast cancer therapy. Carbohydr Polym. 2022 Feb 1;277:118822.

[41] Mishra S, Manna K, Kayal U, Saha M, Chatterjee S, Chandra D, et al. Folic acid-conjugated magnetic mesoporous silica nanoparticles loaded with quercetin: A theranostic approach for cancer management. RSC Adv. 2020 Jun 17;10(39):23148–64.

[42] Ortiz-Islas E, Manríquez-Ramírez ME, Sosa-Muñoz A, Almaguer P, Arias C, Guevara P, et al. Preparation and characterisation of silica-based nanoparticles for cisplatin release on cancer brain cells. IET Nanobiotechnol. 2020 May 1;14(3):191–7.