CHAPTER 2

REVIEW OF LITERATURE

Review of literature covering national and international status has been completed.

1. Abu-Dief et al. (2022) explored the recent advances in the design and synthesis of Mesoporous Silica Nanoparticles (MSNPs) for targeted drug delivery applications. MSNPs possess intrinsic physiochemical stability, a high surface area, low toxicity, and significant loading capacity for various therapeutic agents, making them highly suitable for controlled drug delivery. This study focused on the parameters influencing the functional characteristics of MSNPs, such as particle size, morphology, porosity, and surface functionalization, which directly affect their in vivo absorption, dissemination, and secretion. The authors also highlighted the potential of combining MSNPs with other functional materials to enhance biological compatibility, monitor drug release, and improve tumor cell uptake. These nanoparticles demonstrate promising applications in cancer treatment and other therapeutic areas due to their controllable and targeted drug delivery capabilities.

2. Tao Liao et al., 2021, developed a dual-pH-sensitive chitosan (CHI)/mesoporous silica nanoparticle (MSN)-based anticancer drug delivery system (DDS) with a "tumor-triggered targeting" property. In this design, mesoporous silica nanoparticles loaded with doxorubicin hydrochloride (DOX) were modified with benzimidazole (Bz), while chitosan-graft-β-cyclodextrin (CHI-g-CD) acted as a "gatekeeper" by covering MSNs through host-guest interaction between β-CD and Bz. Targeting peptide adamantane-glycine-arginine-glycine-aspartic acid-serine (Ad-GRGDS) and methoxy poly(ethylene glycol) benzaldehyde (mPEG-CHO) were also grafted onto CHI via pH-sensitive bonds. This system remains "stealthy" at neutral pH but reveals the targeting peptide and positive charge in an acidic tumor environment. The DDS demonstrated efficient DOX release in cancer cells due to pH-induced interactions and exhibited enhanced tumor targeting with reduced cytotoxicity against normal cells, proving effective in both in vitro and in vivo studies for inducing cancer cell apoptosis and inhibiting tumor growth.

3. Jie Chang et al (2024) developed a pH-responsive mesoporous silica nanoparticle-based drug delivery system specifically for targeted breast cancer therapy. Mesoporous silica nanoparticles (MSN-COOH) were synthesized and loaded with doxorubicin (DOX) into the pores of MSN-COOH. The surface of these nanoparticles was further modified with polyethyleneimine (PEI) and anisamide (AA), named DOX@MSN-PEI-AA (DMPA). The targeted drug delivery was achieved by AA-mediated receptor endocytosis, allowing DMPA to specifically enter breast cancer cells. The acidic environment in the lysosomes/endosomes triggered the protonation of PEI, leading to its dissociation from the MSN surface and a controlled release of DOX in the cytoplasm. In vitro and in vivo studies, including anti-tumor and hemolytic experiments, demonstrated that DMPA exhibited precise targeting of breast cancer cells while maintaining excellent safety, making it a promising candidate for breast cancer therapy.

4. Garima Lohiya et al 2021, developed a highly reproducible and monodispersed chitosan-coated, doxorubicin-loaded, aptamer-conjugated Mesoporous Silica Nanoparticle (MSN) drug delivery system targeting breast cancer cells overexpressing EGFR/HER2. The system utilized carboxylated chitosan to impart pH-responsiveness, allowing endo/lysosomal escape, enhanced cytosolic delivery, and tunable drug release kinetics. The partial carboxylation of chitosan facilitated a quicker release of doxorubicin while maintaining the MSN's targeting and release properties. The developed MSNs demonstrated higher uptake and cytotoxicity in triple-negative and HER2-positive breast cancer cells compared to non-targeted MSNs, making this system a promising therapeutic strategy for breast cancer therapy. Characterization included cytotoxicity assays, drug release studies, and receptor-mediated targeting analysis.

5. Senitta Stephen et al., 2021, reviewed the role of Mesoporous Silica Nanoparticles (MSNs) in the development of advanced drug delivery systems. Their study highlighted MSN's biocompatibility, high drug-loading efficiency, and potential for ligand functionalization to enhance therapeutic outcomes in various diseases. The review emphasized MSN’s versatility in delivering small molecules and large biomolecules like peptides and proteins. Additionally, MSNs have been explored in

non-conventional drug delivery systems, including liposomes, microspheres, oro-dispersible films, 3D-printed formulations, and microneedles. However, challenges such as low bulk density, retention of mesoporous structure during processing, and limited in vivo studies were identified as barriers. The study provided a critical analysis of MSN-based systems compared to other functionalized polymers, and future directions were outlined to address existing challenges.

6. García-Fernández et al. (2021) explored the potential of Mesoporous Silica Nanoparticles (MSNs) for pulmonary drug delivery, addressing the significant clinical challenge posed by respiratory diseases. The authors emphasized that conventional lung therapies are hindered by anatomical, physiological, and immunological barriers, leading to reduced drug bioavailability at the target site. MSNs, with their high surface area, tunable pore size, and functionalization capabilities, provide a novel solution to overcome these barriers. The review highlighted the role of nanomedicine in improving drug delivery to the lungs and showcased the application of MSNs in treating various respiratory diseases. Key evaluations included the structural and functional characterization of MSNs for their efficiency in pulmonary drug delivery systems.

7. Hafiz Ahmed et al. 2022, reviewed the biomedical applications of mesoporous silica nanoparticles (MSNs) as drug delivery carriers. The study highlights the unique properties of MSNs, such as their large surface area, pore volume, and surface-active groups, which have been extensively utilized in drug delivery, photodynamic therapy, biosensors, and tissue engineering. The porous structure of MSNs allows for high drug loading, enhancing solubility and therapeutic efficacy. However, the authors emphasize that clinical translation of MSN-based drug delivery systems requires thorough in vivo human studies to assess potential adverse reactions and side effects. The review discusses the dependence of toxicity on MSN characteristics like shape, size, surface chemistry, and charge, and stresses the need for optimizing surface properties to improve biocompatibility. Advances in triggered drug release, including gatekeepers and delivery of large molecules such as proteins and nucleic acids, are also covered. This comprehensive review provides valuable insights into the current

research on MSNs-based drug delivery systems, focusing on tunability, surface functionalization, biosafety, and clinical translation challenges.

8. Hafiz Ahmed et al. 2022 reviewed the biomedical applications of mesoporous silica nanoparticles (MSNs) as drug delivery carriers. They highlighted the unique properties of MSNs, including their large surface area, pore volume, and surface-active groups, which are extensively utilized in drug delivery, photodynamic therapy, biosensors, and tissue engineering. The study emphasized that the porous structure of MSNs facilitates high drug loading, enhancing solubility and therapeutic efficacy. Despite these advantages, the authors noted that clinical translation of MSN-based drug delivery systems requires thorough in vivo human studies to assess potential adverse reactions and side effects. The review discusses how MSN characteristics such as shape, size, surface chemistry, and charge influence toxicity and stresses the need for optimizing these properties to improve biocompatibility. Additionally, advances in triggered drug release, including gatekeepers and the delivery of large molecules like proteins and nucleic acids, are covered. This comprehensive review provides valuable insights into the current research on MSN-based drug delivery systems, focusing on tunability, surface functionalization, biosafety, and clinical translation challenges.

9. Meng-meng Lu et al 2018, designed and synthesized nano silver decorated Mesoporous Silica nanoparticles as Safety tissue adhesives. Herein inorganic nanoparticles glued the tissue with nanobridging effect. These nanoparticles were characterized by TEM, FTIR, different Mesopore Properties, particle size distribution, zeta potential, energy-dispersive X-ray spectroscopy. Furthermore, strength of adhesion, anti-microbial assay, mouse skin wound model, and MTT assays were evaluated in order to determine the tissue adhesion, anti-bacterial property, biodegradability and biocompatibility of the Ag-MSNs. These nanoparticles showed efficient wound closure in comparison to sutures with little systemic toxicity.

10. Pande Vishal et al 2018, synthesized a platform for targeted of mesoporous silica nanoparticles acting as a medium of delivery for Gemcitabine hydrochloride conjugated with folic acid and loaded with dye and characterized by FTIR, TEM, Mercury porosimetry, Particle size analysis and cell line study. High drug-loading

capacity is a key feature of the mesoporous silica platform that was designed in this study and also shows fluorescence in cell line study.

11. Pande Vishal et al 2018, Studied the solubility and dissolution enhancement of poorly water-soluble drug Palperidone by MSNs. They synthesized amine functionalized MSNs and loaded the drug Palperidone with the help of wet impregnation method. The invitro and invivo drug release was studied which was found to be significantly enhanced. The invitro drug release in 120 min for MSN loaded drug was 96% while that of plain drug was 30%. The invivo study also confirmed the enhancement of solubility and dissolution of Palperidone.

12. Haibin Wu et al 2017, synthesized a regenerative wound healing material made up of Ceria nanocrystals decorated mesoporous silica as ROS scavenging tissue adhesive. They characterized the nanoparticles with Particle size, TEM, XRD, STEM, DLS, and Zeta Potential and Adhesion test in Rat wound model and found that the nanoparticles showed high tissue adhesive capacity.

13. Suk ho Hong et al 2017, developed an activatable theranostic agent made up of hollow mesoporous silica nanoparticles loaded with Indocyanine green. Endocytosis route was preferred by the nanoparticles to enter the malignant cells. Once they entered, they became highly fluorescent. Characterization was carried out by using Quantitative analysis of cellular uptake, In vitro cytotoxicity testing, In vitrphototoxicity testing. In case of the selective NIR fluorescence cancers this material is proving effective.

14. Pegah Khosravian et al 2016, fabricated and evaluated folic acid/ methionine functionalize MSNs for delivery of docetaxel. Amine functionalization is carried out by using 3-aminopropyl triethoxy silane. MSNs are evaluated by Ex vivo fluorescence imaging, In vivo distribution of nanoparticles, In vivo fluorescence imaging Infrared spectroscopy, MTT assay, SEM, TEM. The Average diameter of synthesized MSN-NH2 was 49 nm with a narrow size distribution. Functionalized and DTX-loaded MSNs that were designed in this study have a pH-sensitive drug release kinetic along with high drug-loading capacity.

15. Sandy Budi Hartono et al 2016, prepared a system for curcumin bioavailability enhancement; which was intended for oral use. It possessed cubic shaped MSNs. It possessed better release profile and a higher solubility. Physical characterization was carried out by using TEM, XRD, FTIR, In vitro release studies. Higher bioavailability of MSN-A-Cur and MSM-A-Cur was was observed when compared to that of free curcumin. Pore size of 1.8 nm was observed in Amine functionalized MCM-41.

16. Minfeng Huo et al 2016, explain triggered-release drug delivery nanosystems for cancer therapy by intravenous injection. Triggered-release nano-drug release system (TRDDSs) emerges as a promising cancer-therapeutic modality to solve the critical issues of traditional chemotherapy.

17. N. Lashgari et al 2016, explained that the organic-inorganic hybrid nanomaterials have important advantages as solid chemosensors and various innovative hybrid materials modified by fluorescence molecules were recently prepared. On the other hand, the homogeneous porosity and large surface area of mesoporous silica make it a promising inorganic support. SBA-15 as a two-dimensional hexagonal mesoporous silica material with stable structure, thick walls, tunable pore size, and high specific surface area is a valuable substrate for modification with different organic chelating groups. They highlighted the fluorescent chemosensors for ionic species based on modification of the mesoporous silica SBA-15 with different organic molecules, which have been recently developed from our laboratory to provide selective, sensitive, low cost, and rapid response optical sensors.

18. Guilan Qual et al 2015, emphasized that targeting property of lactose was integrated with the excellent drug delivery and endocytotic behaviors of MSNs to build a novel drug delivey system. Docetaxel was selected as a model drug, and fluorescein isothiocyante was used as a dye for the tracking to determine where the corgo willo released. Physical characterization was carried out by using SEM and TEM, cellular uptake of nanoparticles was studied by using confocal microscopy, by using wetness impregnation method drug was incorporated into the mesoporous silica nanoparticles. Cytotoxicity study carried out by using MTT viability assay.

19. Carlos Baleizo et al 2015, development hMSNs for theranostics, carrying fluorescent beacons for traceability and imaging, featuring a smart release control mechanism and able to accommodate large drug loads and deliver their cargo on-demand to a desired location, promises an exceptional platform for precision therapy and diagnosis.

20. Mehdi Esmaeili Bidhendi et al 2023, provided an alternatve for removal of mercury ions (Hg+2) by the use of modified nano porous compounds. Hence, in this context a new modification of mesoporous silica (SBA-15) with 1, 3, 5 (Trithiane) as modifier ligand and its use for the removal of mercury ions from aqueous environment has been investigated SBA-15 and Trithiane were synthesized. The confirmation of the presence of ligand in the silica framework by FTIR spectrum was demonstrated. The current investigation provided a newly modified nano porous compound as an efficient adsorbent for removal of Hg+2 from aqueous environment.

21. Justin Siefker et al 2014, demonstrated recent advances in the synthesis and design of nanostructured MSNs, and provide a light on opportunities for the delivery of biologicals to different organ and tissue compartments. The SBA-15 platform provides a delivery carrier that is inherently separated from the active biologic due to distinct intra and extra particle environments Flexibility in the application of the SBA-15 platform are also discussed.

22. Ebrahim Ahmadi et al 2014, prepared a mesoporous silica nanoparticle as carriers for sustained DDS. Ibuprofen was selected as a model drug. SBA-15 was prepared by hydrolysis and condensation. Surface functionalization is carried out by using 3-aminopropyltriethoxysilane. Liquid-phase grafting method was employed for the loading of Ibuprofen. Physical characterization was performed using SEM and TEM, X-ray diffraction, Thermal gravimetric and differential thermal analysis, In vitro release studies. Best loading efficiency achieved at 40oc, 35h, and stirring rate of 100 rpm.

23. M.J.K. Thomas et al 2010, described Silica nanoparticles (MSNs) with a highly ordered mesoporous structures (103 Å) with cubic Im 3m have been synthesized using triblock copolymers with high poly(alkylene oxide) (EO) segments in acid media. The produced nanoparticles displayed large specific surface area (765cm2/g)

with an average particles size of 120 nm. The loading efficiency was assessed by incorporating three major antiepileptic active substances via passive loading and it was found to varying from 17 to 25%. The state of the adsorbed active agents was further analyzed using differential scanning calorimetry (DSC) and X-ray powder diffraction (XRPD). Dissolution studies revealed rapid release profiles within the first 3 h. The viability of 3T3 endothelial cells was not affected in the presence of MSNs indicating negligible cytotoxicity.

24. Salonee Tawde et al 2020, were formulated an antiarthritic gel containing ginger extract and evaluate its drug release activity. Topical ginger gels were prepared using Carbopol 934 as a gelling agent at varying concentrations, namely 0.5%, 1%, and 1.5% w/w. The gel was analyzed to determine percent purity and cumulative drug release. Results indicated that the 1.5% w/w concentration of Carbopol in the ginger gel exhibited adequate drug release. Antiarthritic gel containing 1.5% w/w of Carbopol demonstrated good consistency, acceptable spreadability, and a favorable drug release profile. The topical herbal ginger gel developed in this study offers a simple, easily formulated, convenient, and economical alternative that merits consideration in the treatment of rheumatoid arthritis.

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