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# Mesoporous Silica Nanoparticle Nanocarriers

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**ABSTRACT**
Mesoporous Silica Based Nanoparticles[MSNPS] are tremendously versatile and it enables to create variety of nanotherapeutic systems for cancer treatment and to treat other diseases.Because of its transparent nature, flexibility in size, low toxicity and various other advantages it makes a very important drug delivery system. In addition it has also shown some gigantic achievements which forced the researchers to believe that it can change the fate of cancer therapy as it is very deadly disease as well as it can also bring great changes in the drug delivery system.In this review the synthesis and use of MSNPs in various diseases have been highlighted.It is used in treating various deadly diseases like cancer, brain tumor and has a significant use in imaging techniques.Well-ordered mesoporous silica materials are becoming widely used in education since since Mobil researchers first discovered them 20 years ago.The use of Adalah MSNPs as "Nanoparticle synthesis" for delivering highly porous nano particles to cells, medications, and other cargos has a variety of uses.
**KEYWORDS:** Mesoporous silica; Therapeutic biomolecules; Brain Cancer Theranostics; Trifunctionalized silica; Toxicity

## I. INTRODUCTION

Since their discovery 20 years ago by Mobil researchers, the education of well-ordered mesoporous silica resources has flourished. Using colloidal chemistry, you can generate nanoparticles that are consistently sized, porous, and dispersible[1]. Various applications of EISA MSNPs as "Nano carriers" for delivery of mesoporous silica nanoparticles to cells, medicines and other cargos [2].

We discuss our recent efforts to develop MSNPs, which are biocompatible nanocarriers with the following properties: (1) highly visible in a variety of imaging modalities; (2) dispersibility; (3) binding specificity to a specific targeted tissue/cell type; (4) ability to load and deliver large levels of diversified cargos; and (5) triggered or untriggered delivery. [3].

## SYNTHESIS OF MSNPs

### 1. PREPARATION BASED ON SOLUTION

The most common kind of MSNP, MCM-41, is made up of cylindrical mesopores that are aligned in an ordered hexagonal pattern[4][5]. Through the use of a liquid crystal template and an alkylammonium salt, most frequently cetyl trimethylammonium bromide, MCM-41 is produced (CTAB). Amphiphilic surfactant molecules self-assemble at the critical micelle concentration to form mssp in aqueous solution and regular liquid crystal mesophases at greater quantities. Surfactant self-assembly produces hybrid nanocomposites in the case of moisture and hydrophilic precursor of soluble silica, including such silicon, Si(OH)4, or polysilicic acids.

By electric and hydrogen bonding interactions, silica precursors are gathered at hydrophilic surfaces to form an amorphous silica mold of the ordered periodical mesophase. Once the surfactant template has been removed by extraction or calcination, the mesoporous product is created. [6].

### 1. Evaporation-Induced Self Assembly

EISA was created in 1997[7] to control the fabrication of continuous coating mesophases by dip-coating. EISA starts with a homogeneous solution of soluble silica and surfactants in ethanol/water, with a starting concentration of surfactant of conc, cmc. Using any evaporative process, including dipcoating, causes the solvent to evaporate [8][9][10][11][12],gradually raises surfactant concentration, causing silica/surfactant micelles to self-assemble and organise into liquid-crystalline mesophases.

Polydopamine (PDA)[13][14], graphene oxide (GO)[15][16], and hydrogel matrix[17][18] are commonly used as internal or external activates for controlled medication release. However, due of the random pH shifts that occurred during their formation, inner trigger release systems—which react to minute changes in the roundings—faced significant challenges in the processes of cancer and inflammation[19]. The consequences of externally induced slow release controlled by

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Continuous illumination, external pH changes, and incident electromagnetic effects are hence the subject of much investigation. [20][21][22].

Mesoporous silica nanoparticles (MSNs) have been popular in recent years as smart lipid nanoparticles for anticancer therapeutics due to their simple functionalization, huge surface area for drug loading, targeted tumor treatment, or bio-imaging agent. [23] [24][25]. In order to create an effective core-shell MSN-based drug delivery system, MSNs are also combined with inorganic nanocrystals (Au, Ag, Fe3O4, MnO, and CuS). [26].

Gold and magnetic NPs are playing a bigger role in core-shell MSNs because to their unique optical and magnetic capabilities in biological applications. These fundamental type MSNs may be useful because to their high loading, cell target selectivity, bio - imaging agents, sensory cues, drug release, and hyperthermia therapy curative nanoparticle carriers. [27][28][29][30][31].

Due to its significant high surface area and -conjugated nanostructures, graphene (GO) is a biocompatible material with excellent solubility in water, physiological stability, and drug - delivery qualities. [32][33]. Polydopamine (PDA) is simple to include into systems for administering cancer drugs, much like polydopamine, which has a distinct chemical structure, strong biocompatibility, and photo - thermal heating effects. [34]. However, plasmonic gold has a low quantum yield and strong surface plasmon resonance, which enables it to collect near-infrared light (NIR) and transform it into heat energy. [35] [36]. Once coupled with PDA or GO nanosheets, plasmonic gold is expected to have additive photothermal thermal effect on the therapy of cancer cells. [37][38][39]. Additionally, combining heat and chemotherapy in one device would be quite effective in getting rid of a lot of cancer cells. [40][41][42].

Tumor accumulation requires direct injection, targeted tumour embolization, or passive targeting in the case of nanocarriers lacking targeting moieties. As a result, quasi nanocarriers frequently result in unfavourable drug release side effects during cancer therapy, such as negative impacts on surrounding cells (or tissues) and inadequate drug buildup in the cutaction. [43] [44]. In this sense, core-shell magnetic Microspheres have the possible to be a successful beleaguered delivery system where medications are delivered in vivo to a specific location under the influence of external magnetic field. [45] Cancer cells may be specifically targeted by surface functionalizing a more sophisticated platform based on its core type MSNs with natural sources ligand for surface receptors, nucleic acids, peptide, non-immunoglobulin scaffolds, or antibodies. [46]In the current cancer treatment, antibodies, a specialised cancer cell targeting medication with low side belongings and a long plasma half-life, may be significant.[47].

**Mesoporous Silica Nanoparticles as Therapeutic Biomolecule Transporters**

After the initial investigation into using nanometric mesoporous silica as a medication delivery medium [48], several more have been published, involving a diverse range of chemical species. Biomacromolecules, for example, serve a crucial function in living organisms since they are accountable for bio recognition [49], signal transduction[50], and replication pathways, as well as the proper development of tissues and organs. Both hormone signalling and the immune system depend on specific affnity interactions between biomacromolecules, demonstrating the relevance of these species (BMs).Using such ligands and receptors for therapeutic purposes, for example, might assist in the regulation of imbalanced systems and the creation of next-generation medicinal nanodevices in oncology[51][52], tumor immunotherapy[53][54][55], and gene therapy[56][57][58], among many other domains.

Among all known materials, nanomaterials (MSNs) have gained attention as possible drug delivery platforms due to their exceptional biocompatibility, degradability, and biological and chemical robustness. Furthermore, MSNs' distinctive porosity structure allows for the establishment of host–guest interactions, which are important for medication delivery since they allow for the creation of safe settings for labile molecules. In addition, modern silica-based nanotechnology allows for the creation of particles with varied diameters[59][60], pore sizes[61], and structures[62], allowing for fine-tuning of the nanosystems' eventual applications, particularly those meant to convey large cargoes.

The generated outer layers of nanostructures may be easily modified using MSNs and equivalent hybrid particles covered with SiO2 to boost biological stability and hence reduce side effects and potential toxicities. [63][64][65].

One of the most significant factors in a successful therapy is particle diameter. The improved permeability and retention effect acts in a typical window of diameters for cancer treatment, which is between 50 and 300 nm. Such values may, however, be narrowed based on the nanosystem's

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final purpose.Smaller particles, for example, would perform better in circumstances where improved trafficking is needed, whereas the diameter must inevitably be raised in nanosystems intended to serve as biomolecule storage. Recently, we investigated how, for the purpose of nanoparticle-based drug delivery, Mesoporous silica-based nanosystems have better pharmacological profiles than free species[66, 67] and are appropriate platforms for mixing two or more chemical species. Regardless of the possible therapeutic benefit, BM integrity and function over the long term may be compromised when they're not adequately shielded from WBCs and immune functions. Despite the fact that MSN pores can be adjusted to accommodate the largest molecules, the limited protection provided by the vast bulk of solid NP emphasises the role of MSN[68] as programming environments for non-viral matrices and protein carriers, whose porous structure can provide a secure cover for the labile molecules. [69].

MSNs, as previously said, have a huge potential influence on biomedicine; in addition to functioning as carriers, they allow for the production of fancy structures with the majority of useful nanomaterials. Notwithstanding its versatility, however, the use of these resources in clinical studies is still imperfect due to the difficulty in making credible comparisons across diverse systems, as Florence explains. Indeed, based on the expanding number of in vivo trials employing MSNs conducted by numerous groups across the world, it is reasonable to expect that they operate well in living systems, and that MSNs will soon be used in clinical practise.

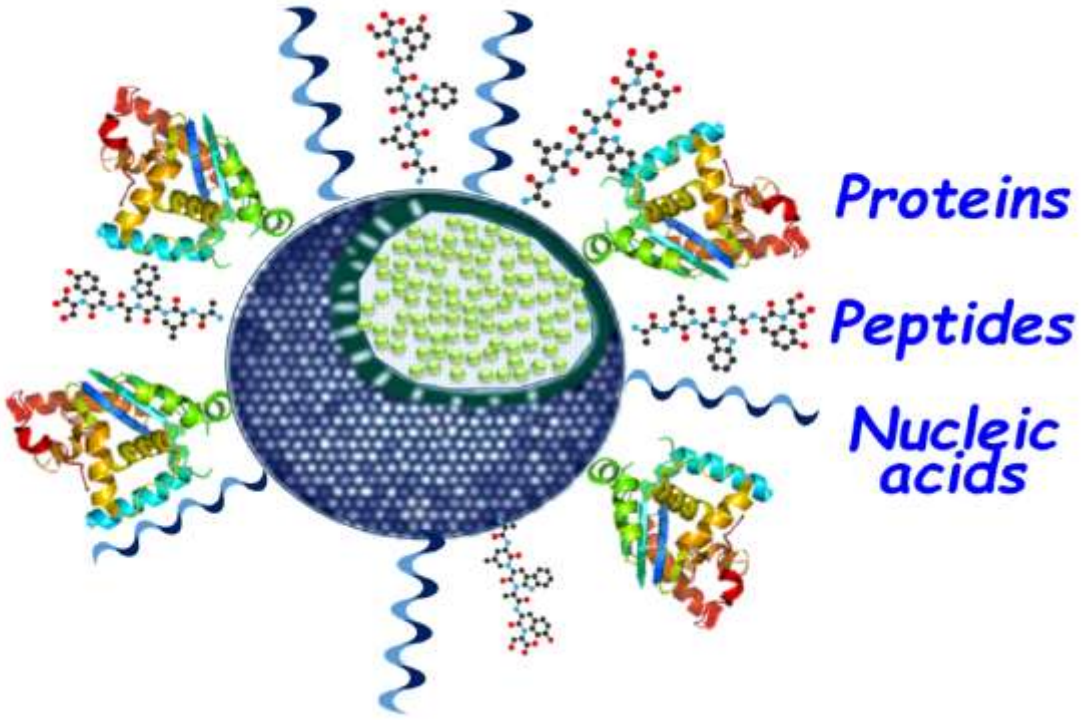


Figure 1 The following are the main types of therapeutic biomolecules that can be delivered utilising mesoporous nanosilica technology[70].

**MSNPs In Cancers**

MSNs have higher potential than traditional drug distribution systems and provide fascinating possibilities for contemporaneous tumour detection and therapy, along with pharmacological and delivery of gene. [71].

**SILICA NANOMATERIALS IN CANCER THERAPY**

The use of nanomaterials provide an excellent platform for cancer detection and diagnosis. Silica-based nanomaterials are significant in cancer treatment because to qualities such as inner pore volume + large surface area,

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programmable and also the pore size, nontoxicity, and biocompatibility.[72].

They have various advantages as a result of these factors.

| Cancer Detection and Diagnosis at the Outset | Used Drug DistributionSystems | MSN-Based Anti-MDR Systems | Reference |
|---|---|---|---|
| Contrast Agents for Imaging | The Passive delivery method is used. | Multiple medications are delivered at the same time. | [73][74] |
| Nano Mesoporous Silica Chips | Lively delivery system is used. | Co-delivery of anticancer medicines/ genes | [75] |
| Fluorescent Silica NPs for Optical Imaging | CR medication transfer methods are used. | Several delivery techniques in combination | [76] |

Early detection and diagnosis are crucial in reducing death and providing suitable and extra real cancer therapy. Tissue biopsy, which includes removing tissues from a patient and examining them for malignant cells, is the most often utilised form of identification. Since the beginning of time, a variety of nanomaterials, including quantum dots (QDs)[77], gold nanoparticles[78], and, finally, silica nanomaterials[79], have been utilised for cancer detection and diagnosis.

Although quantum dots may potentially be applied in biomedicine for in situ optical imaging and drug delivery, further research into their toxicity is needed before they can be extensively used in medical diagnosis/ therapy. [80].

However, because silica NPsare nontoxic, biodegradable plus they have a large loading capacity for a range of drugs, they are good candidates for safe and effective therapy.

**SILICA NANOMATERIALS AS IMAGING CONSTRAST AGENTS**

Magnetic resonance imaging and ultrasound (US) are often applied to identify cancer because of their low cost, capacity for RT monitoring, and minimumradioactivity[81]. The most often used MRI or US agents, however, are tiny molecules made of Ca and gadolinium chelates and metallic ions, being unable to produce high contrast pictures that might aid in the early detection of cancer as a downside [82]. Silica nanoparticles have promise for the future of diagnostic procedures since they have a large drug loading capacity, high strength, and could swiftly break down in the figure in an appropriate manner. Target-specific and non-toxic MRI and US contrast agents are made of silica nanoparticles.

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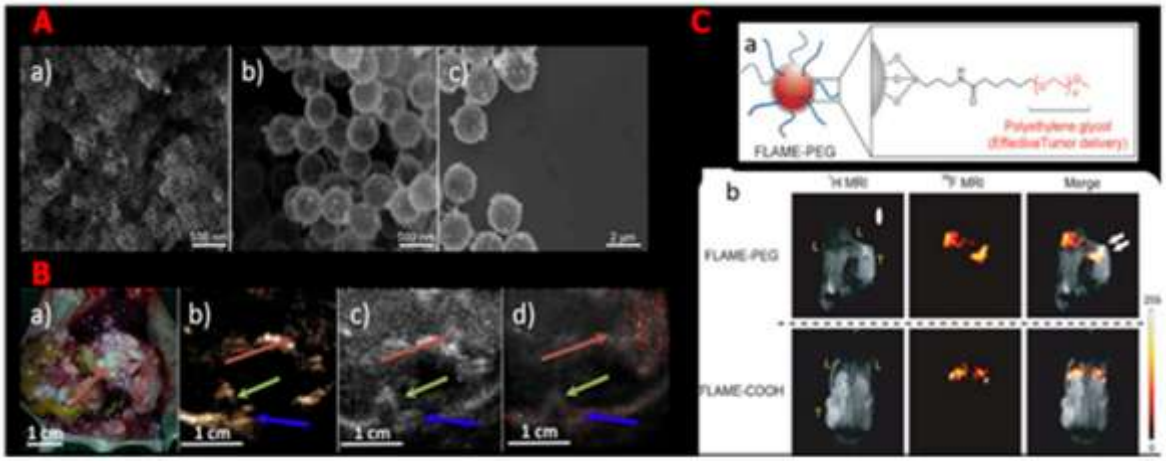


Figure 2 Ultrasound and attractivetimbre imaging difference agents made of silica nanoparticles.

**SILICA CHIPS MESOPOROUS NANOMATERIALS**

High molecular weight proteins can be separated from low molecular weight proteins using nanoporous silica chips[83]. The increasing concentration of low molecular weight proteins enhances signalling. Additionally, mesoporous silica chips' sensitivity and selectivity for sorting low MW proteins and locating cancer biomarkers are enhanced by surface engineering alongwith metallic ions[84] as well as other functional groups[85]. As a result, bi functional mesoporous chips provide a trustworthy signal for the early identification of disorders such as tumours

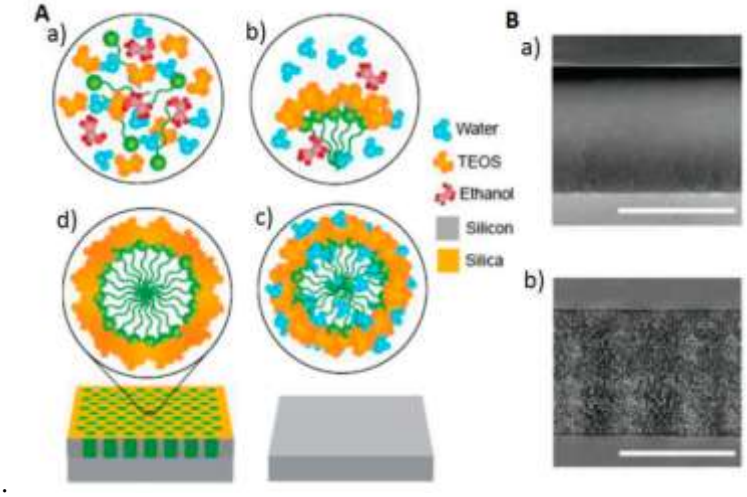


Figure 3 shows the creation and assembling of mesoporous silica proteomic chips. Fresh solution (A), the formation of micelles (B), the spin-coating procedure that causes self-assembly (C), and an enlarged picture of a pore after elevated temperature ageing (D). (B) SEM/TEM cross-sectional images of the GX6 chips on the surfaces of a raw silicon wafer and a silicon wafer covered with MP film (lower). [86].

**Brain Tumour Theranostics using Mesoporous Silica Nanoparticles**

The most lethal type of brain tumour is called glioblastoma multiforme , a high-grade malignant glioma that grows quickly and destroys the nearby brain parenchyma. One of the deadliest cancers is brain cancer due to its strong chemo-resistance, frequent relapses, fast cognitive deterioration, and dismal survival rates. [87][88][89][90According to statistics, only around 5% of patients survive for longer than five years. This is due to three things: Three factors contribute to tumour recurrence: first, the blood-brain barriers (BBB), which blocks the passage of the majority of

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chemotherapy applications; second, the fibrotic nature and fast growth of brain tumours, which results in partial clearance; and third, chemotherapy resistance. Because of this, traditional chemotherapy for brain cancer frequently fails to work. As a result, there is an urgent need to make novel ways for breaking down barriers and increasing the efficacy of brain cancer therapies. [91][92][93][94].For brain cancer theranostics, nanomedicine presents a viable therapeutic prospect. The gradual advancement of nanomaterials has provided a plethora of possibilities for overcoming the numerous restrictions of brain cancer treatment.

In a recent research, Liu et al. created PSiNPs in 3 sizes to penetrate the BBB and assessed them in vivo/ in vitro. Animal tests, The in vivo investigation included both superficial in vivo studies and ex vivo optical imaging following injection into the artery. [95].

A Cy5 fluorophore was integrated into the silica framework of the 100 nm nanoparticles that Bertucci et al. created in a ground-breaking finding. Then, temozolomide (TMZ), a glioma-treating anticancer medication, was added to this. The surface of the particles was subsequently treated with a methacrylate nucleotide (R8-PNA) molecule that specifically targets the miR221 microRNA. The TMZ-loaded mesoporous nanomaterial had stronger pro-apoptotic effects, and the coupling of TMZ and R8-PNA in the nanotubes successfully induced apoptosis in the thing or phenomenon T98G cell line (70.9 percent of apoptotic cells). [96].

**Nanomaterials Made Of Mesoporous Silica Used In Plant Gene Transfer**

Cell markers for bioimaging (fluorescent and compelling resonance imaging)[97] Only a few of the medicinal uses of mesoporous nanoparticles include stimuli-responsive medicine delivery[98], Delivery of proteins and enzymes[99][100], Transfection of RNA or DNA [101][102][103], and multifunctional theranostic agents[104][105] are some more theranostic techniques (MSNs). The susceptibility of biological origin indicators to MSNs, such as digestibility, in vitro cytotoxicity, and biocompatibility, has been established in mammalian systems. Nonetheless, unlike human cells, plant cells have a distinct morphology. Several studies are now being undertaken to investigate nanoparticle phytotoxicity[106][107][108] as well as their influence on plant development. [109][110][111].

Despite a lack of plant sciences study, reports show that nanoparticles, such as single and multi-walled carbon nanotubes, can be used in cell membranes (carbon-coated) [112][113]. Carbon nanotubes [114], nanoconjugates of mesoporous TiO2-alizarin red S [115], [116][117], CdSe/ZnS qds [118], and nanoscale magnetic particles. Numerous pathways exist for the nanoparticles to penetrate plant cells, including drilling new holes and binding to transporter and ion channel proteins [119]. Numerous studies have proposed utilising nanoparticles as drug delivery methods. [120].

Chang et al. (2013) demonstrated that MSNs may infiltrate the cell wall and function as a carrier in Particularly among young roots to use a simple co-culture approach (Figure 4) [121].The carriers benefit from having access to the entire tissue and other crucial organelles. There are several advantages to contemporary technology: I MSNs deliver DNA to deeper layers of the skin such as the cortex and endodermis; Plant cell walls can dissolve without the need of an enzymatic process;[122] MSNs with nanopores show potential as multifunctional vehicles for delivering numerous compounds into cell in intact plants, according to the discovery of an energy-independent method for MSN absorption. MSNs may also go to organelles like as chloroplasts and nuclei, where they're being targeted for distribution.[123]

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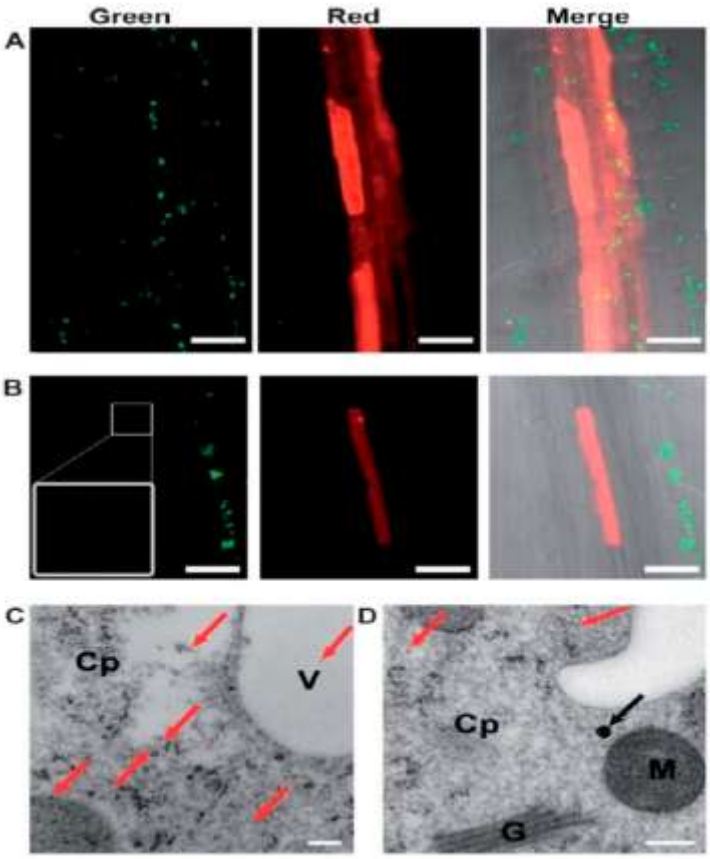


Figure 4: Gene distribution (MSN-mediated). (A,B) Confocal microscopy was used to visualise Arabidopsis root cells 48 hours following DNA-MSN therapy (1:100 ratio). Both cortical (B) and endodermal (A) cells showed expression of genes (mCherry protein; red). The cells that expressed mCherry have TMAPS/F-MSNs (B, green channel). After DNA-MSN complexes incubation, root cell TEM shows immunogold-labeled mCherry protein, 50 mm scale bars (C,D). The gold-labeled mCherry proteins are shown by red arrows. The same cell contains both mCherry protein (red arrows) and TMAPS/F-MSNs (black arrows) (D). The scale bars of 200 nm are employed. The letters G, Cp, M, and V stand for the Golgi apparatus, cytoplasm, mitochondria, and vacuole, respectively.

**Tri-functionalized Silica Nanomaterial in Comprehensive Cancer Thernostics**

According to Shih-Hsun et al., the development of three silica nanoparticles (MSNs) capable of integrating the triad of target, imaging, and treatment in a single unit was a significant accomplishment in the field of theranostics. (Figure 5). Mesoporous silica nanoparticles have been modified to include contrast agents, Pharmacological cargos employed as therapeutic mediators, as well as biotechnological binders for highly focused particle transport (MSNs). [124]. ATTO647N, a near-infrared (NIR) fluorescence juxtaposition agent, was introduced directly into the nanomaterial's silica structure to assess the opacity of most tissue at close (NIR) wavelengths and to improve the surface accessible for succeeding targeting ligands and conjugating pharmaceuticals. State troopers (PdTPP), an o2 precious metal-based photocatalyst, were fused in mesoporous nanoparticle nanochannels to facilitate photodynamic therapy (PDT). The allows for a reduction PdTPP was internalised when mesoporous nanomaterials' surface cRGDyK peptides were used to target cancer cells' overexpressed avb3 integrins (Figure 6). Cells from the theranostic area that were evaluated in vitro had a very strong therapeutic benefit in addition to good targeting and minimal harm. [125]. A photosensitizer (PS) and a particular wavelength of light are used in photodynamic therapy, a cutting-edge cancer treatment technique[126]. Mesoporous silica nanomaterial canals may be filled with photosensitizer (PS) in large numbers, and to target

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MSNs or increase their reactivity, the exterior layer of the nanomaterials can be chemically changed. [127]. In order to achieve maximum cytotoxicity, the temporary one O2 must immediately interact with particles in intra-cellular pathways, and PS can be protected from damaging environments thanks to the unique structure of the nanomaterials. Protoporphyrin IX, a well-studied photosensitizer (PS), was easily absorbed by cells and induced phototoxicity that was affected by the amount of time exposed and the brightness of the light. The primary benefit of photodynamic therapy is that it only results in cytotoxicity in the regions where the radiation is applied, making it an excellent method for the treatment of cancercells outside of these regions are unaffected. The silica nanoparticles' well-organized mesoporous structure increased the energy transfer rate by 93%. Breast cancer prototypes were tested in vitro and in vivo, and the cytotoxicity generated by 1 O2 as a result of Intracellular energy transmission was also extremely efficient.[128].

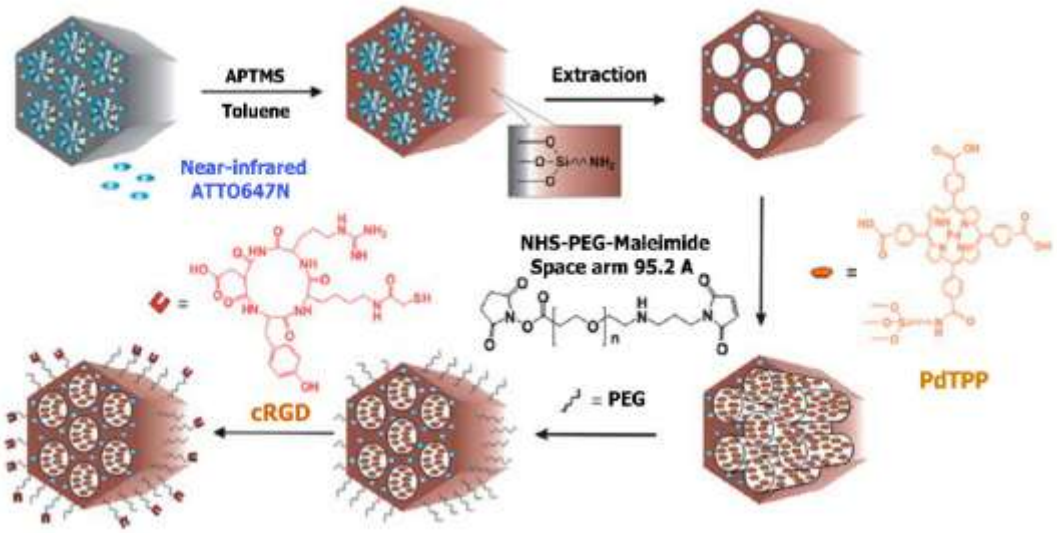


Figure 5: A647@MSN-RGD-PdTPP, a mesoporous silica nanomaterial (MSN) with three functionalities, was created. In that sequence, a cancer targeting ligand, atto 647N, and a photodynamic treatment photosensitizer (APTMS-PdTPP) were utilised to functionalize the nanomaterials (cRGD)[129].

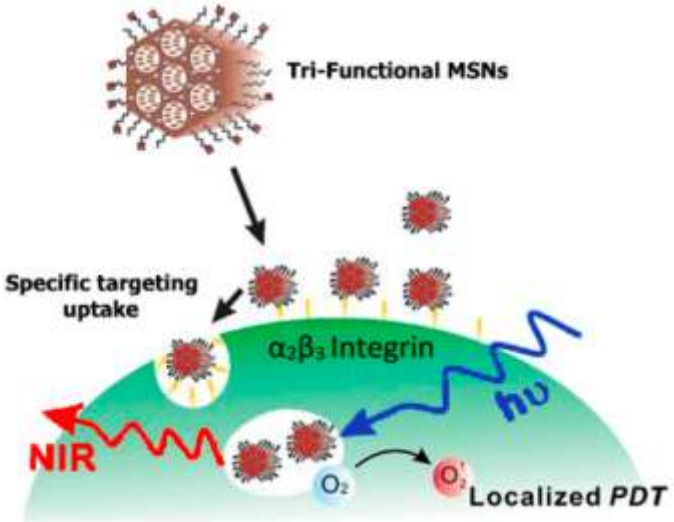


Figure 6 Tri-functionalized mesoporous nanomaterials that have separate domains for localised photodynamic treatment photosensitizers, traceable imaging, and competent targeted delivery[138].

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**TOXICITY OF MSNPS**

Any application of a nanocarrier must consider nanoparticle toxicity. Over a century has been spent studying the toxicity of crystalline and amorphous silicon dioxide, particularly in relation to silicosis. [130][131][132][133], and much more recently, the toxicity of nanoparticles has been carefully researched since, as compared to coarse grained silicaThe increased surface-to-volume ratio of nanoparticles may result in improved cellular interactions and novel toxicity pathways.[134]. Despite several studies on the dangers of crystalline and amorphous silicas [135][136][137][138]The mechanism(s) through which exposure to silica results in silicosis is yet unclear, and literature descriptions are frequently contradictory. When surface silanol (SiOH) groups are dissociated to create SiO, they can form hydrogen bonds with filmmechanisms [140] may interact with positive charge tetraalkylammonium-containing phospholipids electrostatically[139] (above the isoelectric point of silica at pH 2-3). Both these interactions result in strong contacts and it may result in membranes lysis. When electrons on the glass substrate come into contact with water, they form superoxide radicals (ROS), including the hydroxyl radical HO•, one of humanity's greatest more reactive species[141]. ROS can harm cells by rupturing cell walls (necrosis) or causing programmed cell death (apoptosis). ROS can stimulate the production of cytokine and other proinflammatory cytokines in addition to promoting mutation and carcinogenesis at sub - lethal levels.

## II. CONCLUSION

A drug could be administered to the target site of action in a variety of ways. MSNPs provide a number of benefits and act as a vehicle for the administration of medications. When compared to other nanocarriers, it has demonstrated advantage for the transport of anticancer drugs in terms of cancer therapy. It is also used in brain cancer and plant gene delivery. Its use in oral medication administration has also been demonstrated in studies. MSNPs based drug delivery system can also get conjugated with multifunctional molecules, which can be used in several platforms of drug delivery.

## REFERENCES

[1]. Mesoporous Silica Nanoparticle Nanocarriers: Biofunctionality and Biocompatibility DERRICK TARN,‡ CARLEE E. ASHLEY,)MIN XUE,‡ ERIC C.CARNES,§ JEFFREY I. ZINK,*ANDC. JEFFREY BRINKER*, §,^, † 2013, 46, 3, 792–801, https://doi.org/10.1021/ar3000986

[2]. Mesoporous Silica Nanoparticle Nanocarriers: Biofunctionality and Biocompatibility DERRICK TARN,‡ CARLEE E. ASHLEY,)MIN XUE,‡ ERIC C.CARNES,§ JEFFREY I. ZINK,*ANDC. JEFFREY BRINKER*, §,^, † 2013, 46, 3, 792–801, https://doi.org/10.1021/ar3000986

[3]. Mesoporous Silica Nanoparticle Nanocarriers: Biofunctionality and Biocompatibility DERRICK TARN,‡ CARLEE E. ASHLEY,)MIN XUE,‡ ERIC C.CARNES,§ JEFFREY I. ZINK,*ANDC. JEFFREY BRINKER*, §,^, † 2013, 46, 3, 792–801, https://doi.org/10.1021/ar3000986

[4]. Kresge, C. T.; Leonowicz, M. E.; Roth,W. J.; Vartuli, J. C.; Beck, J. S. Orderedmesoporous molecular sieves synthesized by a liquid-crystal template mechanism. Nature 1992, 359,710–712.

[5]. Beck, J. S.; Vartuli, J. C.; Roth, W. J.; Leonowicz, M. E.; Kresge, C. T.; Schmitt, K. D.; Chu,C. T. W.; Olson, D. H.; Sheppard, E. W. A new family of mesoporous molecular sieves prepared with liquid crystal templates. J. Am. Chem. Soc. 1992, 114, 10834–10843.

[6]. Mesoporous Silica Nanoparticle Nanocarriers: Biofunctionality and Biocompatibility DERRICK TARN,‡ CARLEE E. ASHLEY,)MIN XUE,‡ ERIC C.CARNES,§ JEFFREY I. ZINK,*ANDC. JEFFREY BRINKER*, §,^, † 2013, 46, 3, 792–801, https://doi.org/10.1021/ar3000986

[7]. Brinker, C. J.; Lu, Y. F.; Sellinger, A.; Fan, H. Y. Evaporation-induced self-assembly:Nanostructures made easy. Adv. Mater. 1999, 11, 579–585.

[8]. Guo, Y. X.; Soyez, H.; Dunn, B.; Huang, M. H.; Zink, J. I. Continuous formation of supported cubic and hexagonal mesoporous films by sol gel dip-coating. Nature 1997, 389,364–368.

[9]. Huang, M. H.; Dunn, B. S.; Zink, J. I. In situ luminescence probing of the chemical and structural changes during formation of dip-coated lamellar phase sodium dodecyl sulphate sol_gel thin films. J. Am. Chem. Soc. 2000, 122, 3739–3745.

[10]. Lu, Y. F.; Fan, H. Y.; Stump, A.;Ward, T. L.; Rieker, T.; Brinker, C. J. Aerosol-assisted self-assembly of mesostructured

spherical nanoparticles. Nature 1999, 398, 223–226.
[11]. Fan, H. Y.; Lu, Y. F.; Stump, A.; Reed, S. T.; Baer, T.; Schunk, R.; Perez-Luna, V.; Lopez,G. P.; Brinker, C. J. Rapid prototyping of patterned functional nanostructures. Nature 2000,405, 56–60.
[12]. Zhang Q, Liu J, Yuan K, Zhang Z, Zhang X, Fang X. A multi- controlled drug delivery system based on magnetic mesoporous Fe3O4 nanopaticles and a phase change material for cancer thermo- chemotherapy. Nanotechnology. 2017;28(40):405101. doi:10.1088/ 1361-6528/aa883f
[13]. Ho CC, Ding SJ. The pH-controlled nanoparticles size of polydopamine for anti-cancer drug delivery. J Mater Sci Mater Med. 2013;24 (10):2381–2390. doi:10.1007/s10856-013-4994-2
[14]. Weaver CL, LaRosa JM, Luo X, Cui XT. Electrically controlled drug delivery from graphene oxide nanocomposite films. ACS Nano. 2014;8(2):1834–1843. doi:10.1021/nn406223e
[15]. He D, He X, Wang K, Zou Z, Yang X, Li X. Remote-controlled drug release from graphene oxide-capped mesoporous silica to cancer cells by photoinduced pH-jump activation. Langmuir. 2014;30(24):7182–7189. doi:10.1021/la501075c
[16]. Li J, Mooney DJ. Designing hydrogels for controlled drug delivery. Nat Rev Mater. 2016;1(12):16071.
[17]. Pimenta AFR, Ascenso J, Fernandes JCS, Colaco R, Serro AP, Saramago B. Controlled drug release from hydrogels for contact lenses: drug partitioning and diffusion. Int J Pharm. 2016;515(1– 2):467–475. doi:10.1016/j.ijpharm.2016.10.047
[18]. Chen FM, Liu X. Advancing biomaterials of human origin for tissue engineering. Prog Polym Sci. 2016;53:86–168. doi:10.1016/j. progpolymsci.2015.02.0041
[19]. Rodzinski A, Guduru R, Liang P, et al. Targeted and controlled anticancer drug delivery and release with magnetoelectric nanoparticles. Sci Rep. 2016;6(1):20867. doi:10.1038/srep20867
[20]. Han R, Yi H, Shi J, et al. pH-responsive drug release and NIR- triggered singlet oxygen generation based on a multifunctional core–shell–shell structure. Phys Chem Chem Phys. 2016;18 (36):25497–25503. doi:10.1039/C6CP05308D
[21]. Zeng X, Liu G, Tao W, et al. A drug-self-gated mesoporous antitumor nanoplatform based on pH-sensitive dynamic covalent bond. Adv Funct Mater. 2017;27(11):1605985. doi:10.1002/adfm.201605985
[22]. Baeza A, Manzano M, Colilla M, Vallet-Regí M. Recent advances in mesoporous silica nanoparticles for antitumor therapy: our contribution. Biomater Sci. 2016;4(5):803–813. doi:10.1039/C6BM00039H
[23]. Cheng W, Nie J, Gao N, et al. A multifunctional nanoplatform against multidrug resistant cancer: merging the best of targeted chemo/gene/ photothermal therapy. Adv Funct Mater. 2017;27(45):1704135. doi:10.1002/adfm.201704135
[24]. Zhou Y, Quan G, Wu Q, et al. Mesoporous silica nanoparticles for drug and gene delivery. Acta Pharm Sin B. 2018;8(2):165–177. doi:10.1016/j.apsb.2018.01.007
[25]. Wang Y, Gu H. Core–shell-type magnetic mesoporous silica nanocomposites for bioimaging and therapeutic agent delivery. Adv Mater. 2015;27(3):576–585. doi:10.1002/adma.201401124
[26]. Gao Q, Xie W, Wang Y, et al. A theranostic nanocomposite system based on radial mesoporous silica hybridized with Fe3O4 nanoparticles for targeted magnetic field responsive chemotherapy of breast cancer. RSC Adv. 2018;8(8):4321–4328. doi:10.1039/C7RA12446E
[27]. Yang C, Guo W, Cui L, et al. pH-responsive magnetic core–shell nanocomposites for drug delivery. Langmuir. 2014;30(32):9819–9827. doi:10.1021/la501833u
[28]. Yu X, Zhu Y. Preparation of magnetic mesoporous silica nanoparticles as a multifunctional platform for potential drug delivery and hyperthermia. Sci Technol Adv Mater. 2016;17(1):229–238. doi:10. 1080/14686996.2016.1178055
[29]. Ansari L, Malaekeh-Nikouei B. Magnetic silica nanocomposites for magnetic hyperthermia applications. Int J Hyperthermia. 2017;33 (3):354–363. doi:10.1080/02656736.2016.1243736
[30]. Zeng X, Luo M, Liu G, et al. Polydopamine-modified black phosphorous nanocapsule with enhanced stability and photothermal performance for tumor multimodal

treatments. Adv Sci. 2018;5 (10):1800510. doi:10.1002/advs.201800510

[31]. Jiang JH, Pi J, Jin H, Cai JY. Functional graphene oxide as cancer- targeted drug delivery system to selectively induce oesophageal cancer cell apoptosis. Artif Cells Nanomed Biotechnol. 2018;46(sup3): S297–s307. doi:10.1080/21691401.2018.1492418

[32]. Tran AV, Shim K, Vo Thi TT, Kook JK, An SSA, Lee SW. Targeted and controlled drug delivery by multifunctional mesoporous silica nanoparticles with internal fluorescent conjugates and external polydopamine and graphene oxide layers. Acta Biomater. 2018;74:397– 413. doi:10.1016/j.actbio.2018.05.022

[33]. Wang Z, Duan Y, Duan Y. Application of polydopamine in tumor targeted drug delivery system and its drug release behavior. J Control Release. 2018;290:56–74. doi:10.1016/j.jconrel.2018.10.009

[34]. Hogan NJ, Urban AS, Ayala-Orozco C, Pimpinelli A, Nordlander P, Halas NJ. Nanoparticles heat through light localization. Nano Lett. 2014;14(8):4640–4645. doi:10.1021/nl5016975

[35]. Karampelas IH, Liu K, Alali F, Furlani EP. Plasmonic nanoframes for photothermal energy conversion. J Phys Chem C. 2016;120 (13):7256–7264. doi:10.1021/acs.jpcc.5b12743

[36]. GhavamiNejad A, SamariKhalaj M, Aguilar LE, Park CH, Kim CS. pH/NIR light-controlled multidrug release via a mussel-inspired nanocomposite hydrogel for chemo-photothermal cancer therapy. Sci Rep. 2016;6:33594. doi:10.1038/srep33594

[37]. Jiang W, Mo F, Jin X, et al. Tumor-targeting photothermal heating- responsive nanoplatform based on reduced graphene oxide/mesoporous silica/hyaluronic acid nanocomposite for enhanced photodynamic therapy. Adv Mater Interfaces. 2017;4(20):1700425. doi:10.1002/ admi.201700425

[38]. Tao W, Zhu X, Yu X, et al. Black phosphorus nanosheets as a robust delivery platform for cancer theranostics. Adv Mater. 2017;29 (1):1603276. doi:10.1002/adma.201603276

[39]. Ma Y, Liang X, Tong S, Bao G, Ren Q, Dai Z. Gold nanoshell nanomicelles for potential magnetic resonance imaging, light-triggered drug release, and photothermal therapy. Adv Funct Mater. 2013;23(7):815–822. doi:10.1002/adfm.201201663

[40]. Liu H, Chen D, Li L, et al. Multifunctional gold nanoshells on silica nanorattles: a platform for the combination of photothermal therapy and chemotherapy with low systemic toxicity. Angewandte Chemie. 2011;50(4):891–895. doi:10.1002/anie.201002820

[41]. Jiang W, Mo F, Lin Y, Wang X, Xu L, Fu F. Tumor targeting dual stimuli responsive controllable release nanoplatform based on DNA- conjugated reduced graphene oxide for chemo-photothermal synergetic cancer therapy. J Mater Chem B. 2018;6(26):4360–4367. doi:10.1039/C8TB00670A

[42]. NDong C, Tate JA, Kett WC, et al. Tumor cell targeting by iron oxide nanoparticles is dominated by different factors in vitro versus in vivo. PLoS One. 2015;10(2):e0115636. doi:10.1371/journal.pone.0115636

[43]. Rosen JE, Chan L, Shieh DB, Gu FX. Iron oxide nanoparticles for targeted cancer imaging and diagnostics. Nanomedicine:NBM. 2012;8(3):275–290. doi:10.1016/j.nano.2011.08.017

[44]. Wu M, Huang S. Magnetic nanoparticles in cancer diagnosis, drug delivery and treatment. Mol Clin Oncol. 2017;7(5):738–746.

[45]. Blanco E, Kessinger CW, Sumer BD, Gao J. Multifunctional micellar nanomedicine for cancer therapy. Exp Biol Med. 2009;234(2):123– 131. doi:10.3181/0808-MR-250

[46]. Alibakhshi A, Abarghooi Kahaki F, Ahangarzadeh S, et al. Targeted cancer therapy through antibody fragments-decorated nanomedicines. J Control Release. 2017;268:323–334. doi:10.10 16/j.jconrel.2017.10.0

[47]. Vallet-Regi, M.; Rámila, A.; del Real, R.P.; Pérez-Pariente, J. A New Property of MCM-41: Drug Delivery

[48]. System. Chem. Mater. **2001**, 13, 308–311.

[49]. Yang, J.; Li, L.; Kopeˇcek, J. Biorecognition: A key to drug-free macromolecular therapeutics. Biomaterials **2019**, 190, 11–23.

[50]. Sever, R.; Brugge, J.S. Signal Transduction in Cancer. Cold Spring Harb. Perspect. Med. **2015**, 5, a006098.

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Volume 7, Issue 4 July-Aug 2022, pp: 787-802 www.ijprajournal.com ISSN: 2456-4494

[51]. Núñez-Lozano, R.; Cano, M.; Pimentel, B.; de la Cueva-Méndez, G. 'Smartening' anticancer therapeutic
[52]. nanosystems using biomolecules. Curr. Opin. Biotechnol. **2015**, 35, 135–140.
[53]. Castillo, R.R.; Lozano, D.; González, B.; Manzano, M.; Izquierdo-Barba, I.; Vallet-Regí, M. Advances in mesoporous silica nanoparticles for targeted stimuli-responsive drug delivery: An update. Expert Opin.
[54]. Drug Deliv. **2019**, 16, 415–439.
[55]. Dempke, W.C.M.; Fenchel, K.; Uciechowski, P.; Dale, S.P. Second-and third-generation drugs for
[56]. immuno-oncology treatment—The more the better? Eur. J. Cancer **2017**, 74, 55–72.
[57]. Topalian, S.L.; Taube, J.M.; Anders, R.A.; Pardoll, D.M. Mechanism-driven biomarkers to guide immune
[58]. checkpoint blockade in cancer therapy. Nat. Rev. Cancer **2016**, 16, 275–287.
[59]. Ribas, A.;Wolchok, J.D. Cancer immunotherapy using checkpoint blockade. Science **2018**, 359, 1350–1355.
[60]. Ahuja, N.; Sharma, A.R.; Baylin, S.B. Epigenetic Therapeutics: A NewWeapon in theWar Against Cancer.Annu. Rev. Med. **2016**, 67, 73–89.
[61]. Das, S.K.; Menezes, M.E.; Bhatia, S.; Wang, X.-Y.; Emdad, L.; Sarkar, D.; Fisher, P.B. Gene Therapies for Cancer: Strategies, Challenges and Successes. J. Cell. Physiol. **2015**, 230, 259–271.
[62]. Fukuhara, H.; Ino, Y.; Todo, T. Oncolytic virus therapy: A new era of cancer treatment at dawn. Cancer Sci.**2016**, 107, 1373–1379.
[63]. Yamada, H.; Urata, C.; Aoyama, Y.; Osada, S.; Yamauchi, Y.; Kuroda, K. Preparation of colloidal mesoporous silica nanoparticles with di_erent diameters and their unique degradation behavior in static aqueous systems.Chem. Mater. **2012**, 24, 1462–1471.
[64]. Yamada, H.; Urata, C.; Ujiie, H.; Yamauchi, Y.; Kuroda, K. Preparation of aqueous colloidal mesostructured and mesoporous silica nanoparticles with controlled particle size in a very wide range from 20 nm to 700 nm.Nanoscale **2013**, 5, 6145–6153.
[65]. Kneževi´c, N.Ž.; Durand, J.-O. Large pore mesoporous silica nanomaterials for application in delivery of
[66]. biomolecules. Nanoscale **2015**, 7, 2199–2209.
[67]. Wu, S.H.; Lin, H.P. Synthesis of mesoporous silica nanoparticles. Chem. Soc. Rev. **2013**, 42, 3862–3875.
[68]. Lindén, M. Biodistribution and Excretion of Intravenously Injected Mesoporous Silica Nanoparticles: Implications for Drug Delivery E_ciency and Safety. In The Enzymes; Elsevier: Amsterdam, The Netherlands,2018; Volume 43, pp. 155–180.
[69]. Croissant, J.G.; Fatieiev, Y.; Khashab, N.M. Degradability and Clearance of Silicon, Organosilica,
[70]. Silsesquioxane, Silica Mixed Oxide, and Mesoporous Silica Nanoparticles. Adv. Mater. **2017**, 29, 1604634
[71]. Castillo, R.R.; Vallet-Regí, M. Functional Mesoporous Silica Nanocomposites: Biomedical applications and Biosafety. Int. J. Mol. Sci. **2019**, 20, 929.
[72]. Castillo, R.R.; Colilla, M.; Vallet-Regí, M. Advances in mesoporous silica-based nanocarriers for co-delivery and combination therapy against cancer. Expert Opin. Drug Deliv. **2017**, 14, 229–243.
[73]. Castillo, R.R.; Baeza, A.; Vallet-Regí, M. Recent applications of the combination of mesoporous silica nanoparticles with nucleic acids: Development of bioresponsive devices, carriers and sensors. Biomater. Sci.**2017**, 5, 353–377.
[74]. Narayan, R.; Nayak, U.; Raichur, A.; Garg, S. Mesoporous Silica Nanoparticles: A Comprehensive Review on Synthesis and Recent Advances. Pharmaceutics **2018**, 10, 118.
[75]. Vallet-Regí, M.; Balas, F.; Colilla, M.; Manzano, M. Bone-regenerative bioceramic implants with drug and protein controlled delivery capability. Prog. Solid State Chem. **2008**, 36, 163–191.
[76]. Rafael R. Castillo, Daniel Lozano, and María Vallet-Regí Mesoporous Silica Nanoparticles as Carriers for Therapeutic Biomolecules Pharmaceutics. 2020 May; 12(5): 432.Published online 2020 May 7. doi: 10.3390/pharmaceutics12050432
[77]. Samuel Kesse, Kofi Oti Boakye-Yiadom, et al. Mesoporous Silica Nanomaterials: Versatile Nanocarriers for Cancer Theranostics and Drug and Gene Delivery.Pharmaceutics. 2019 Feb; 11(2): 77.Published online 2019 Feb 13. doi: 10.3390/pharmaceutics11020077
[78]. Samuel Kesse, Kofi Oti Boakye-Yiadom, et al. Mesoporous Silica Nanomaterials:

Versatile Nanocarriers for Cancer Theranostics and Drug and Gene Delivery.Pharmaceutics. 2019 Feb; 11(2): 77.Published online 2019 Feb 13. doi: 10.3390/pharmaceutics11020077

[79]. Liberman, A.; Martinez, H.P.; Ta, C.N.; Barback, C.V.; Mattrey, R.F.; Kono, Y.; Blair, S.L.; Trogler, W.C.;Kummel, A.C.; Wu, Z. Hollow silica and silica-boron nano/microparticles for contrast-enhanced ultrasound to detect small tumors. Biomaterials 2012, 33, 5124–5129.

[80]. Matsushita, H.; Mizukami, S.; Sugihara, F.; Nakanishi, Y.; Yoshioka, Y.; Kikuchi, K. Multifunctional core–shell silica nanoparticles for highly sensitive 19F magnetic resonance imaging. Angew. Chem. 2014, 126, 1026–1029.

[81]. Bouamrani, A.; Hu, Y.; Tasciotti, E.; Li, L.; Chiappini, C.; Liu, X.; Ferrari, M. Mesoporous silica chips for selective enrichment and stabilization of low molecular weight proteome. Proteomics 2010, 10, 496–505.

[82]. Yin, F.; Zhang, B.; Zeng, S.; Lin, G.; Tian, J.; Yang, C.; Wang, K.; Xu, G.; Yong, K.-T. Folic acid-conjugated organically modified silica nanoparticles for enhanced targeted delivery in cancer cells and tumor in vivo.J. Mater. Chem. B 2015, 3, 6081–6093.

[83]. Gazouli, M.; Lyberopoulou, A.; Pericleous, P.; Rizos, S.; Aravantinos, G.; Nikiteas, N.; Anagnou, N.P.;Efstathopoulos, E.P. Development of a quantum-dot-labelled magnetic immunoassay method for circulating colorectal cancer cell detection. World J. Gastroenterol. 2012, 18, 4419.

[84]. Zheng, T.; Pierre-Pierre, N.; Yan, X.; Huo, Q.; Almodovar, A.J.; Valerio, F.; Rivera-Ramirez, I.; Griffith, E.;Decker, D.D.; Chen, S. Gold nanoparticle-enabled blood test for early stage cancer detection and risk assessment. ACS Appl. Mater. Interfaces 2015, 7, 6819–6827.

[85]. Wu, X.; Wu, M.; Zhao, J.X. Recent development of silica nanoparticles as delivery vectors for cancer imaging and therapy. Nanomed. Nanotechnol. Biol. Med. 2014, 10, 297–312.

[86]. Cai, W.; Gao, T.; Hong, H.; Sun, J. Applications of gold nanoparticles in cancer nanotechnology. Nanotechnol. Sci. Appl. 2008, 1, 17.

[87]. Wu, X.; Wu, M.; Zhao, J.X. Recent development of silica nanoparticles as delivery vectors for cancer imaging and therapy. Nanomed. Nanotechnol. Biol. Med. 2014, 10, 297–312.

[88]. Jasanoff, A. MRI contrast agents for functional molecular imaging of brain activity. Curr. Opin. Neurobiol.2007, 17, 593–600.

[89]. Wu, X.; Wu, M.; Zhao, J.X. Recent development of silica nanoparticles as delivery vectors for cancer imaging and therapy. Nanomed. Nanotechnol. Biol. Med. 2014, 10, 297–312.

[90]. Liberman, A.; Martinez, H.P.; Ta, C.N.; Barback, C.V.; Mattrey, R.F.; Kono, Y.; Blair, S.L.; Trogler, W.C.;Kummel, A.C.; Wu, Z. Hollow silica and silica-boron nano/microparticles for contrast-enhanced ultrasound to detect small tumors. Biomaterials 2012, 33, 5124–5129.

[91]. Matsushita, H.; Mizukami, S.; Sugihara, F.; Nakanishi, Y.; Yoshioka, Y.; Kikuchi, K. Multifunctional core–shell silica nanoparticles for highly sensitive 19F magnetic resonance imaging. Angew. Chem. 2014, 126, 1026–1029.

[92]. Sprintz, M.; Tasciotti, E.; Allegri, M.; Grattoni, A.; Driver, L.C.; Ferrari, M. Nanomedicine: Ushering in a new era of pain management. Eur. J. Pain Suppl. 2011, 5, 317–322.

[93]. Bouamrani, A.; Hu, Y.; Tasciotti, E.; Li, L.; Chiappini, C.; Liu, X.; Ferrari, M. Mesoporous silica chips for selective enrichment and stabilization of low molecular weight proteome. Proteomics 2010, 10, 496–505.

[94]. Rozhkova, E.A. Nanoscale materials for tackling brain cancer: Recent progress and outlook. Adv. Mater.2011, 23, H136–H150.

[95]. Wang, Y.; Wang, K.; Zhao, J.; Liu, X.; Bu, J.; Yan, X.; Huang, R. Multifunctional mesoporous silica-coated graphene nanosheet used for chemo-photothermal synergistic targeted therapy of glioma. J. Am. Chem. Soc.2013, 135, 4799–4804.

[96]. Sonali; Agrawal, P.; Singh, R.P.; Rajesh, C.V.; Singh, S.; Vijayakumar, M.R.; Pandey, B.L.; Muthu, M.S.Transferrin receptor-targeted vitamin E TPGS micelles for brain cancer therapy: Preparation, characterization and brain distribution in rats. Drug Deliv. 2016, 23, 1788–1798.

[97]. Agrawal, P.; Singh, R.P.; Kumari, L.; Sharma, G.; Koch, B.; Rajesh, C.V.; Mehata, A.K.; Singh, S.; Pandey, B.L.;Muthu, M.S.

TPGS-chitosan cross-linked targeted nanoparticles for effective brain cancer therapy. Mater. Sci.Eng. C 2017, 74, 167–176.

[98]. Pinhão, M.S. Characterization of the Toxic Potential of Nanomaterials Using in vitro Cell Models.Ph.D. Thesis, Universidade de Lisboa, Lisboa, Portuguese, 2014.

[99]. He, Q.; Shi, J. MSN Anti-Cancer Nanomedicines: Chemotherapy Enhancement, Overcoming of Drug Resistance, and Metastasis Inhibition. Adv. Mater. 2014, 26, 391–411.

[100]. Sonali; Singh, R.P.; Singh, N.; Sharma, G.; Vijayakumar, M.R.; Koch, B.; Singh, S.; Singh, U.; Dash, D.;Pandey, B.L. Transferrin liposomes of docetaxel for brain-targeted cancer applications: Formulation and brain theranostics. Drug Deliv. 2016, 23, 1261–1271.

[101]. Agrawal, P.; Singh, R.P.; Sharma, G.; Mehata, A.K.; Singh, S.; Rajesh, C.V.; Pandey, B.L.; Koch, B.; Muthu, M.S.Bioadhesive micelles of d- α-tocopherol polyethylene glycol succinate 1000: Synergism of chitosan and transferrin in targeted drug delivery. Colloids Surfaces B Biointerfaces 2017, 152, 277–288.

[102]. Liu, D.; Lin, B.; Shao,W.; Zhu, Z.; Ji, T.; Yang, C. In vitro and in vivo studies on the transport of PEGylated silica nanoparticles across the blood–brain barrier. ACS Appl. Mater. Interfaces 2014, 6, 2131–2136.

[103]. Bertucci, A.; Prasetyanto, E.A.; Septiadi, D.; Manicardi, A.; Brognara, E.; Gambari, R.; Corradini, R.; DeCola, L. Combined Delivery of Temozolomide and Anti-miR221 PNA Using Mesoporous Silica Nanoparticles Induces Apoptosis in Resistant Glioma Cells. Small 2015, 11, 5687–5695.

[104]. Lu, C.-W.; Hung, Y.; Hsiao, J.-K.; Yao, M.; Chung, T.-H.; Lin, Y.-S.;Wu, S.-H.; Hsu, S.-C.; Liu, H.-M.; Mou, C.-Y.Bifunctional magnetic silica nanoparticles for highly efficient human stem cell labeling. Nano Lett. 2007, 7,149–154.

[105]. Lin, Y.-S.; Tsai, C.-P.; Huang, H.-Y.; Kuo, C.-T.; Hung, Y.; Huang, D.-M.; Chen, Y.-C.; Mou, C.-Y. Well-ordered mesoporous silica nanoparticles as cell markers. Chem. Mater. 2005, 17, 4570–4573.

[106]. Singh, N.; Karambelkar, A.; Gu, L.; Lin, K.; Miller, J.S.; Chen, C.S.; Sailor, M.J.; Bhatia, S.N. Bioresponsive mesoporous silica nanoparticles for triggered drug release. J. Am. Chem. Soc. 2011, 133, 19582–19585.

[107]. Lin, Q.; Huang, Q.; Li, C.; Bao, C.; Liu, Z.; Li, F.; Zhu, L. Anticancer drug release from a mesoporous silica based nanophotocage regulated by either a one-or two-photon process. J. Am. Chem. Soc. 2010, 132,10645–10647.

[108]. Lee, C.H.; Cheng, S.H.; Huang, I.P.; Souris, J.S.; Yang, C.S.; Mou, C.Y.; Lo, L.W. Intracellular pH-responsive mesoporous silica nanoparticles for the controlled release of anticancer chemotherapeutics. Angew. Chem.2010, 122, 8390–8395.

[109]. Slowing, I.I.; Trewyn, B.G.; Giri, S.; Lin, V.Y. Mesoporous silica nanoparticles for drug delivery and biosensing applications. Adv. Funct. Mater. 2007, 17, 1225–1236.

[110]. Chen, Y.-P.; Chen, C.-T.; Hung, Y.; Chou, C.-M.; Liu, T.-P.; Liang, M.-R.; Chen, C.-T.; Mou, C.-Y. A new strategy for intracellular delivery of enzyme using mesoporous silica nanoparticles: Superoxide dismutase.J. Am. Chem. Soc. 2013, 135, 1516–1523.

[111]. Radu, D.R.; Lai, C.-Y.; Jeftinija, K.; Rowe, E.W.; Jeftinija, S.; Lin, V.S.-Y. A polyamidoamine dendrimer-capped mesoporous silica nanosphere-based gene transfection reagent. J. Am. Chem. Soc. 2004, 126, 13216–13217.

[112]. Ashley, C.E.; Carnes, E.C.; Epler, K.E.; Padilla, D.P.; Phillips, G.K.; Castillo, R.E.; Wilkinson, D.C.;Wilkinson, B.S.; Burgard, C.A.; Kalinich, R.M. Delivery of small interfering RNA by peptide-targeted mesoporous silica nanoparticle-supported lipid bilayers. ACS Nano 2012, 6, 2174–2188.

[113]. Xia, T.; Kovochich, M.; Liong, M.; Meng, H.; Kabehie, S.; George, S.; Zink, J.I.; Nel, A.E. Polyethyleneimine coating enhances the cellular uptake of mesoporous silica nanoparticles and allows safe delivery of siRNA and DNA constructs. ACS Nano 2009, 3, 3273–3286.

[114]. Cheng, S.-H.; Hsieh, C.-C.; Chen, N.-T.; Chu, C.-H.; Huang, C.-M.; Chou, P.-T.; Tseng, F.-G.; Yang, C.-S.;Mou, C.-Y.; Lo, L.-W. Well-defined mesoporous nanostructure modulates three-dimensional interface energy transfer for two-photon activated photodynamic therapy. Nano Today 2011, 6, 552–563.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 4 July-Aug 2022, pp: 787-802 www.ijprajournal.com ISSN: 2456-4494

[115]. Tu, H.L.; Lin, Y.S.; Lin, H.Y.; Hung, Y.; Lo, L.W.; Chen, Y.F.; Mou, C.Y. In vitro studies of functionalized mesoporous silica nanoparticles for photodynamic therapy. Adv. Mater. 2009, 21, 172–177.
[116]. Lee, C.W.; Mahendra, S.; Zodrow, K.; Li, D.; Tsai, Y.C.; Braam, J.; Alvarez, P.J. Developmental phytotoxicity of metal oxide nanoparticles to Arabidopsis thaliana. Environ. Toxicol. Chem. 2010, 29, 669–675.
[117]. Slomberg, D.L.; Schoenfisch, M.H. Silica nanoparticle phytotoxicity to Arabidopsis thaliana. Environmental science & technology 2012, 46, 10247–10254.
[118]. Parsons, J.G.; Lopez, M.L.; Gonzalez, C.M.; Peralta-Videa, J.R.; Gardea-Torresdey, J.L. Toxicity and biotransformation of uncoated and coated nickel hydroxide nanoparticles on mesquite plants. Environ.Toxicol. Chem. 2010, 29, 1146–1154.
[119]. Chang, F.-P.; Kuang, L.-Y.; Huang, C.-A.; Jane, W.-N.; Hung, Y.; Yue-ie, C.H.; Mou, C.-Y. A simple plant gene delivery system using mesoporous silica nanoparticles as carriers. J. Mater. Chem. B 2013, 1, 5279–5287.
[120]. Villagarcia, H.; Dervishi, E.; de Silva, K.; Biris, A.S.; Khodakovskaya, M.V. Surface chemistry of carbon nanotubes impacts the growth and expression of water channel protein in tomato plants. Small 2012, 8,2328–2334.
[121]. Lin, D.; Xing, B. Phytotoxicity of nanoparticles: Inhibition of seed germination and root growth. Environ.Pollut. 2007, 150, 243–250.
[122]. Kurepa, J.; Paunesku, T.; Vogt, S.; Arora, H.; Rabatic, B.M.; Lu, J.; Wanzer, M.B.; Woloschak, G.E.; Smalle, J.A.Uptake and distribution of ultrasmall anatase TiO2 Alizarin red S nanoconjugates in Arabidopsis thaliana.Nano Lett. 2010, 10, 2296–2302.
[123]. Chang, F.-P.; Kuang, L.-Y.; Huang, C.-A.; Jane, W.-N.; Hung, Y.; Yue-ie, C.H.; Mou, C.-Y. A simple plant gene delivery system using mesoporous silica nanoparticles as carriers. J. Mater. Chem. B 2013, 1, 5279–5287.
[124]. Liu, Q.; Chen, B.; Wang, Q.; Shi, X.; Xiao, Z.; Lin, J.; Fang, X. Carbon nanotubes as molecular transporters for walled plant cells. Nano Lett. 2009, 9, 1007–1010.
[125]. Serag, M.F.; Kaji, N.; Venturelli, E.; Okamoto, Y.; Terasaka, K.; Tokeshi, M.; Mizukami, H.; Braeckmans, K.;Bianco, A.; Baba, Y. Functional platform for controlled subcellular distribution of carbon nanotubes.ACS Nano 2011, 5, 9264–9270.
[126]. Etxeberria, E.; Gonzalez, P.; Baroja-Fernandez, E.; Romero, J.P. Fluid phase endocytic uptake of artificial nano-spheres and fluorescent quantum dots by sycamore cultured cells: Evidence for the distribution of solutes to different intracellular compartments. Plant Signal. Behav. 2006, 1, 196–200.
[127]. Corredor, E.; Testillano, P.S.; Coronado, M.-J.; González-Melendi, P.; Fernández-Pacheco, R.; Marquina, C.;Ibarra, M.R.; de la Fuente, J.M.; Rubiales, D.; Pérez-de-Luque, A. Nanoparticle penetration and transport in living pumpkin plants: In situ subcellular identification. BMC Plant Biol. 2009, 9, 45.
[128]. Zhu, H.; Han, J.; Xiao, J.Q.; Jin, Y. Uptake, translocation, and accumulation of manufactured iron oxide nanoparticles by pumpkin plants. J. Environ. Monit. 2008, 10, 713–717.
[129]. Rico, C.M.; Majumdar, S.; Duarte-Gardea, M.; Peralta-Videa, J.R.; Gardea-Torresdey, J.L. Interaction of nanoparticles with edible plants and their possible implications in the food chain. J. Agric. Food Chem. 2011,59, 3485–3498.
[130]. Nair, R.; Varghese, S.H.; Nair, B.G.; Maekawa, T.; Yoshida, Y.; Kumar, D.S. Nanoparticulate material delivery to plants. Plant Sci. 2010, 179, 154–163.
[131]. Chang, F.-P.; Kuang, L.-Y.; Huang, C.-A.; Jane, W.-N.; Hung, Y.; Yue-ie, C.H.; Mou, C.-Y. A simple plant gene delivery system using mesoporous silica nanoparticles as carriers. J. Mater. Chem. B 2013, 1, 5279–5287.
[132]. Samuel Kesse, Kofi Oti Boakye-Yiadom, et al. Mesoporous Silica Nanomaterials: Versatile Nanocarriers for Cancer Theranostics and Drug and Gene Delivery.Pharmaceutics. 2019 Feb; 11(2): 77.Published online 2019 Feb 13. doi: 10.3390/pharmaceutics11020077
[133]. Samuel Kesse, Kofi Oti Boakye-Yiadom, et al. Mesoporous Silica Nanomaterials: Versatile Nanocarriers for Cancer Theranostics and Drug and Gene Delivery.Pharmaceutics. 2019 Feb; 11(2): 77.Published online 2019 Feb 13. doi: 10.3390/pharmaceutics11020077

[134]. Cheng, S.-H.; Lee, C.-H.; Chen, M.-C.; Souris, J.S.; Tseng, F.-G.; Yang, C.-S.; Mou, C.-Y.; Chen, C.-T.; Lo, L.-W.Tri-functionalization of mesoporous silica nanoparticles for comprehensive cancer theranostics—The trio of imaging, targeting and therapy. J. Mater. Chem. 2010, 20, 6149–6157.
[135]. Samuel Kesse, Kofi Oti Boakye-Yiadom, et al. Mesoporous Silica Nanomaterials: Versatile Nanocarriers for Cancer Theranostics and Drug and Gene Delivery.Pharmaceutics. 2019 Feb; 11(2): 77.Published online 2019 Feb 13. doi: 10.3390/pharmaceutics11020077
[136]. Samuel Kesse, Kofi Oti Boakye-Yiadom, et al. Mesoporous Silica Nanomaterials: Versatile Nanocarriers for Cancer Theranostics and Drug and Gene Delivery.Pharmaceutics. 2019 Feb; 11(2): 77.Published online 2019 Feb 13. doi: 10.3390/pharmaceutics11020077
[137]. Samuel Kesse, Kofi Oti Boakye-Yiadom, et al. Mesoporous Silica Nanomaterials: Versatile Nanocarriers for Cancer Theranostics and Drug and Gene Delivery.Pharmaceutics. 2019 Feb; 11(2): 77.Published online 2019 Feb 13. doi: 10.3390/pharmaceutics11020077
[138]. Hanahan, D.;Weinberg, R.A. Hallmarks of cancer: The next generation. Cell 2011, 144, 646–674.
[139]. Cheng, S.-H.; Hsieh, C.-C.; Chen, N.-T.; Chu, C.-H.; Huang, C.-M.; Chou, P.-T.; Tseng, F.-G.; Yang, C.-S.;Mou, C.-Y.; Lo, L.-W. Well-defined mesoporous nanostructure modulates three-dimensional interface energy transfer for two-photon activated photodynamic therapy. Nano Today 2011, 6, 552–563.
[140]. Cheng, S.-H.; Lee, C.-H.; Chen, M.-C.; Souris, J.S.; Tseng, F.-G.; Yang, C.-S.; Mou, C.-Y.; Chen, C.-T.; Lo, L.-W.Tri-functionalization of mesoporous silica nanoparticles for comprehensive cancer theranostics—The trio of imaging, targeting and therapy. J. Mater. Chem. 2010, 20, 6149–6157.
[141]. Cheng, S.-H.; Lee, C.-H.; Chen, M.-C.; Souris, J.S.; Tseng, F.-G.; Yang, C.-S.; Mou, C.-Y.; Chen, C.-T.; Lo, L.-W.Tri-functionalization of mesoporous silica nanoparticles for comprehensive cancer theranostics—The trio of imaging, targeting and therapy. J. Mater. Chem. 2010, 20, 6149–6157.
[142]. Castranova, V.; Vallyathan, V. Silicosis and coal workers' pneumoconiosis. Environ. Health Perspect. 2000, 108, 675–684.
[143]. Donaldson, K.; Borm, P. J. A. The quartz hazard: A variable entity. Ann. Occup. Hyg. 1998,42, 287–294.
[144]. Elias, Z.; Poirot, O.; Dani~A.re, M. C.; Terzetti, F.; Marande, A. M.; Dzwigaj, S.; Pezerat, H.;Fenoglio, I.; Fubini, B. Cytotoxic and transforming effects of silica particles with different surface properties in Syrian hamster embryo (SHE) cells. Toxicol. In Vitro 2000, 14,409–422.
[145]. Rimal, B.; Greenberg, A. K.; Rom, W. N. Basic pathogenetic mechanisms in silicosis:Current understanding. Curr. Opin. Pulm. Med. 2005, 11, 169–173.
[146]. Meng, H.; Xue, M.; Xia, T.; Ji, Z.; Tarn, D. Y.; Zink, J. I.; Nel, A. E. 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, 4131–4144.
[147]. Castranova, V.; Vallyathan, V. Silicosis and coal workers' pneumoconiosis. Environ. Health Perspect. 2000, 108, 675–684.
[148]. Donaldson, K.; Borm, P. J. A. The quartz hazard: A variable entity. Ann. Occup. Hyg. 1998,42, 287–294.