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Review Article

Mesoporous Silica Nanoparticles: A Promising Portal for Diagnosis and Treatment for Chronic Diseases

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ABSTRACT

Nanotechnology is a promising technology in the creation of novel strategies in the field of the healthcare domain. Nano distribution of pharmaceuticals emerging new features for enhanced targeted drug delivery in the diagnosis of chronic disorders like cancer, AIDs and Alzheimer's disease. Numerous types of nanocarriers were established in the Nanotechnology. Mesoporous Silica Nanoparticles (MSNs) are an inorganic form of nanoparticle having specific characteristics like tunable pore size, particle size, suitable morphology and surface functionalization. These attributes show effective loading of therapeutic agents, including micro molecules, genes, proteins and peptides through chemical bonding. Through improved bioavailability, controlled medication release, focused drug delivery and lesser adverse effects, mesoporous silica nanoparticles have largely advanced in the treatment of chronic illnesses. MSNs have many applications, especially in the medical field like Bioimaging, target specificity, pH stimuli response and Thernostatics, etc., Cancer is the most prevailing disease across the world, in various therapies were established using MSNs to increase the medicine's solubility and better delivery of the medication. By integrating poorly soluble medications into their hollow structure, MSNs increase their bioavailability. It allows for lower dosage forms and reduces adverse side effects.

Keywords: Bioimaging, Biomedical applications, Bio-sensing and cell tracing, Controlled release, pH stimuli responsiveness, Targeted drug delivery, Theranostics.

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INTRODUCTION

In recent decades, Nanotechnology has been developing substantial advances in the formulation, analysis, manufacturing process, and use of components, structures, devices, and systems at the nanoscale. Nanotechnology is one of the most promising technologies of the 21st and researchers have explored it as a novel approach to medical research. Especially, emerging advanced tools in the medical field by developing nanomedicine and nano drug delivery systems for target drug delivery to improve treatment efficiency in various chronic disorders.[1] Nanoparticulate drug delivery system terminus gene therapy, cancer therapy, AIDS therapy and Alzheimer's therapy also play a role in crossing the blood-brain.[2] While formulating nanoparticles as a delivery system, the main objectives are to attain control over particle size, surface characteristics and API divulge to attain site-targeted drug pursuit and pertinent therapeutic rate and dosage regimen. The drug administered using nano-sized drug carriers is termed Nanocarriers and offers targeted drug delivery. These strategies are effective in poorly soluble, unstable or systemically toxic medications as they extend blood half-lives and reduce side effects. In medical advancements, Mesoporous Silica Nanoparticles (MSNs) an inorganic form of nanoparticles were developed. MSNs provide diverse opportunities in research and development.[3] MSNs are made up of silica, which essentially promotes surface modification through interaction between the silanol group and drug functional groups.[4] Different types of MSNs are shown in Figure 1. MSNs are analyzed by a large range of tunable specific surface area, pore size, alterable particle size, morphology and accessible surface functionalization. Components for nano platform development and components in MSNs-based Theranostics platforms is shown in Figure 2. Cancer is a startling public wellness quandary that impacts millions of people around the globe. WHO's 2022 census revealed 9.7 million cancer deaths and 20 million new malignancy diagnoses, according to the International Agency for Research on Cancer (IARC). In 2050, there will likely be about 35 million new instances of cancer. Cancer mortality rate doubles in 2050 in high HDI Countries. Diagnosing cancer is daunting because cancer cells can disrupt normal cells mechanisms by increasing their number and differentiate at astonishing rates, spread to other organs and easily obtain resistance against standard therapies. Several types of diagnosis are performed such as Conventional

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cancer therapies i.e., Surgeries, chemotherapy and radiotherapy for different kinds of cancers.

Furthermore, these conventional therapies endanger malignant resurgence as they often fail to destroy the complete malignant cell and may also infect the healthy cells and organs during therapies. To overcome this requires the creation of a novel treatment effectively and safely to target tumor cells selectively and explicitly. Over decades emerging nanotechnology in the medical field developed a new approach to diagnosing cancer. The development of mesoporous silica nanoparticles is a novel method for achieving the desired medication delivery without showing severe side effects. MSNs modified as effective carriers for different varieties of anti-cancer agents like small molecules, macromolecules, genes, proteins, etc.[8]

BREAST CANCER

According to IARC, majorly three major types of cancers that affect huge members across the world. In these, Breast cancer poses a challenge to women's mortality rates. Numerous sorts of chemotherapy medicaments have been utilized to diagnose breast cancer, which includes fulvestrant, methotrexate, tamoxifen, vincristine, vinblastine and Taxol.[9] As an antimetabolite agent, the MTX antagonizes the dihydrofolate reductase binding proteins and suppresses proliferation in the multiplication of cells by inhibiting Thymidine synthesis.[10] Due to the hydrophobic nature of MTX, a solution with a physiological pH of 2.95, the point at which it is indicates an antagonistic charge and drug molecules are trapped by the opposite charge through electrostatic interactions.[11,12] Several investigations demonstrate that approaches to distributing medications, involving MTX is delivered *in vitro* using both organic and inorganic nanocarriers adroitly as well as tidily.[13] These innovations promote medication loading capacity and efficiency through a constant release profile. Often major medication delivery implementation endures crucial obstacles to obtaining apt LC by sustaining the carriers specifically less than 100nm. Large particle sizes exceeding 200 nm are established using PEGylated chitosan nanocarriers, that contain polymeric nanostructures with a high capability for loading of MTX.[14] In contrast, reducing the particle size and adapting the newly developed inorganic form of nanocarriers i.e., During the distribution of MTX in high LC, MSNs of the MCM-41 type were also utilized; the particle dimensions exceeded around 20 μm.[15] One of the key problems in drug delivery is that malignant cell growth antagonizes the medication administered at a lesser concentration. The cytotoxic impact of MTX injected by MSN-PMAA has been identified at greater drug concentrations.[16] MSNs are the most advantageous nanocarrier sowing to regulated medication release, precise medication administration, reduced harmful consequences, increased bioavailability, regulated pore dimensions, volume of penetration, high surface area, and reduced drug degradation.[17] This approach describes the enhanced drug delivery of MTX, by various tactics of MSNs' amine alteration has been examined to develop cancer therapy.

LUNG CANCER

The second most challenging cancer is Lung Cancer, also known as Bronchogenic carcinoma caused mainly by the consumption of tobacco worldwide, which can lead to infections that can occur among the air passages. It is anticipated that pulmonary carcinoma, the most prevalent and fatal kind of cancer globally, will rise in prevalence on a global scale as the use of tobacco is increasing.[18-22] Oat cell carcinoma and Non-Small-Cell Lung Carcinoma (NSCLC), the last-mentioned which is again divided into two types of pulmonary cancer stemming from the initial cell. A range regarding current treatments for lung cancer includes biological therapy, targeted drug therapy, radiation treatment, chemotherapy, radio-frequency ablation, and operation.

Chemotherapy, which stops the development of malignant cells often are comprised of a wide range of drugs.[23,24] Issues such as poor permeability, chemical stability, or solubility are examples that are said to behaving unsatisfactory physical and chemical attributes of the medication that can impact drug metabolism and also pharmacokinetics or drug safety.[25,26] Nanoparticle-mediated targeted gene therapy is revolutionizing the treatment of cancer patients worldwide. Lately, Mesoporous Silica Nanoparticles (MSNs) have acquired much awareness for siRNA's delivery into cells. Another collaborative delivery plan has been suggested to reduce the quantity of each medication and attain a combined impact of cancer treatments. In the ongoing research, researchers have examined the potency of collaborative delivery of lung cancer. Therefore, foresee this innovative technique may be extremely helpful to lung carcinoma treatment in the coming days.[27] There's a spike in concern about utilizing nanoparticles that have been inorganically synthesized for distinct life sciences utilizations. Mesoporous silica nanoparticles have lately captivated an essential focus on biomedical applications because of their beneficial structural properties.[28] Mesoporous silica nanoparticles are regarded as potential moieties for siRNA delivery as they provide space for a site of binding and a wide surface area to house siRNA. Because of this purpose, mesoporous silica nanoparticles are generally altered with positively charged (cationic) polymers such as Poly-L-lysine (PLL) or Polyethyleneimine (PEI) for binding negatively charged (anionic) nucleic acids through electrostatic forces.[29,30] There is ongoing interest in advancing the development of molecularly targeted treatment approaches for lung cancer. In the latest studies, researchers have used MSNs as drug delivery vectors and loaded them with photosensitizer chlorine e6 (C6) and conjugated cisplatin prodrug for the combined activity to vanquish cisplatin resistance against lung cancer.[31] In alternative approaches, due to increased oxidative stress in lung cancer cells, camptothecin-loaded redox-responsive nanohybrids employing

gold nanoparticles and MSNs may have a growth-inhibiting impact.[32]

MSN ROLE IN CERVICAL CANCER

Cervical cancer is most prevailing in women. The symptoms are bleeding between periods, lower back pain, foul smell discharge and abnormal discharge. It is caused by Human Papillomavirus (HPV). Many treatments are used such as chemotherapy etc., for the cure of cervical cancer but it may show some side effects. So as an alternative approach, MSNS-formulated medication can be used in treating it. A sequence PAP-LP-MSN and AP-PAP-MSN are two types of naturally modified, MCM-41 type mesoporous silica nanoparticle materials that were developed and characterized. They had varying pore diameters (5.7 nm).[33,34] They employed a phenanthridine activity embedded in an oligonucleotide to selectively decorate the inner pore surface of AP-PAP-MSN and the outer particle surface of PAP-LP-MSN.[35] Although the chemical phenanthridinium itself is impermeable to cell membranes, we demonstrate that live human cervical carcinoma cells (HeLa: Stands the name of a Black woman Henrietta Lacks) may actually internalize both phenanthridine-immobilized PAP-LP-MSN and AP-PAP-MSN materials. We discovered that the phenanthridium groups on the outside of the PAP-LP-MSN nanomaterials could bind to HeLa cell cytosolic oligonucleotides, particularly messenger RNAs, and produce a substantial decrease in cell growth. Conversely, the cellular hazard of AP-PAP-MSN, which had comparable oligonucleotide embedding molecules rooted inside the pores, was considerably decreased once HeLa cells endocytosed it. They anticipate that the approach of promoting mesoporous silica nanoparticle geometry regulation with the specific modification of the two distinct faces (inner porous areas and outer granule areas) will end up in an entirely novel type of small device. Mesoporous silica nanoparticles loaded with photo sensitizer curcumin the resulting drug will increase anticancerous activity against cervical cancer HeLa cells about 3,4 folds time increased activity can be seen.

MSN'S ROLE IN HIV

MSNs are also used in the treatment of HIV. The drugs that are used in the Highly active antiretroviral therapy [HAART] i.e., Ritonavir poor soluble and have high permeability. Due to the lipophilicity of the drug shows a very slow dissolution rate.[36,37] RTV is examined to increase in systemic level for various PI, leading in lesser administration frequency although greater doses may lead to an increase in the toxicity effects in patients which may lead to an increase in side effects.[38,39] Hence it is necessary to adapt innovative formulation methods to increase the bioavailability of drugs. Therefore, majorly recognized formulation for implementing BCS class 2 drugs to attain much greater bioavailability in order to make them more permeable. The

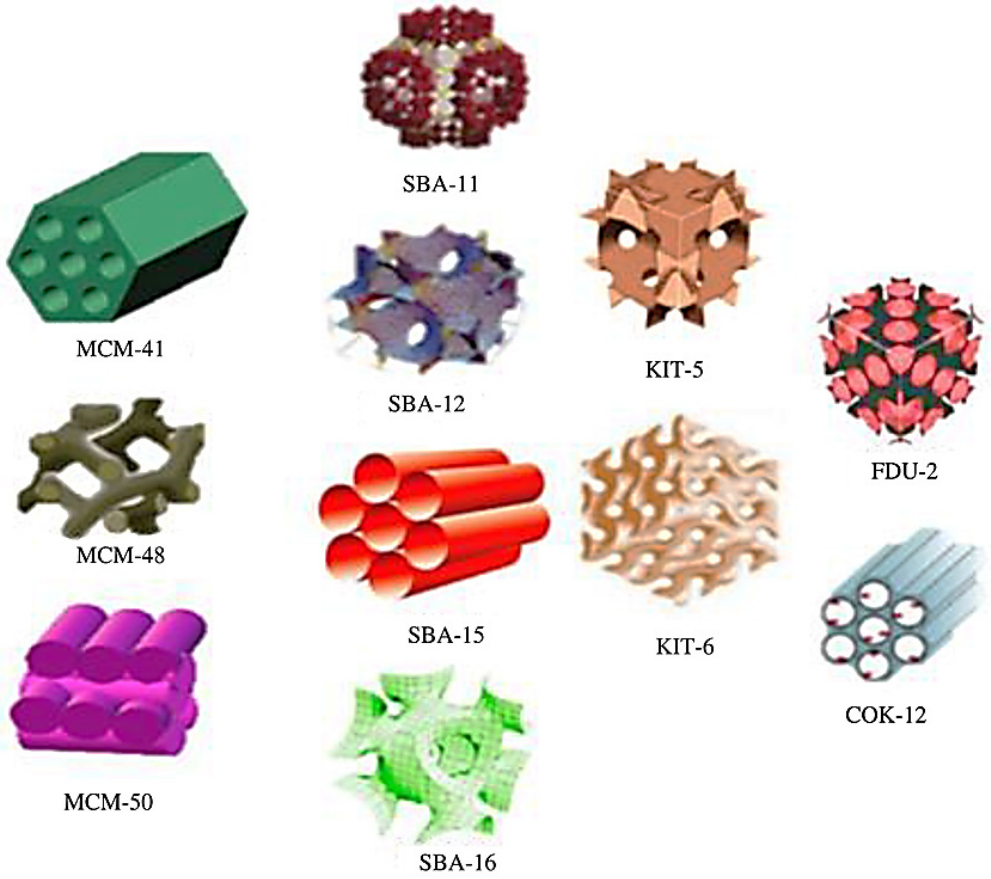

Figure 1: MSN's Role in Cancer Diagnosis (Retrived from Tella JO *et al*., 2022).[4]

duration of dispersion as well as biological absorption of ritonavir were found by granular self-micro-emulsifying medication transport,[40] micron-sized particles[41-43] including complexes.[44,45] From the previous decennium, mesoporous silica nanoparticles are regarded as one unsurpassed, unique strategy for weakly water-soluble drugs to amplify dissolution and bioavailability. Literature poll displays the numerous weakly water-soluble drugs, for example, atorvastatin,[46] celecoxib,[47] Itraconazole,[48] carbamazepine[49] and masitinib[50] can also victoriously loaded to different mesoporous silica nanoparticle types for many kinds of applications, that include regulated medication or DNA departure, bioavailability and solubility enhancement, and selective transporters. Mesoporous silica nanoparticles also have some very impressive properties, such as a larger contact area, increased medication absorption capacity, the ability to change the drug's transparency to an opaque form, a decrease in tiny particles to the nano-meter level that improves the reliability of medications inside the spaces between particles, and the ability to easily modify the pores in accordance with medication release behaviour, which results in an essential medications delivery technique. MSN surface has an unrestrained hydroxyl group which simply interacts with the specific functional group of drug molecules. Because of these characteristics, MSNs have opened an innovative opportunity in the distribution of medications.[51,52] Current insights, morphological and particle dimensions MSNs is to improve the solubility and rate of dispersion of an antibiotic ritonavir, so it eventually influences its bioavailability.

MSN'S ROLE IN ALZHEIMER'S DISEASE

MSNs have recently also been prominent in the diagnosis of neurodegenerative diseases presuming cognitive impairment, by utilizing curcumin's biological assets, which are considered to enhance its curative properties. In the streptozotocin-induced Alzheimer's Disease [AD] hypothesis, curcumin-loaded MSNS with a mixture of thermos-responsive hydrogel substantially improved memory loss and obtained suitable mucoadhesive properties.[53] Both MSN-CCM [Mesoporous silica nanoparticles loaded with curcumin] and HG@MSN-CCM [Hydrogel encapsulated Mesoporous silica nanoparticles with Curcumin]possessed a high permeability rate in the pig nasal cavity, according to an *ex vivo* investigation; additionally, this study explained that the design formula may be an intriguing option for cognitive impairment diagnostics.[54]

Mesoporous silica nanoparticles are used in many applications owing to the pore nature and size, shape and connectivity of mesoporous particles is described in Tables 1 and 2. Utilizing mesoporous silica nanoparticles towards biological implementation encompasses use as imaging and medical judgment agents, explicitness high dissolvability and potency for loading plus delivery regarding the extreme concentrations concerning distinct particles, including:

X-RAYING ALONG WITH BIOMARKING TOOLS

The mesoporous silica nanoparticles can be utilized to quantify biological processes about a long moment whenever applied within a sub therapeutic dose also can easily be removed out of human anatomy once the x-raying procedure is done. The extensive usage of silica-grounded- nano-sensors is seen in optical resonance imaging and MRI or both together.[55] The characteristics of these are biological dispersion, malignant cell aiming efficacy, cellular toxicity and integration track as well as the process for the diagnosis was determined exceptionally by the forthright way regarding the X-raying of mesoporous silica nanoparticles. Main stuff could be bound accompanied along with remedial elements nanocrystals of quantum also stain molecule similar fluorescein-5-isothiocyanate also Isothiocyanate-Conjugated Rhodaime B (RITC). They are familiar with infrared fluorescent probes including Alexa Flour 700 nm and DyLight 680 fluorophore. The luminous mesoporous silica nanoparticles that result can produce greater resolution and obtain statistical data as well as hyperspectral depictions.

SELECTIVE BINDING

Mesoporous silica nanoparticles may be used in targeted site to reduce off-target attachment while enhancing high-affinity binding to specific cellular units or layers. The pair of docile and proactive aiming particularity play a dominant part in enhancing biological attainability.[56] Targeting the particularity belonging to mesoporous silica nanoparticles reduces the dose quantity of a therapeutic agent completely eradicating the poisonous impacts of the therapeutic agent and altering its dosing.[57]

Slow focusing rises the penetrability inside the malignant circulatory channels and also permeates the Assembling of nanocarriers at malignant sites. Also, it lowers medical effectiveness, therapeutic agent exploration as well as various pharmacological agent inhibition forms because of the shortage of cellular selectivity.[58] Combining nanocarriers might be higher via site-specific targeting to form a specific and selective connection with therapeutic agents along the binding area.[59] It can occur when malignant cells are greater exposed to receptors as compared to healthy cells.[60] It demonstrates in the case of mesoporous silica nanoparticles are layered by a positively charged copolymer, these causes a rise in the grasp of mesoporous silica nanoparticles.[61]

In targeted engagement overlay Alterations in mesoporous silica nanoparticles by particular aiming therapeutic agents heighten selectivity from the pharmacological agents to the tumor living unit as compared to thriving units.[62] The main objective is bioactive drugs similarly to folic vitamins, Arg-Gly-Asp polypeptide as well as iron transport protein can be utilized.[63] The best example is, vitamin B9 as folic acid sensor is widely used at various forms of oncogenic cells including breast endometriosis colon, rectal, lung also ovaric.[62,64] Higher efficacy therapeutic

release obtains greater selectivity as well as ligand bond it also can be obtained greater surface-linked drug concentrations molecules these finally enhance polyvalent binding effects.[61]

Ability to fill and transport a large quantity of distinct compounds

Enter the cell via endocytosis and micropinocytosis; MSNs can realize the loading of different kinds of high-concentration classes of multiple cargoes, respectively with a substantial circumference and by managing mesoporous silica nanoparticles chemical composition.[65-67]

Dispersion property

For biomedical applications, MSN should be dispersive because of the accumulation and durability should prevented owing of the integration of cells, which makes it impossible to regulate its distribution throughout the body and results in elevated lethality due to the expanded dimension of compounds.[56] MSN circumference alteration,[68] amino acids and compound covering[69] and a membrane of encapsulation can all reduce the accumulation of molecules.[66,67,70] By employing these techniques, bulkiness and repellent properties are accomplished, leading to the establishment of a steady aqueous distribution of MSNs.[56]

Bio-sensing via cellular imaging

Either in situ or *ex situ*, MSNs' microscopic molecule diameter with adaptable surface chemistry serves as a detection array for identifying targets inside particular cells.[71] Dispersion-associated concerns like intramolecular intensity and luminescence can be prevented by micron-sized particles because mesoporous silica nanoparticles tend to operate their surface with more cellular-detecting compounds or alternative site-directing chemicals, they are a fantastic tool for cellular imaging.[72]

Biomedical photonics

Through the precise exterior appearance of MSNs, a translucent silica-polymer that has low-temperature extension and good durable properties can be formed.[73] Such greater-translucent MSN polymers are used in electronic gadgets such as Optical waveguide film, photovoltaic cell surrounds, and also lenses for Oled.

CYCLODEXTRIN-FUNCTIONALIZED MSNS

MSNs employ an externally triggered regulated ejection mechanism. The mercapto-acetic acid-encapsulated Cyclodextrin tiny particles had been scientifically synthesized as detachable curbs to inhibit MSNs and incorporated medications and synapses. The encapsulated components were freed from the channel after the disulfide bond between Mesoporus silica nanoparticles and Cyclodextrin curbs was broken with the aid of several di-sulfide-decreased chemicals.[74] As broadly known, several individuals worldwide are affected by carcinoma, arguably regarding a life-threatening illness. The prevalent diagnosis for cancer is surgery, chemotherapy, radiotherapy, etc., but many of the patients are affected with major side effects.[75] The propensity in recent times is to innovate utilizing Molecular engineering with the combination of diverse pharmaceutical and technical areas, with the primary goal of tackling and curing malignancy is described in Table 3.

In the process of research in cancer therapy, many inorganic and organic carriers such as quantum dots, phospholipid bilayers, Biopolymer nanocarriers, Polymeric nano assemblies and ferrofluids had demonstrated. Furthermore, distinct nanoporous solids are scrutinized as nanoporous mediators, comprising graphene, bauxite, quartz, etc., with their limited biocompatibility. For instance, with openings that varied from 2 to 7 nm, mesoporous bauxite was identified as an ideal material. Mesoporous carbon tiny particles comprising doxorubicin and ibuprofen have been explored for Multimodal therapy cures for breast carcinoma.[76-81]

Therefore, most of the investigations describe that the MSNs are promising nanomaterials used for cancer treatment. MSNs show the targeted drug delivery with enhanced biocompatibility. MSNs have many significant features such as site-specific drug delivery, Imaging biomarkers and smart drug delivery. An intriguing using of the exterior of silica with pores to trigger the release of medications was the strategy in the target site. The controllable release of drugs occurs merely when stimulus from the outside and inside are present, as they have optimal receptivity with no side effects. The feature of multi-functionalizing the surface, MSNs release the drug at specific sites.[76,82]

Some of the nano-systems along with MSNs, can be enclosed in malignant through simple diffusion determines the Enhanced Permeability and Retention effect (EPR). Many studies state that mesoporous silica nanoparticles are biocompatible. The main goal is to achieve targeted drug delivery without severe side effects in tumor diagnosis.[75,82]

MSN usage in Nanomedicine is effective in therapeutics, diagnostics and theragnostic treatment. MSN is also used as a carrier of genetic material and ribonucleic acid. Pharmacogenomics treatment of malignancy aims to provide accurate treatment by reducing the adverse effects of drugs. MSN includes many therapeutic applications for disorders like Hyperglycemia, Autoimmune Disorder and AIDs.[77,83-85]

This nanocarrier core shell is designed by scientists and attracts great attention to research in cancer therapy, where each of the three coatings is sensitive to a different stimulus. MSN representsthe central system. The initial shell is composed of the hyaluronan-fluorescein isothiocyanate layer with a catalytic response, the second disulfide-SiO_2 shell is for glutathione responses and the third zwitter ionic exterior shell is pH-level sensitive. As long as the negative nanocarrier can connect with the positive cellular membrane, the enhanced permeation and

absorption of the nanocarriers surrounding the cancerous cells causes the zwitterionic outer layer to become influenced by pH and turn positive, aiding cellular recovery. After being taken inside the cancerous cells, the high amount of cytoplasmic glutathione may form a link with disulfide to eliminate SiO_2, exposing the hyaluronan, which would initiate the drug's release. This study's objective was to create a medication delivery system coated with various materials of different actions to encourage prolonged periods of blood circulation, efficient cancer uptake and medication release triggered via various impulses. More directly, MSNs work as a primary element in a drug delivery system for anticancer drugs, as the disulfide bonds and hyaluronan regulate the drug release by degradation due to the high presence of glutathione and hyaluronidase in cancerous cells. The insertion of Fluorescein Isothiocyanate (FITC) also allows for drug monitoring and live imaging of cancer cells.[86] MSN-hydroxyapatite drug nanocarriers also provide good loading capacity and biocompatibility with remarkable anti-tumor therapeutic potentials, which may be valid evidence that silica-based. That is to say, creating safe bio-drug systems might expand the knowledge of nanoparticles.[75,85]

MSNs can also significantly emerge in antimicrobial platforms. It demonstrates the incorporation of the antibiotic clofazimine with accruable pores of MSNs with polar and non-polar surfaces. These characteristics show an ideal strategy for controlling the drug release that doesn't impact loading capacity.[87]

Another excellent use of silica-based mesoporous nano-biomaterials is in bone tissue regenerative medicine, which greatly affects human wellness. A huge portion of mankind suffers from osteoporosis and a strong demand for a disorder to treat the situation arises. The most common treatment is rebuilding the bone through surgical treatment by implanting a suitable natural or synthetic material. Such implantable material must be biocompatible, osteo-inductive and osteo-conductive and it has to be osteo-integrated in the damaged bone tissue, where it has to stimulate new bone-cell formation using cells, extracellular matrix, interaction within cells, cellular signaling and growth factors. MSNs were demonstrated to be spectacular medicines and biomolecules using nanocarriers for both *in vitro* and *in vivo* delivery. Moreover, mesoporous silica nanoparticles are widely being used as acrylic implants of bone strengthened

Table 1: Different types of MSNs and their characteristics.[5]

Types of MSNs	Size of MSNs	Structure	Characteristics
MSN as Spheres	25-200 nm	Spheres	High pore volume and surface area. Flexible surface chemistry Low cytotoxicity. Used as an oral dosage form. Rapid clearance from blood. Cancer treatment.
MSN as Rod	AR 2-8	Rod	High surface area. High cellular uptake. High drug loading. As a carrier for MRI contrast agents, it is used in bacterial infection treatment.
MSN as Dendrimers	50-300 nm	Dendrimers	Large size. High drug loading. Idea for loading siRNA/mRNA and insulin in diabetes and also used in the treatment of cervical cancer. Used in mRNA vaccine preparation.
MSN as Donut	S 10 nm	Donut	Limited for surface conjugation only. Not suitable for drug loading.
MSN as Hollow	50-300 nm	Hollow	Biocompatible layer for coating nanoparticles. Application for theranostic drug delivery.
MSN as Bowl	200-300 nm	Bowl	Large size. High cellular uptake. Limited application for drug delivery. Used in the treatment of vein thrombosis.
MSN as Disc	150-600 nm	Disc	Preferential adhesion to vascular endothelial. Broad application for drug delivery.

with polymers.[88] A new combination of hydroxyapatite and mesoporous silica was studied as a potential material for a polymer matrix containing a drug nanocarrier and filler material for the development of a poly(lactide-co-glycoside)/mesoporous SiO_2-hydroxyapatite composite material for application as a drug releasing scaffolds for bone regeneration.[89] The bone, as a natural substrate, is very complex and there is a relationship between the growth factors and the bone regeneration that is also possible to be obtained. As a result, researchers are looking forward to designing tissue engineering for bone that could solve the problems posed by traditional methods of treatment.[88]

Multi-stimuli responsive MSNs

Once the multiple stimuli are combined synergistically, therapeutically triggered delivery systems designed to be operated by them can be employed for the accurate dosing of medications to a targeted site within the body. The functionalization and engineering of MSNs imply that a minimum of two types of reactive molecules or comprising functional groups must be incorporated into the same nano-machine. Feasible pore caps may then be opened by one or the other impulses or concurrently by both. Additionally, creating a cascade of stimuli may be feasible when the procedure of unblocking mesoporous silica nanoparticles is triggered by one stimulus or results in the sequential release of different payloads. The Quantum dots of graphene developed are incorporated in MSN for chemo-Photothermal Therapy (PTT). The Graphene Quantum Dots-Mesoporous Silica Nanoparticles (GQD-MSNs) determine temperature-responsive release and pH characteristics and when exposed to radiation, it efficiently produces heat to destruct malignant cells. Doxorubicin-loaded Graphene Quantum Dots-Mesoporous Silica Nanoparticles (DOX-loaded GQD-MSNs). Inhibit increased absorption efficacy, cell toxicity and greater cytoplasmic accumulation in 4T 1 breast carcinoma cells.[90] More importantly, the conjugation of tumor-targeting ligands with the gatekeepers permits the preparation of drug delivery that responds to stimuli with highly regulated medication release and targeted delivery to particular tumour cells.

As a proof-of-concept, Multipurpose MSNs for focused doxorubicin delivery to specific tumor cells. In this work, amino β-Cyclodextrin (β-CD) rings were adhered to the surface of the MSNs via disulfide bonds was used as a cap to occlude drug moieties inside the mesopores. In this work, Polyethylene glycol-conjugated with Adenovirus (Ad) units and folate molecules were respectively grafted onto the MSNs through the Adenovirus/β-cyclodextrin complexation. The multifunctional MSNs modified with the targeting units of folate were encapsulated. The experiments performed demonstrate an effective process for cellular uptake of the doxorubicin-loaded nanoparticles by HeLa cancer cells that are abundant in folate receptors through receptor-mediated endocytosis. In the same circumstances, the human embryonic kidney's folate-receptor-deficient 293 normal

Table 2: Applications of MSNs.[55-73,90,91]

Applications	Use	References
Imaging and diagnostic agents	Optical resonance imaging and MRI or both together	55
Target specificity	Decreases attachment to the intended organ or tissue that is inconsequential and boosts precise affinity.	56-64
Ability to load along with deliver a high concentration of different molecules	MSNs enter cells via endocytosis, enabling the effective loading of various cargoes.	65-67
Dispersion property	MSN should be dispersive for its stability and its aggregation should be prevented because distribution becomes difficult and causes high toxicity.	56,66-70
Bio-Analysis for Cellular Pathway Mapping	MSNs act as a detector device for both in the laboratory and in living cells detection of objectives among cellular units.	71,72
CDS nanoparticle-capped MSNs	Stimuli-responsive controlled release system	73
Multi-stimuli responsive MSNs	The multiple stimuli are combined synergistically, therapeutically triggered delivery systems designed for increased transport of medicaments to targeted sites within organs.	90, 91

Table 3: MSNs in Biomedical Applications.[75-96]

Uses	Diseases	References
MSNs release the drug at specific sites without severe side effects in tumor diagnosis. MSN is also used as a carrier for DNA and RNA, nanocarriers also provide good loading capacity and biocompatibility with remarkable anti-tumor therapeutic potentials.	Cancer, Hyperglycemia, bone inflammation and AIDs	76-82
MSNs have widely been utilized to strengthen polymers in plexiglass for bone grafts, bone tissue engineering,	bone tissue disorders	83-89
Accurate MSN voids embedding of the antimicrobial clofazimine with aqueous and lipophilic facades.	Microbial infections	90-95

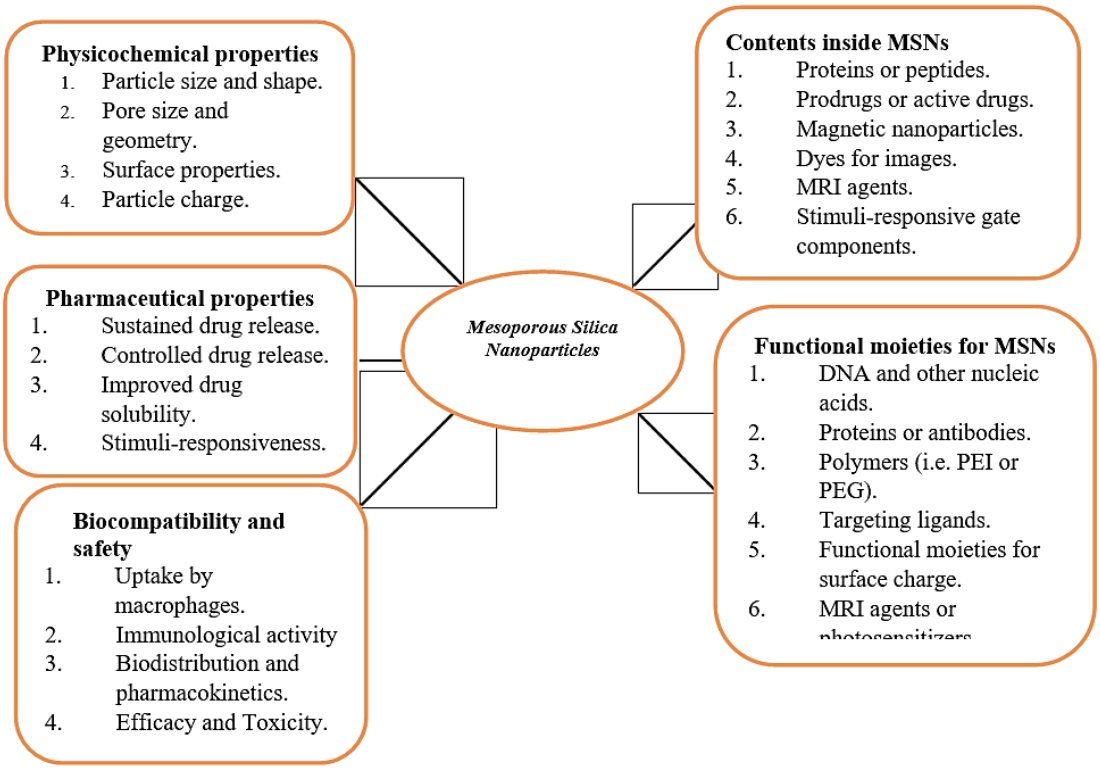

Figure 2: Components for nano platform development and components in MSNs-based Theranostics platforms.[4]

cells showed lesser endocytosis. The key cellular absorption mechanism was through endocytosis, which may cause the acidic pH of endosomes to cause the release of loaded doxorubicin into the cancer cells. After the endosomal escape of nanoparticles and its leakage into the cytoplasm of malignant cells, a large amount of growth-stimulating hormone may be entrapped in the cytoplasm and contribute to the cleavage of disulfide bonds to break the β-CD capping rings, thus promoting more drug release in cancer cells' cytoplasm. Because these multifunctional MSNs are highly effective at cellular absorption through receptor-mediated endocytosis and stimuli-triggered drug release, they may be able to significantly suppress the proliferation of cancer cells. A few of the various materials have been affixed to MSNs for various cancer therapeutic applications.[91]

Used as a carrier for theragnostic

One of the most beneficial nanostructures for therapeutic applications is mesoporous silica nanoparticles. Mesoporous silica nanoparticles have been enhanced to integrate a variety of depiction agents, comprising organic hues, Up-Conversion Particles (UCNPs), MRI juxtaposition agents, and CT (Computed Tomography) juxtaposition agents.

One of the finest and most prominent diagnostic imaging procedures is a Magnetic Resonance Imaging (MRI) tactic that provides sharp, vivid contrary imaging among particular primary tissues and the cells and tissues around them because they are less expensive, have lower radiation and have the ability to conduct real-time scrutiny.[92] Mesoporous silica nanoparticles

containing inorganic nanoparticles, such as gadolinium (Gd) chelates, Fe_3O_4, or manganese oxide, have been used for MRI.[93] In some cases, pH-responsive theragnostic nanoplatforms based on Feo-OH-incorporated mesoporous silica nanoparticles have been reported. The synthesized Ferrous with Mesoporous silica nanoparticles contain turn-on-able T1 MRI accomplishment which can rejoin solid tumours acidic microenvironment to activate T1 signals by promoting ferric ions (Fe^{3+}).[94] Theragnostic nanoplatforms are able to recognize explicit diagnosis and be spoke pharmaceutical initiatives simultaneously. A pioneering versatile mesoporous silica nanoparticles erected by rendering the acetals immobile on the superficial surface of Mesoporous Silica Nanoparticles, pairing to minuscule Lanthanide-infused frequency shifting nanoparticle, and then incorporated with the antineoplastic drug was improved for therapeutics and imaging.[95] Fluorescence dye-based fluorescence optical imaging and fluorescent probes, fluorescent and bioluminescent proteins have gained significant attention in theragnostic. Trimethylammonium groups changed Mesoporous silica nanoparticles adsorbed with indocyanine green were made regarding optical imaging *in vivo*. The biological distribution of MSNs-TA-ICG *in vivo* in rats was demonstrated.[96] Magnetic core-MSNs for computed tomography determined with technetium 99 m were described for previous and distinct Melanoma diagnosis with single photon emission computed tomography.[97]

CONCLUSION

Mesoporous Silica Nanoparticles (MSNs) have proven immense potential in the recognition and management of chronic diseases because of their unique physicochemical properties. Because of its substantial surface area, tunable pore size, and superior biocompatibility, MSNs can be used as targeted delivery systems for diagnostic and therapeutic agents. Targeted delivery through these nanoparticles reduces systemic adverse effects as well as enhance the therapeutic efficiency of medications, especially for chronic conditions like cancer, AIDs and Neurodegenerative disease. MSNs are incredibly versatile for targeted therapy because of their surface functionalization potential, which makes it easier to conjugate specific ligands. Furthermore, they ensure prospective drug delivery due to their ability to encapsulate both hydrophilic and hydrophobic drugs and their controlled-release mechanisms. MSNs have been considered as an essential tool for theranostics because of the simultaneous imaging and therapy made feasible by the integration of diagnostic agents within them. To optimize their therapeutic potential, despite numerous advantages, issues such possible toxicity, biodistribution, and long-term clearance need to be resolved. The goal of current study is to get beyond these restrictions by using sophisticated delivery systems, biodegradable formulations, and surface modifications. MSNs offering innovative strategies to drug delivery and diagnostics have the potential to completely transform the treatment of chronic disorders. The integration of them into clinical practice is anticipated to be accelerated by current advancements in MSN technology and new insights into their biological interactions, delivering prospective for enhanced patient satisfaction and targeted therapy.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

MSNs: Mesoporous Silica Nanoparticles; **UCNPs:** Up-Conversion Particles; **β-CD:** β-cyclodextrin; **HPV:** Human Papilloma Virus; **IARC:** International Agency for Research on Cancer; **NA:** Not Applicable.

SUMMARY

The distinct physicochemical characteristics of Mesoporous Silica Nanoparticles (MSNs) are making them a potential and adaptable platform for the diagnosis and treatment of chronic illnesses. Because of their vast surface area, homogeneous pore diameters, and highly organized, porous structure, these nanoparticles can contain a variety of therapeutic agents, including proteins, nucleic acids, imaging agents, and small molecule medicines. Because of this, MSNs are perfect for applications including controlled release and diagnosis. MSNs can be designed to release their payloads in a controlled and sustained manner, which is particularly advantageous for the treatment of chronic diseases that call for long-term medicine.

MSNs can be modified to incorporate imaging agents like radionuclides, magnetic nanoparticles, or fluorophores in diagnostic applications. This enables non-invasive monitoring and diagnosis of chronic illnesses like cancer, heart disease, and neurological conditions. Because of their small size, they can travel through the bloodstream and gather at specific locations, where they help with high-resolution imaging using methods like PET, MRI, and fluorescence imaging. Effective treatment of chronic illnesses depends on the early detection and tracking of disease development, both of which are made possible by this tailored imaging capabilities.

MSNs may transfer medications, proteins, and nucleic acids therapeutically, which is very helpful in the treatment of complicated chronic illnesses like cancer or neurological diseases. They make it possible to encapsulate several therapeutic compounds, facilitating combination therapy that can improve results and address disease heterogeneity. Furthermore, MSNs are an essential part of personalized medicine because of their

capacity to be customized for certain disease locations or patient requirements, improving bioavailability and increasing therapeutic effects according to a person's genetic and environmental characteristics.

allegedly their potential, a number of obstacles need to be overcome before MSNs are routinely applied in therapeutic settings. Concerns regarding long-term toxicity, stability inside the body, and possible accumulation in organs are among them; these require more research. Regulatory obstacles and production scalability are other obstacles to their clinical translation. MSNs have the potential to completely transform the diagnosis and treatment of chronic illnesses, opening up new possibilities for more efficient, individualized, and focused treatments, provided that research is continued to address these challenges.

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