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Mesoporous Silica Nanoparticles as an Effective Carrier in the Biomedical Field

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ABSTRACT

Mesoporous silica nanoparticles exhibit the most promising approach in the biomedical field. As compared with the other carriers mesoporous silica nanocarriers could achieve high release profiles of drugs by Improving the loading efficiency in various drug delivery systems. The unique feature of the mesoporous material such as surface characteristics, pore size, pore-volume, high loading capacity & surface functionalization makes a better alternative in the biomedical sector. Also, the mesoporous carriers are safe & biocompatible pharmaceutical excipients they are used in diagnosis, targeted drug delivery & in the biomedical field.

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INTRODUCTION

Nanotechnology has been developed as an important component in science and technology. The development of advances in the field of nanotechnology has a great impact on the diagnosis of disease as well as their treatment.

Nanotechnology has a wide application in the field of nanomedicines the use of nanocarriers for the development of nanomedicines, nanocarriers have the unique feature of modification of surface and surface charge, modification in their particle size, shape and the pore volume ratio. The main advantage of the use of nanocarriers is their particle size range has great importance in the drug absorption process due to smaller particle size range the surface area of the particle is larger and significantly the absorption is getting increase & hence increase in bioavailability of the drug moiety.

It has been proved that the nanocarriers are biodegradable and nontoxic biocompatible there are the main advantages for the oral drug delivery of drug molecules. The nanoparticles such as carbon dots, iron oxide nanoparticles gold nanoparticles & metal oxides, etc. are widely used for the diagnosis and treatment of disease. Out of which silica nanoparticles are gained wide popularity from recent few years. (1)

The silica nanoparticles are available in their different sizes range i.e. micro, meso & macro. The mesoporous silica nanoparticles have various advantages than that of other nanocarriers. Its advantage of uniform size, pore volume & modification its possible on the surface of it. The presence of pore i.e. internal & external pore makes it a distinctive & promising drug carrier.

Due to their high pore volume present on the MSNs increases the efficiency of loading of the drug, because pore morphology is greatly influenced drug loading & drug release. The mesoporous silica nanoparticles keep the drug in the amorphous state which facilitate drug distribution and the drug dissolution and chemical stability and inertness make better control of drug loading as well as release.

The mesoporous silica nanoparticles also have the main advantage is chemical as well as a physical modification on the surface, addition of appropriate functional groups on the surface of MSNs enhances the efficiency loading capacity of the drug molecule and hence will enhance the bioavailability. (1,2)

Drug loading & release process from the MSNs:

In the case of an advanced drug delivery system, the nanosystem which is designed for the improvement of drug solubility, and dissolution rate also make the drug available at the specific target site and decreases the adverse effect associated with the drug. Two important concepts i.e. drug loading capacity and drug release rate that determines the performance of the drug delivery system. The most widely used method for loading of drug molecules into the pores of MSNs is the adsorption method, soaking of MSNs into drug solution, mainly the drug having poor-aqueous solubility are preferred. Pore size is another important parameter to increase the adsorption of drug molecules.

Various physicochemical characteristics of the drug molecules polarity, rate of degradation of drug, weak ionic interaction, early release of drug from carrier molecule before reaching to the specific site, etc. To overcome such problems the recent studies have focused on the novel drug delivery system. (1,41)

Applications of Mesoporous silica nanoparticles in Biomedical Field:

1. Mesoporous silica nanoparticles used as a carrier for drug delivery system:

The mesoporous material is used as a carrier for various targeted drug delivery system due to the specific structural arrangement they can reach to the specific site without any loss & achieve the target. The silica-based porous material is used as an effective carrier for poor absorption. The drugs which are come under this class restrict the oral dosing. To improve the solubility and the absorption of such insoluble drugs the design of a suitable carrier is an important aspect.

For efficient drug delivery of the therapeutic molecules, mesoporous silica nanoparticle idesigned as an efficient drug reservoir for the loading of poorly water soluble drugs. The mesoporous material is having high surface area and the large pore volume provides a platform for the encapsulation of hydrophobic drugs. The drug having amorphous nature or non-crystalline both can remain within the pores of MSNs. Due to the mesoporous state of the silica molecules facilitates the drug dissolution also the chemical stability and inertness of the mesoporous material provide the controllable drug encapsulation and controllable release of the drug molecules.

Most of the anticancer drugs that come under class II and class IV have poor water solubility are belong to a class of hydrophobic drugs. This low solubility problem is a critical barrier for the absorption of the drug and bioavailability can limit the oral administration. Therefore it's an important issue to overcome the solubility of the therapeutic molecules; the mesoporous silica carriers are widely accepted without the use of organic solvent. (3)

1.1 PH responsive drug delivery:

Many of the drugs are having a release pattern based on the particular pH range. Also, some of the drugs may alter their response when they go into a different pH environment. For the oral administration of drugs, the environment of the pH range in GIT is an important aspect of the release and delivery of drugs. Controllable release of drugs depends upon the pH range is a promising way of treating the disease. There are various drugs formulated as a pH-controlled drug delivery system. Treating of disease through the nanoparticles the pH change is occurs based upon the internalization of the particles into cancer cells.

Mesoporous silica material is a promising approach for the pH responsive drug delivery system. The surface of the mesoporous silica nanoparticles is modified by the pH directing agent for the controllable release of the drug. Also, the surface coating strategy is used for the mesoporous material into which the drug is incorporated the loaded guest molecule is protected via a pH change. The modification on the surface of the mesoporous silica nanoparticles, the pores present on the nanoparticles are capped which is a great advantage for the pH sensitive drug molecules (4,5). A report states that the pH responsive drug and carrier depends upon the mesoporous silica nanoparticles. A pH responsive release of the ibuprofen is achieved by modifying the surface structure of the mesoporous silica material by positively charged chitosan in pH range, 4.0 to 7.4 chitosan prevents Ibuprofen release at pH 7.4.

Also, the drug molecule Raloxifene hydrochloride inside the chitosan has significant accumulation in the tumor cell by forming the pH responsive nanoparticles (8,11,12).

1.2 Temperature directing system:

It is important to design a temperature-responsive drug delivery that can only release drug that can only release drugs at temperature 37ºC, and the drug encapsulated during circulation. The change in temperature is useful for the release of drug from the MSN.

The temperature of the site of inflammation & the tumor tissue site is higher than that of normal body tissues. By using this temperature difference between cancer cells & normal cells, smart drug delivery can be used to increase the release of drug in tumors. Other than this temperature-responsive drug delivery in which tumor site is could be heated externally to improve the release of drugs at the tumor site.

Poly (acrylamide) swell with an increase in temperature based on poly N-isopropyl acrylamide (PNIPAM) & ordered mesoporous material developed. PNIPAM is a temperature-sensitive polymer because it is having the hydrophilic-hydrophobic transitions at lower critical solution temperature (LCST) it is the most widely used polymer in biomedical applications. In this polymer system, there is a breakdown of the hydrogen bund between PNIPAM and water when the temperature is above LCST at 25ºC and the polymer chain is getting shrinks, the pores are getting opened for the drug loading whereas below LCST there is the formation of hydrogen bonds leads to swelling of the polymer chain and sealing of pores tend to prevent the release of drug.(14,16,42)

1.3 Enzyme directed drug delivery:

Enzymes are important in many of the physiological as well as pathophysiological processes. If these enzymes are not regulated then it leads to the disease condition.

Enzymes play an important role in the reaction, Enzyme the reaction at mild temperature and pH condition it is beneficial in the formulation of nanomedicines. So, to achieve the controllable drug delivery system the mesoporous silica nanoparticles (MSN's) based enzyme-responsive drug delivery is designed for the anticancer drugs, in which the enzyme sensitive moieties are introduced and capped on the surface of mesoporous material it can be recognized and get degraded by the enzyme overexpression inside the tumor cell and after that drug gets releases from the MSN's.

The enzyme such as lipase, phospholipase, glycosidases, or protease is related to all metabolic processes so they are used in the enzyme-mediated drug delivery system. (14,16)

1.4 Magnetic drug delivery:

The magnetic responsive nanocarriers are providing the real-time release of the drug, by the oscillating magnetic field. The magnetic nanoparticles are target to the specific site of the tissue by the external magnetic field. It is one of the best options for the controllable drug delivery system.

The mesoporous silica-based magnetic responsive drug delivery is developed by encapsulation of the magnetic particles within the silica matrix .the use of magnetic mesoporous silica nanoparticles used to control the localization of the external magnetic field. (19)

The magnetic field responsive drug release depends upon the temperature, and it depends upon the magnetic nanoparticles embedded in mesoporous silica which is having the ability to generate the thermal energy by the application of the external magnetic field. (17)

An alternative magnetic field is employed for the controlled release of the drug fluorescein. The fluorescein loaded magnetic mesoporous silica nanoparticles are functionalized with 15 base pairs of the oligonucleotides, after that the system was capped with the super magnetic ion oxide which avoids the premature release of fluorescein trapped into the silica matrix. The application of the external magnetic field causes the dehybridization of oligonucleotide temperature is increase allowing the release of fluorescein molecule. When the applied magnetic field is stopped then hybridization between the complementary stand has occurred and the temperature is fall that shows the on-off behavior of nanodevices. (18)

1.5 Ultrasound Responsive Drug Delivery:

Ultrasound is one of the advantageous approaches for drug delivery. The ultrasound has the ability of deep tissue permeation and countable delivery of the drug. The ultrasound irritations also can increase the drug release efficiency from both degradable and non-biodegradable polymers. (19) The silica nanoparticles based drug delivery system is could be directed by the ultrasound.

In this drug delivery, the system is composed of polydimethylsiloxane (PDMC) acts as a gatekeeper which prevents the early release. When such a system exposed to the ultrasound system for 10min, the sustainable drug delivery of the therapeutic molecule was observed. From this, we conclude the mesoporous silica nanoparticles which act as an effective system for the ultrasound responsive drug delivery. (27)

2. Mesoporous silica nanoparticles in Anticancer therapy:

Cancer is the most leading disease and the primary cause of death. Most of the chemotherapeutic agents which fall under the low solubility class and have poor effectiveness and high side effects. Some of the drugs are having a short shelf life and low bioavailability issue. To overcome such a problem the mesoporous silica plays an important role to solve such issues. The mesoporous silica is having good biocompatibility, high aqueous solubility, and has stable chemical properties. Its surface can also be modified and has high loading efficiency.

The mesoporous silica can reach the tumor target site in the treatment of cancer; provide a better release of the drug at a specific site of the target. Mesoporous silica material can enter into tumors passively by an increase in permeability and retention effect can be actively targeted, and increase the time of circulation and availability. The major advantage of the MSNs is that it is having low toxicity and it is safe in cancer therapies.

HBS aptamer-functionalized mesoporous silica carbon-based –DOX loaded system was used for the photothermal therapy in human growth factor receptor-2 (HER-2) in breast cancer. The uptake of MSNs based nanoparticles was comparatively more than that of normal epithelial cells and after conducting the cytotoxicity study it was determined that the inhibition of cell is highest as compared to photothermal therapy and chemotherapy. (19,28)

3. Mesoporous silica nanoparticles in tissue engineering:

The application of mesoporous silica nanoparticles is a relatively new field that gained more interest in the research (21). Mesoporous silica has provided a flexible platform for the controlled delivery of drug tissue engineering and stem cell therapy. In the field of regenerative medicines provides a promising tool for the treatment of disease and to replace the damaged or lost tissues. Tissue engineering using stem cell that guides the cell proliferation, cell formation, and functional tissues differentiation.

4. Stem cell imaging-

Endogenous and Exogenous cell transplantation is used as a potential therapy in many of the disease conditions. In the cell transplantation to target and monitor the cell is a critical step. The uses of mesoporous silica material are suitable candidates for the increased stability of incorporated imaging drugs and enhance the resolution.

Mesoporous silica nanoparticles are used as a suitable carrier for the imaging agents, or also it acts as a coating over the material which is developed for the MRI, optical and photoacoustic imaging. MSNs imaging has been developed initially for cancer therapy. In stem cell therapy the mesoporous material used for MRI imaging which analyzed the cell behavior after the transplantation process. The mesoporous silica nanoparticles in tissue engineering are focused on bone tissue formation and also in the osteogenic differentiation. The modified surface of MSNs increases the behavior pattern of osteoclasts. The application of tissue engineering is to increase the biocompatibility and bio functionality of imaging agents. (22)

5. Protein adsorption and separation:

The mesoporous silica nanoparticles are having a high surface and can modify the surface which is a promising tool for the adsorption of various protein molecules. The interaction between the protein molecules and nanoparticles mainly studied for the influence of the size of mesoporous silica nanoparticles on the activity of enzymes and the adsorption of protein molecules. The in-vivo uptake and the release of cytochrome C by the MSN were studied. Cytochrome C was loaded in MSNs which crosses the cell membrane and release in the cytoplasm. The cytochrome C which is acts as an active enzyme in aqueous solution. (23)

6. Mesoporous silica nanoparticles in genetic engineering:

DNA molecule is used widely for therapy, genetic investigation, and diagnosis. Genetic engineering is the most growing field in drug delivery. DNA extraction and purification are important steps in therapy.

The use of nanotechnology in the field of genetics is the most important concept in gene therapy. The use of silica-based nanoparticles for the detection of DNA and separation purification. The DNA molecule is adsorbed onto the surface of silica nanoparticles, this

adsorption interaction includes electrostatic repulsion, hydrogen bonding, and this interaction makes the surface more specific and efficient.

Functionalized silica nanoparticles are mainly important for the delivery of genes. Two steps are required for efficient delivery of gene first is the loading of a gene on silica carrier which required efficient affinity between the silica nanocarriers and the gene. DNA molecules are having a negative charge on the surface, so the silica surface is modified by the addition of functional groups like the amino group make it positive for better interaction.

The second step is gene release; there should be weak interaction between the gene molecule and nanoparticles. Silica-based plasmid DNA and plasmid DNA alone were injected into the mouse brain. It was determined that the silica nanoparticle-based DNA show a gene expression and the gene signature was well protected and well transferred into nuclei of a cell. (24)

7. Mesoporous silica nanoparticles in photodynamic therapy:

The basic principle behind photodynamic therapy is irradiating the radiation on a specific wavelength upon which cell death has occurred. The use of photodynamic therapy is used as an alternative to chemotherapy and radiotherapy.

Mesoporous silica nanoparticles are gained more attention for the tumor-targeted cells. The specific targeting of the tumor cell is occurred by incorporating some photosensitizers on MSNs. There is a covalent interaction that takes place between the MSNs and the photosensitizers further the surface of mesoporous silica it may modify for the cancer cell-specific uptake.

The incorporation of photosensitizer material on the surface of MSNs prevents unwanted irradiation and prevents the toxicity. The successful therapeutic outcome obtained by incorporation of photosensitizers on MSNs upon irradiation. (25)

8. Mesoporous silica directed Biosensors:

Mesoporous silica material is having multiple features like there small size, shape, pore structure, surface chemistry, etc. because of these unique characteristics, it is used as an attractive tool for the detection of the various analyte. Mesoporous silica nanoparticles are having high pore size and optical transparency so they are used as a promising option for the biosensing applications.

Mesoporous silica nanoparticles that provide an area for the immobilization of sensing agents in both inside the pores and outside of surface which leads a fast response(25). H_2O_2 and NO_2 was detected by the immobilization of hemoglobin and myoglobin in MSNs electrodes. (26,27)

CONCLUSION

In the conventional treatments of diseases such as cancer, conventional chemotherapy is the main approach in the treatment of cancer. But the major drawback of the chemotherapy is, it will cause several harmful side effects due to high dose administration of therapeutic agent causes nonspecific uptake of the active agent by healthy cells. The nonspecific uptake of drugs by healthy cells is a major obstacle in the treatment of cancer. Therefore, it is important to deliver the therapeutic molecule at a specific target with the choice of suitable carriers. Mesoporous silica nanoparticle is one of the promising candidates for the delivery of various drug molecules in many disease states. Mesoporous silica nanoparticle is important in targeted drug delivery due to its unique physical and chemical properties and also conjugation of various functional groups on MSNs successful drug delivery can be achieved.

Various functional groups attached on the surface of the molecule which allows more flexibility in the drug delivery system. It is important to develop the biodegradable, non-toxic, safe, and high target efficiency of the drug delivery system Mesoporous silica is an important direction and main objective. Application of Mesoporous material produces great attention for the formulation of poorly water-soluble drugs. MSN improves the dissolution rates as well as stabilizes the formulation during subsequent storage conditions and enhances the bioavailability of poorly soluble drugs. The valuable property of mesoporous silica nanoparticles that, the possibility to use and combined different materials and merge various functionalities which are important to obtain multifunctional medicine in multimodal imaging and simultaneous diagnosis of disease and therapy.

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