International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 804-811 www.ijprajournal.com ISSN: 2249-7781

Mesoporous Silica Nanoparticle: A Targeted Drug Delivery System

Nilesh S. Pendbhaje[*1], Akanksha S. Wagh[2], Pooja G. Avhale, Rupali V. Nirmal[4], Ashwini A. Jamdhade[5]

1: Head of Department, Diploma in Pharmacy, SRE'S, Sanjivani College of Pharmaceutical Education and Research, Kopargaon

2: Student, Diploma in Pharmacy, SRE'S, Sanjivani College of Pharmaceutical Education and Research, Kopargaon

3: Student, Diploma in Pharmacy, SRE'S, Sanjivani College of Pharmaceutical Education and Research, Kopargaon

4: Lecturer Diploma in Pharmacy, SRE'S, Sanjivani College of Pharmaceutical Education and Research, Kopargaon

5: Lecturer Diploma in Pharmacy, SRE'S, Sanjivani College of Pharmaceutical Education and Research, Kopargaon

Date Of Submission: 01-05-2021 Date Of Acceptance: 10-05-2021

ABSTRACT: Mesoporous silica-nanoparticles (MSNs) have gotten a lot of attention in the last decade because of their possible biomedical applications. MSNs as drug delivery systems (DDSs) have major advantages over conventional drug nanocarriers due to their optimised mesoporous structure and high surface area.Because of their unique characteristics, these ordered porous materials have gotten a lot of attention as drug carriers. They are cost efficient since they can be synthesised using a relatively easy method. Furthermore, the morphology, pore size and volume, and particle size can all be altered by regulating the parameters during the synthesis.MSNs as drug carriers for the treatment of different diseases have seen a dramatic rise in research in recent years, suggesting their possible benefits in drug delivery. Its widespread use for the loading of small molecules as well as macromolecules like proteins, siRNA, and other similar molecules has rendered it a versatile carrier.In recent years, researchers have made numerous changes to the structure of MSNs in order to investigate their potential in drug-resistant chemotherapy and antimicrobial therapy. We addressed the synthesis of these multitalented nanoparticles as well as the factors that influence the size and morphology of this wonder carrier in this study.

Keywords- Mesoporous silica nanoparticles,nanocarriers,nanomedicine,nano biomolecule,

I. INTRODUCTION:

modern nanotechnology has evolved as the principal component of science in the current century over the years , diagnosis of disease and it's therapy is constantly leaping milestones due to the application of nanotechnology in the field of biomedicine the evaluation of nanomedicine and green technology for itsproduction have been a great boon and shifted paradigms in therapy and tissue engineering Owings to the advantages of nanocarriers such as a high surface area to volume ratio unique features of surface modification and engineering to obtain particle of various size , shapes and different chemical characteristics. Silica nanoparticles with mesoporous referred to as mesoporous silica nanoparticles have gained wide popularity over the recent year an exhaustive set of literatures are available and research is still underway in evaluating new avenues for:

1) Use of MSNs in drug delivery
2) MSNs in improving the solubility of drug
3) The ultimate goal is to enable more effective and patient friendly treatment regiment by reducing drugs concentration and dosing frequency by offering easier administration an improving safetydelivery system have been applied to prolong the circulation time and bioavailability of certain drug molecules but addressing the drug deliveryvehicle to specific tissue or cellstill lies in the formulation based on liposomes are already on the market but a variety of other delivery system are emerging mesoporous silica nanoparticles. The

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 804-811 www.ijprajournal.com ISSN: 2249-7781

interaction between nanoparticles and various cell and tissue of the human body will ultimately determine the medical applicability of the technology

The soluble molecules or drug using nanoparticulate drug carriers adds another level of complexity as these nanoparticles may dissolve aggregate and interact with biomolecule cell and tissue according to their chemical compounds the first report using MSM-41 type mesoporous silica nanoparticles as drug delivery systems in 2001 the last ten year have witnessed an exponential increase in research on biomedical applications of MSNs. It has been one the hottest areas in nanobiotechnology and nanomedicine for designing biocompatible MSNs and multifunctional counterpart in disease diagnosis and therapy as nanocarriers, mesoporous silica nanoparticles with unique mesoporous structure have been explored as effective drug delivery systems for a variety of therapeutic agents to fight against various kinds of disease including
1) Diabetes2) inflammation 3) cancer.

Origin of mesoporous silica material:

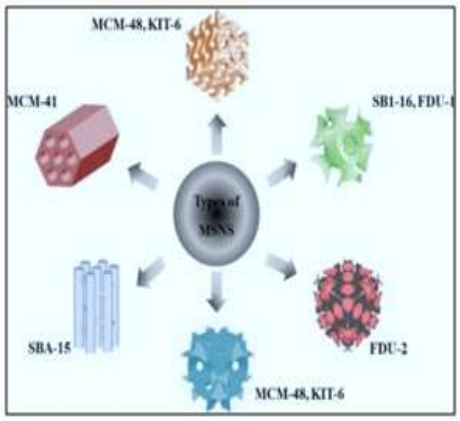
The synthesis of mesoscopic materials dates back to 1970's mobile research and development corporation was the first to synthesize mesoporous solid from aluminosilicate gels using liquid crystal template mechanism in the year 1992 they designated it as MCM-41 as per IUPAC, mesoporous materials are defined as the one having a pore size in the range of 2-50nm and ordered arrangement of pores giving an ordered structure to its(1) Several effort are underway to utilise this technology for cancer therapy.

Generally, MCM-41 is hexagonal with a pore diameter of 2.5 to 6 nm wherein cationic surfactants were used as template. MCM-41 is one of the most widely explored materials for drug delivery. MCM-48 has a cubic arrangementwhereas MCM-50 has a lamella like arrangement (2)highly order mesoporous structure of SBA-15 has also been widely used for biomedical purpose this was first synthesized by University of California Santa Barbara and hence named SantaBarbara amorphous type of material. This is different from MSM in that they possess larger pores of 4.5-30 nm and thicker silica wall (3) FSM-16 that is folded sheet of mesoporous material are another type of mesoporous material which are synthesized using quaternary ammonium surfactant as a template and layered polyciliateKane miteOtsuka etc demonstrated the FMS-16 could be used for pharmaceutical application other than as an adsorbent and for catalysis (4).

Properties of mesoporous silica:

MSNs present well defined and tenable physiochemical property including particle size pore size pore volume surface area volume areapore structure and surface functionality. The porous structure of MSMs provide cavities that can host and release a great variety of biomolecule an therapeutic agent in fact the versatility ofMSNs in size morphology and texture has fuelled their application as a controlled drug delivery nanocarriers (4)In this sense mesoporous silica nanoparticle can be produced with different particle diameter differentporediameter differentporocitywith magnetic nanoparticle imbedded into their skeleton or even growing themesoporous network from different metal nanoparticlescores. the pore size of MSNs is a limiting factor of the molecule that could be introduced into the mesoporousin term of size the pore diameter can be turned from 2 to 30nanometre depending on the susurrant employ as a templatesynthesiscondition employed in this sense MSNs with large pore diameter up to 50 nanometre are employed for the absorption and delivery of the protein, enzyme, antibiotic and nucleic acid(5) different porous morphologies and texture for MSNs have been reported ,such as MCM-41 like hexagonal, cubic,concentric, foam like radial, or worm like porosity.in fact it has been reported that controlling the morphology of the MSNs pores permits To selectively load different molecule of various size and similarly tune the cargo release together will the Metrixdissolution kinetics

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 804-811 www.ijprajournal.com ISSN: 2249-7781



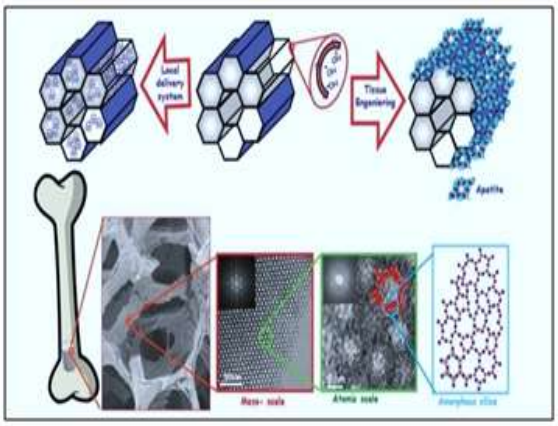


Fig.no.01: Structure of MSN's Fig.no.02: Delivery system in MSN's

A schematic representation of two main application of MSMs in biomedicine drug delivery an bone tissue engineering bottom MSMs are constituted of amorphous silica at atomic scale with an order meso structure that can be employed to many facture 3D scaffold with certain micro porosity useful for bone tissue engineeringsynthetic path for synthesis of MSNs in which the surfactant molecules are initially dissolve in water to then add dropwise the silica precursor that would condensate around the surfactant template then after the sole gel process take place and the Silica nanoparticles are formed the surfactantremove lead to monodispersedspherical MSN(6).

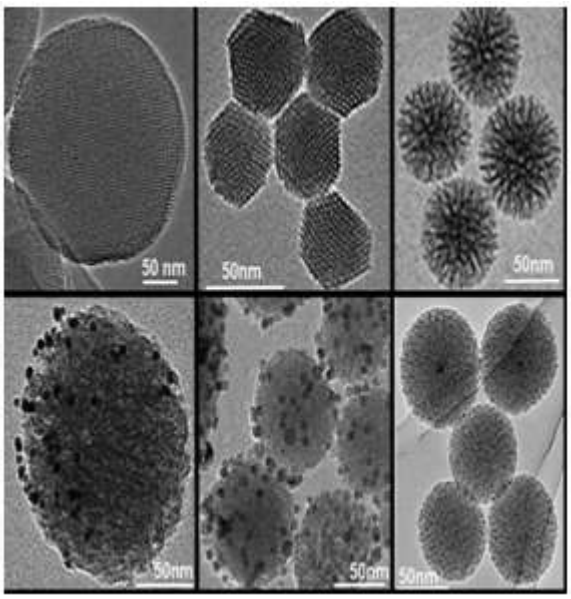


Fig.no.03: Diverse size of MSNs

Synthesis of MSNs:

Some of the Methods used to synthesise silica nanoparticle are reverse micro emulsion and flame synthesis and widely utilised sol gal method fordecay the sol gel process is widely applied to produce silica glassand ceramic material due to its ability to form pure and homogenous product at mild condition the process involves hydrolysis and condensation of metal alkoxides(si(oR)4) such as Tetra ethyl orthosilicate (TEOS),si(oc2H5)4) or inorganic salt such as a sodium silicate in the presence of mineral acid (HCl)or base (NH3)as a catalyst. The general reaction TEOS that lead to the formation of silica particle in the sol can be written as

Si(oc2H5)4+H2o- si(oc2H5)3. oH+c2H5oH

=Si-o-H+H-o-si watercondensation=si-o-si+H2O

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 804-811 www.ijprajournal.com ISSN: 2249-7781

Si. oc2H5+H-o-si alcohol condensation si-o-si=c2H5oH (7)

The hydrolysis of TEOS molecules forms silanol groups the condensation /polymerization between the silanol groups. Or between silanol groups and ethoxy group creates siloxane bridges that form silica structure. The formation of silica particles can be divided into two stages nucleation and growth (8)

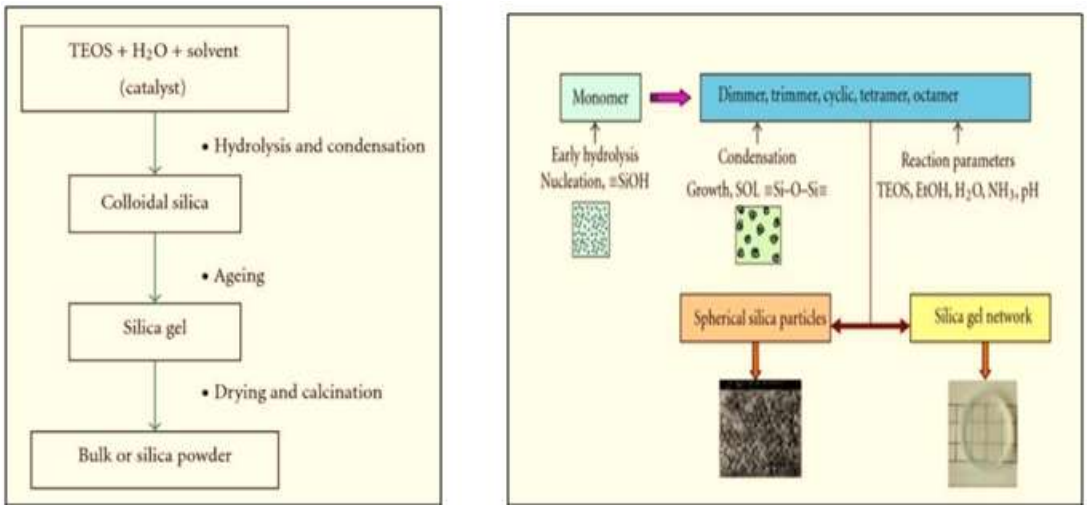


Fig.no.04: Synthesis of MSN's

Targeting therapy using MSN-based drug delivery systems:

Tremendous effects have been made using MSNs an drug delivery system for cancer targeted therapy although it was reported that 50 and 250 tnanometre silica nano particles has higher blood distribution and higher blood liver ratio thenpegylated solid lipid nanoparticle and polycyanoacrylate nanoparticle more result with the opposite outcome were reported we designed pegylated silica nanoparticle with a diameter of 125 nanometer as carrier of docetaxel for liver cancer therapy with high leading capacity passive targeting ability and decrease of targeting distribution the silica nanoratnanoratt encapsulated docetaxel has significantly decreased liver toxicity and haematologicaltoxicityBybio conjugating MSNs with specific targeting ligands active targeting to cancer cells or angiogenic endothelial cells has been realized .which have now been paid attention for MSNs based drug delivery systems and should be critically researched first it should select the active targeting ligands with high specificity but suitable affinity to their receptors for a giventumor type ,low affinity would result in suboptimal targeting efficiency whereas extraordinarily ability because of the strong tendency of ligands to be sequestered by the tumor cells near blood vessels .the grafting density of ligands on to nanoparticles should be carefully designed multivalent binding can increase the avidity between ligands and receptor for multiple interactions but multivalent ligands presentation may increase the immunogenicity and recognition of nanoparticles by RES.(9)

After targeting to tumor tissue MSNs can enter in to cancer cell via energy dependent cellular uptake. particlesize, surface properties and surface bioconjugation with ligands specifically binding with cellular receptor after entering in to cells the nanoparticles would release the loaded chemotherapeutic drug or therapeutic macromolecules which have different mechanisms to kill cancer cell and need be delivered into corresponding subcellular organellesAlthough the passive and active targeting have been designed, targeting efficiency is not as idea as expected no matter which targeting strategy to use, the particle size, shape and surface property of MSNs have a profound impact on the ability of particles to overcome the in vivo biological barrier, reach tumor tissue enter into tumor cell release loaded therapeutic agents for therapy.(10)

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 804-811 www.ijprajournal.com ISSN: 2249-7781

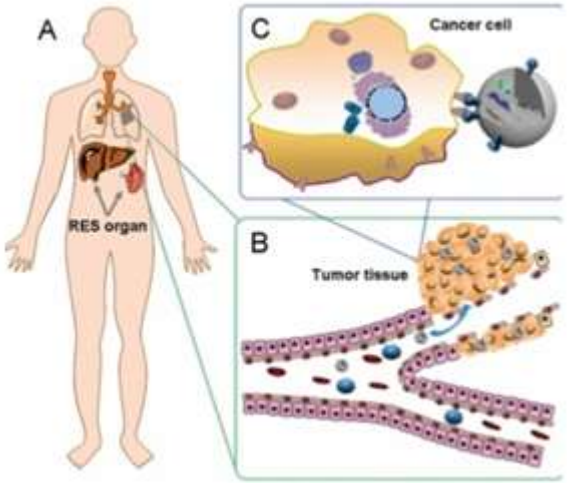


Fig.no.7: Targeting therapy using MSN's

Targeting anti-tumor therapy using MSNs

Based on the Globo can 2008 about 12.7 million cancer cases and 7.6 million cancer deaths are estimated to have occurred in 2008. Cancer has been the leading cause of death in economically developing countries. There exists an enormous challenge for preventing and curing cancer at present. Recent advances in nanotechnology have offered new opportunities for cancer prevention, detection and treatment. fornanobasedcancer targeting therapy. One of the biggest challenges is to achieve sufficiently high local drug concentration in the tumor while spring healthy tissue the final therapeutic index is determine by biodistribution, metabolism and clearance of nanoparticles drug delivery systems. (11)

- Systematically administered nanoparticleswould encounter different compartmental barrier before reaching the desired location barrier are highly efficient for the removing foreign materials including nanoparticles from the body understanding of these biological barriers is necessary for designing nanoparticles with ability to by pass the barriers and reach cancer cell the nanoparticles would be adsorbed with opsonin protein in the blood , including complement protein laminin, fibronectin apolipoprotein thrombospondin subsequently ,the absorbed protein can interact with specific plasma membrane receptor on phagocytic cell and the opsonized nanoparticles would be rapidly removed from the circulation by phagocytic cell especially kupffer cells in liver and splenic red pulp macrophage. This is the main clearance pathway for nanoparticles larger thanthe renal threshold limit of about 10nm.
- After circulating to the desired location nanoparticles need extravasate from the vasculature into the interstitial space of solid tumor tissue the abnormal vascular structure of tumor endows substantial advantages for nanoparticular drug delivery systems with size ranging from around 30 to 40 nm intensive tumor targeting.
- Particle size, hydrophobicity/hydrophilicity and surface chemistry of nanoparticle would greatly influence the vascular permeability of the transported nanoparticle the potential limitations of passive targeting promote the development of more advanced active targeting because of the high metabolic demands for rapid proliferation (12).
- **MSNs in bone tissue engineering**: Bone disorders are of significant concern due to increase in the median age of our population. It is in this context that tissue engineering has been emerging as a valid approach to the current therapies for bone regeneration/substitution. Tissue-engineered bone constructs have the potential to alleviate the demand arising from the shortage of suitable autograft and allograft materials for augmenting bone healing. Silica based mesostructured nanomaterial possessing pore sizes in the range 2–50 nm and surface reactive functionalities have elicited immense interest due to their exciting prospects in bone tissue engineering. In this review we describe application of silica-based mesoporous nanomaterials for bone tissue engineering. We

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 804-811 www.ijprajournal.com ISSN: 2249-7781

summarize the preparation methods, the effect of mesopore templates and composition on the mesopore-structure characteristics, and different forms of these materials, including particles, fibres, spheres, scaffolds and composites. Also, the effect of structural and textural properties of mesoporous material on development of new biomaterials for production of bone implants and bone cements was discussed. Also, application of different mesoporous materials on construction of manufacture 3-dimensional scaffolds for bone tissue engineering was discussed. It begins by giving the reader a brief background on tissue engineering, followed by a comprehensive description of all the relevant components of silica-based mesoporous biomaterials on bone tissue engineering, going from materials to scaffolds and from cells to tissue engineering strategies that will lead to "engineered" bone (13)

- MSNs for Improvement of Solubility of Drugs MSNs owing to their modifiable surface chemistry can act as carriers for poorly soluble drugs and tackle their solubility issues.Bukhara et proved this potential of MSNs by loading thepoorly soluble drug fenofibrate and assessing them in healthy human volunteers. The volunteers weremonitored for a period of 96 h post dosing and their plasma samples were collected and assessed forthe pharmacologically active metabolite fen fibric acid. A significant increase in Cmax with a point estimate of 177% and a reduction in tmax were observed for fenofibrate formulation following single oral administration. No serious adverse events were reported and none of the volunteers discontinued the study. This demonstrates that the MSNs could also be used as a possible alternative to other carriers to improve the solubility and bioavailability of drugs. Enhanced oral bioavailability of telmisartan (TEL) was achieved by loading it into MSNs. Based on the results obtained by the study on beagle. Dogs, Zhang et al. set forth a basis to use MSNs as a drug carrier for poorly soluble drugs. In microcellular uptake studies showed that TEL-MSN showed an enhanced uptake in Caco-2 cells resulting in accumulation in the cell membrane as compared to TEL-mesoporous silica microparticles.
- Biocompatibility of MSNs in Humans the biocompatibility of silica nanoparticles has long been a topic of controversy as studies conducted by researchers have yielded variable results. Nevertheless, the Food and Drug Administration (FDA) approval of hybrid silica nanoparticles for bioimaging marks an event of utmost importance. These particles were found to be ~7 nm in size within which fluorescent dye, Cy5 was incorporated. These particles were labelled with 124I and surface functionalized with peptide cyclo-(Arg-Gly-Asp-Tyr) (cRGDY) to selectively target integrin-expressing tumours.C dots were synthesized in such a way that they had limited reticuloendothelial system (RES) uptake and promote renal excretion. Preliminary experiments on in vivo safety by Choi et al. (Cornell University) revealed that these fluorescent silica nanoparticles were safe and did not show any toxicity in mice. These particles were also found to be an effective bioimaging probe for cancer imaging. Burns et al. carried out in vivo biodistribution studies of the developed C dots in nude mice wherein nanoparticles were injected intravenously. The particles were found to show rapid renal clearancewithin 45 min of injection and majority of these particles accumulated in the liver. To further modify theclearance, the particles were coated with methoxy-terminated poly (ethylene glycol) chains. By carefulmanipulation of the surface features of C dots, they can be used for wide variety of biomedical applications including imaging and therapy Based on the encouraging results of pre-clinical (16)studies, these nanoparticles received approval from the FDA as an Investigational New Drug (IND)to conduct the human clinical trial, phase I. The first human clinical trials suggested its safety forhuman use. A pilot clinical trial was conducted in five metastatic melanoma patients to assess thepharmacokinetic (PK) profile of C dots following a single injection dose. The PK profiles, renalexcretion, metabolic profile assessment in patients suggested that the particles were well tolerated, preferentially accumulated in the tumour site and were found to be safe for human use. A study wherein the potential of ordered mesoporous silica nanoparticles (OMS) in enhancing the bioavailability of fenofibrate in man was conducted by Bukhara and collaborators which can be considered as another breakthrough step acting as a trigger in evoking interest among

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 2 Mar-Apr 2021, pp: 804-811 www.ijprajournal.com ISSN: 2249-7781

the researchersfor the use of MSNs for biomedical applications. Promising results obtained by them in their preclinicalstudies prompted them to complement those results with clinical studies. Fenofibrate was loaded into OMS and these were subsequently enclosed within capsules. The study was carried out with12 volunteers who were administered a single dose of fenofibrate OMS and the marketed formulationof fenofibrate, Lipanthyl®. Safety assessment was performed by periodic monitoring of the vital signs,12-lead electrocardiogram (ECG) and blood biochemical parameters in the subjects. The PK profilerevealed an increasein the rate and extent of absorption of fenofibrate when incorporated in OMS ascompared to the marketed product. In addition, the formulation was found to be well tolerated in the volunteers ensuring the safety of the developed OMS formulation (17)

II. CONCLUSION:

The mesoporous materials have shown an outstanding potential in Nanomedicines. Mesoporous silica-nanoparticleshas become excellent nanoplatforms to design smart drug delivery systems for biomedical applicationsMSNPs with their unique mesoporous structure offer advantages that may allow clinically applicable Nano formulations for disease diagnosis and therapy. MSNPs possess easily tenable particle size, uniform pore size, high pore volume greater surface area and simple mesoporous or hollow structure. MSNPs provide excellent nanoplatforms to design smart drug delivery systems for biomedical applications. With respect to drug delivery systems, they have an extraordinarily high drug loading capacity and stimuli-responsive drug release profiles. MSNPs have relatively high in vitro and in vivobiocompatibility.

III. ACKNOWLEDGMENT:

Authors wish to express their sincere thanks to Hon. Mr. Amit Dada Kolhe, Ex. Trustee, Sanjivani Rural Education Society's, Kopargaon, for their constant support and encouragement. We will also like to thank to the Principal and staff of Sanjivani College of Pharmaceutical Education and Research (Diploma) for their constant support.

Abbreviations:

MSNs=mesoporous silica nanoparticles
DDS = drug delivery systems
CBZ=carbamazepine
OXC=oxcarbazepine
RES=reticuloendothelial system
FDA=food and drug administration

REFERENCES:

[1]. Krukemeyer, M. G., Krenn, V., Huebner, F., Wagner, W., & Resch, R. (2015). History and possible uses of nanomedicine based on nanoparticles and nanotechnological progress. J NanomedNanotechnol, 6(6), 336.
[2]. Mudshinge, S. R., Deore, A. B., Patil, S., &Bhalgat, C. M. (2011). Nanoparticles: emerging carriers for drug delivery. Saudi pharmaceutical journal, 19(3), 129-141.3
[3]. Kankala, R. K., Zhang, Y. S., Wang, S. B., Lee, C. H., & Chen, A. Z. (2017). Supercritical fluid technology: An emphasis on drug delivery and related biomedical applications. Advanced healthcare materials, 6(16), 1700433.
[4]. Kankala, R. K., Zhu, K., Sun, X. N., Liu, C. G., Wang, S. B., & Chen, A. Z. (2018). Cardiac tissue engineering on the nanoscale. ACS Biomaterials Science & Engineering, 4(3), 800-8184.
[5]. Gong, T., Xie, J., Liao, J., Zhang, T., Lin, S., & Lin, Y. (2015). Nanomaterials and bone regeneration. Bone research, 3(1), 1-7.
[6]. Alhariri, M., Azghani, A., &Omri, A. (2013). Liposomal antibiotics for the treatment of infectious diseases. Expert opinion on drug delivery, 10(11), 1515-1532.
[7]. Deshpande, P. P., Biswas, S., &Torchilin, V. P. (2013). Current trends in the use of liposomes for tumor targeting. Nanomedicine, 8(9), 1509-1528.
[8]. Puri, A., Loomis, K., Smith, B., Lee, J. H., Yavlovich, A., Heldman, E., & Blumenthal, R. (2009). Lipid-based nanoparticles as pharmaceutical drug carriers: from concepts to clinic. Critical Reviews™ in Therapeutic Drug Carrier Systems, 26(6)
[9]. Gad, A., Kydd, J., Piel, B., & Rai, P. (2016). Targeting cancer using polymeric nanoparticle mediated combination chemotherapy. International journal of nanomedicine and nanosurgery, 2(3).
[10]. Cheng, C. J., Tietjen, G. T., Saucier-Sawyer, J. K., & Saltzman, W. M. (2015). A holistic approach to targeting disease with polymeric nanoparticles. Nature reviews Drug discovery, 14(4), 239-247.

[11]. Han, Y. H., Kankala, R. K., Wang, S. B., & Chen, A. Z. (2018). Leveraging engineering of indocyanine green-encapsulated polymeric nanocomposites for biomedical applications. Nanomaterials, 8(6), 360.
[12]. Madaan, K., Kumar, S., Poonia, N., Lather, V., & Pandita, D. (2014). Dendrimers in drug delivery and targeting: Drug-dendrimer interactions and toxicity issues. Journal of pharmacy &bioallied sciences, 6(3), 139.
[13]. Hiemenz, J. W., & Walsh, T. J. (1996). Lipid formulations of amphotericin B: recent progress and future directions. Clinical infectious diseases, 22(Supplement_2), S133-S144.
[14]. Gill, P. S., Wernz, J., Scadden, D. T., Cohen, P., Mukwaya, G. M., von Roenn, J. H., ... & Ross, M. E. (1996). Randomized phase III trial of liposomal daunorubicin versus doxorubicin, bleomycin, and vincristine in AIDS-related Kaposi's sarcoma. Journal of Clinical Oncology, 14(8), 2353-2364.
[15]. Barenholz, Y. C. (2012). Doxil®—the first FDA-approved nano-drug: lessons learned. Journal of controlled release, 160(2), 117-134.
[16]. Batist, G., Barton, J., Chaikin, P., Swenson, C., & Welles, L. (2002). Myocet (liposome-encapsulated doxorubicin citrate): a new approach in breast cancer therapy. Expert opinion on pharmacotherapy, 3(12), q-1751.
[17]. Junghanns, J. U. A., & Müller, R. H. (2008). Nanocrystal technology, drug delivery and clinical applications. International journal of nanomedicine, 3(3), 295.